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Research Article

THE EFFECTS OF THE ANXIETY LEVELS OF TYPE 2 DIABETES MELLITUS PATIENTS ON THEIR TREATMENT ADHERENCE IN THE COVID-19 PANDEMIC PERIOD

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Abstract: *This study was conducted to investigate the effects of the anxiety levels of Diabetes Mellitus (DM) patients on their treatment adherence in the COVID-19 pandemic period. The sample of this descriptive and cross-sectional study consisted of 313 DM patients who presented to the internal medicine outpatient clinic between 01.01.2021 and 01.06.2021. The data were collected using a Personal Information Form, the Coronavirus Anxiety Scale (CAS), and the Morisky Medication Adherence Scale (MMAS-8). Descriptive statistics, Mann-Whitney U test, Kruskal-Wallis test, and Spearman's correlation test were used to analyze the data. The mean CAS score of the DM patients was 7.89±3.87, while their mean total MMAS-8 score was 4.06±1.56. It was determined that the patients who were using oral antidiabetic medications, those adhering to their medication and diet treatment, and those who were not COVID-19 had higher levels of anxiety. There was a negative significant relationship between the MMAS-8 and CAS scores of the patients ($p<0.05$). It was determined that as the anxiety levels of the DM patients increased in the pandemic process, their treatment adherence levels decreased. To reduce the anxiety levels and increase the treatment adherence of DM patients during the COVID-19 pandemic period, sufficient information, psychosocial support, and a multidisciplinary approach should be provided.*

Keywords*: COVID-19, Anxiety, Diabetes Mellitus, Type 2, Treatment Adherence.*

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1. Introduction

The Coronavirus Disease-2019 (COVID-19) was declared an international public health emergency and a pandemic on 11 March 2020 by the World Health Organization as it spreads rapidly from person to person and has high mortality rates [1]. According to the daily reports of the Turkish Ministry of Health, the total numbers of deaths due to COVID-19 per day are 1,275 in Turkey and 81,258 in the world [2]. It has been emphasized that the virus causing COVID-19 (SARS-CoV-2) continues to show its effects by mutating significantly affects the health of individuals with chronic diseases such as Diabetes Mellitus (DM) [3-6]. In Turkey, the COVID-19-related mortality rate of hospitalized diabetic patients was reported as 13.6% [2]. In studies conducted with DM patients with COVID-19, it has been reported that a comorbid disease like DM may require intensive care treatment, and it increases the risk of death [7, 8]. According to the International Diabetes Federation (IDF), among chronic diseases that are considered the greatest global health problem of the twenty-first century, DM

is a significant one with high treatment costs, morbidity rates, and mortality rates. According to the IDF data, one in every 10 people are diabetic, there are 537,000,000 diabetes patients in the world, and there are 9,020,900 such patients in Turkey [9]. DM was reported as the second-most frequently encountered condition in COVID-19 patients (IDF, 2020) and major comorbidity of COVID-19 infection [3].

Acute complications caused by DM include diabetic ketoacidosis, hyperglycemic hyperosmolar non-ketotic coma (HHNC), and hypoglycemia. Its chronic complications include microvascular complications such as diabetic retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as cardiovascular diseases, cerebrovascular events, and coronary artery diseases [10-12]. It has been determined that while DM patients are dealing with these acute and chronic complications, issues like quarantine, isolation and social media news brought about by COVID-19 increase the anxiety, fear, concern and stress experienced by these patients. Unfortunately, the COVID-19 pandemic period has been a period where DM patients have had difficulties in accepting their disease, adhering to their treatment, and changing their lifestyles [13, 14]. Previous studies investigating the effects of COVID-19 in DM patients have reported that 20-40% of DM patients have depression, anxiety, stress, and eating disorders [5, 14]. It has also been stated that COVID-19 increases the disease burden in DM patients [11], more than half of patients experience high levels of anxiety [15, 16], they have long-term permanent symptoms due to COVID-19 (chest pain, shortness of breath, cough, fatigue, loss of appetite, burnout, neurocognitive dysfunctions), and they have difficulty in managing their disease [3]. In the management of diabetes, one of the important issues is the management of diabetes treatment. The main elements of diabetes treatment management include medication, diet, exercise, personal management education, and self-check [17]. Medication adherence requires individual behaviors (e.g., taking one's medication, adhering to diet, making lifestyle changes) and taking general health precautions. Studies in the literature have shown that DM patients often do not adhere to their treatment [18-21]. It has been found that anxiety and depression affect the medication, diet and daily living activities of DM patients, and the frequency of their complications and their mortality rates have increased in the COVID-19 pandemic period [4, 7, 8, 22-24]. Restrictions caused by the pandemic period, stress, and experiencing moods such as fears, concerns or anxiety about death lead diabetic patients to experience more anxiety, prevent them from utilizing hospital services as much as they need to and interrupt their treatments [5, 13,15, 22].

This study was conducted to determine the effects of the COVID-19-related anxiety levels of DM patients on their treatment adherence in the COVID-19 pandemic period.

The research questions were as follows:

1. What are the anxiety levels of DM patients in the COVID-19 pandemic period?
2. What are the treatment adherence levels of DM patients in the COVID-19 pandemic period?
3. Do the sociodemographic and disease-related characteristics of diabetic patients affect their anxiety and treatment adherence in the COVID-19 pandemic period?
4. Is there a relationship between the anxiety levels and treatment adherence levels of DM patients in the COVID-19 pandemic period?

2. Material and Methods

2.1. Study Design

A descriptive and cross-sectional design was used in this study.

2.2. Setting and Sample

The population of this study consisted of DM patients presenting to the internal medicine outpatient clinic of the Ilgın State Hospital between 01.01.2021 and 01.06.2021. To determine the

sample size required for this study, the 1528 patient records at the DM outpatient clinic for the six previous months were taken as a basis and based on the formula for a known population, the minimum required sample size was calculated as 307 in a 95% confidence interval and with an error margin of 5%. The sample consisted of 313 patients who met the following inclusion criteria of the study: (a) Being 18 years old or older, (b) having been monitored with the diagnosis of DM for the least one year, (c) being a patient followed for at least 3 months (d) using at least 1 oral antidiabetic/insulin, (e) being literate, (f) being able to communicate, (g) not having a psychiatric problem (patients who were found to have no psychiatric problems in the patient file and verbally declared that they did not have any psychiatric disease), (h) and agreeing to participate in the study. Among the exclusion criteria of the study; (a) it including being under the age of 18, (b) filling in the forms incompletely, (c) having a psychiatric problem, (d) not volunteering to participate in the study.

2.3. Data Collection Instruments

The data were collected using a Personal Information Form, the Coronavirus Anxiety Scale (CAS), and the Morisky Medication Adherence Scale (MMAS-8).

2.3.1 Personal Information Form

The data collection form, which was prepared based on the literature [6,17, 21, 25-27], had a total of 25 questions including 12 questions on the sociodemographic characteristics of the participants (age, sex, education status, marital status, status of having children, income status, place of residence, disease duration, comorbidities, habits), 4 questions about the COVID-19 pandemic period (COVID-19 contact/positivity status, status of attending follow-ups in the COVID-19 pandemic period, blood sugar levels in the COVID-19 pandemic period), and 9 questions about DM and its treatment.

2.3.2 Coronavirus (COVID-19) Anxiety Scale (CAS)

CAS is a 5-point Likert-type scale that was developed by Lee et al. [28] It has 5 items and one dimension. Each item is scored based on the response options of "0" not at all, "1" rare, less than a day or two, "2" several days, "3" more than 7 days, and "4" nearly every day over the last 2 weeks. The validity and reliability study of the scale in Turkish was conducted by Biçer et al. [29]. The minimum and maximum scores of the scale are 0 and 20. Scores of 9 or higher indicate high levels of anxiety. While Biçer et al. [29] reported the Cronbach's alpha coefficient of the scale as 0.83, in this study, this coefficient was found as 0.73.

2.3.3 Morisky Medication Adherence Scale (MMAS-8)

MMAS-8 was tested for validity and reliability by Morisky. A revision was made to increase the validity and reliability of the scale, and the number of items was increased to 8 [30]. In Turkey, the validity and reliability study of the scale was carried out by Sayıner [31]. In the scale, 7 items are in the form of closed-ended questions with two options (yes/no), while one item is in the form of a closed-ended question with 5 options.

Positive responses to the items that are about concepts that would affect treatment adherence positively are marked as 1 point, while negative responses are marked as 0 points. A response of "no" to items 1, 2, 3, 4, 6 and 7 is marked as 1 point, while a response of "yes" to item 5 is marked as 1 point. Item 8 has multiple options, where only one response option (never/rarely) indicating high medication adherence is scored as 1 point when marked, and all other options that indicate low medication adherence are scored as 0 points. A score of 8 shows high adherence, a score of 6-7 shows medium adherence, and a score lower than 6 shows low adherence. The Cronbach's alpha coefficient of the scale was reported as 0.78, while in this study, the Cronbach's alpha coefficient was found as 0.72.

2.4. Data Collection

The data were collected face-to-face by using protective equipment and complying with the 1.5-meter distancing rule due to the ongoing COVID-19 pandemic. DM patients were informed by the researchers about the objective, process and data collection instruments of the study. They were informed that participation was voluntary, and they provided consent. It took each participant about 10-15 minutes to complete the data collection forms.

2.5. Ethical Statement

Ethics committee approval was gained from the Ethics Committee for Non-Interventional Clinical Studies at Selcuk University (Decision Number:2020/25) and the Scientific Research Platform of the Ministry of Health (Protocol number: 2020-12-08T11_10_22).

2.6. Data Analysis

The data were analyzed using the SPSS 24.0 (Statistical Package for the Social Sciences) software. The descriptive statistics of the data were calculated, and the Kolmogorov-Smirnov test was used to test normal distribution. The Cronbach's alpha coefficient was calculated as a measure of reliability. For the non-normally distributed variables, the Mann-Whitney U test was used in the comparison of two independent groups, whereas Kruskal-Wallis and Bonferroni tests were conducted to compare more than two groups. Spearman's correlation test was used to test correlations. The level of statistical significance for the statistical analyses was accepted as $p<0.05$.

3. Results

It was determined that 54.3% of the participants were in the age group of 36-64, 60.4% were women, 80.5% were married, 48.9% were working at a job, 52.1% had a medium level of income, 68.1% were living in districts, and 40.3% were primary-secondary school graduates (Table 1).

The participants who were 65 years old or older, those who had higher education degrees, those who were single, those who were not working, those with a good income level and those living in cities had significantly higher mean MMAS-8 scores ($p<0.05$) (Table 1). No significant relationship was found between the sociodemographic characteristics of the participants and their mean CAS scores ($p>0.05$) (Table 1).

Table 1. Distributions of the mean CAS and MMAS-8 Scores of the Type 2 DM Patients Based on their Sociodemographic Characteristics (n=313)

Sociodemographic Characteristics	**n**	**%**	**CAS** $\bar{X}$ **± SD**	**MMAS-8** $\bar{X}$ **± SD**
Age[2]				
18-35 years	4	1.3	9.25±2.62	3.33±1.15[a]
36-64 years	170	54.3	7.84±3.63	3.69±1.28[b]
65 years or older	139	44.4	7.92±4.17	4.80±1.54[c]
χ^2/p			χ^2=0.946, p=0.623	χ^2=29.722, p=0.000**, c>b>a
Sex[1]				
Female	189	60.4	8.04±3.72	4.32±1.52
Male	124	39.6	7.66±4.08	4.31±1.55
z/p			z=-1.137, p=0.256	z=-0.714, p=0.475

Table 1. continued.

Sociodemographic Characteristics	**n**	**%**	**CAS** $\bar{X} \pm SD$	**MMAS-8** $\bar{X} \pm SD$
Education Status[2]				
Illiterate	42	13.4	7.76±4.81	3.37±1.25[a]
Primary-secondary school	126	40.3	7.86±3.58	4.01±1.43[b]
High school	118	37.7	8.00±3.86	4.49±1.59[c]
Higher education	27	8.6	7.44+3.70	4.97±1.44[d]
χ^2/p			χ^2=1.197/ p=0.754	χ^2=28.573 p=0.000**, d>c>b>a
Marital Status[1]				
Married	252	80.5	7.79±3.61	4.08±1.50
Single	61	19.5	8.31±4.78	5.02±1.42
z/p			z=-0.403/ p=0.687	z=-4.442/ p=0.000**
Working Status[2]				
Housewife	149	47.6	8.06±3.81	4.21±1.57[a]
Working	153	48.9	8.69±3.89	3.88±1.52[b]
Not working	11	3.5	8.01±3.17	4.40±1.71[c]
χ^2/p			χ^2=0.213/p=0.418	χ^2=22.493/ p=0.000**, c>a>b
Income Status[2]				
Good	119	38.0	8.49±3.82	4.60±1.51[a]
Medium	163	52.1	7.54±3.96	4.25±1.48[b]
Bad	31	9.9	7.45±3.34	3.96±1.53[c]
χ^2/p			χ^2=4.727/p=0.094	χ^2=10.630/ p=0.005*, a>b>c
Place of Residence[2]				
City				
District	19	6.0	6.47±2.48	4.92±1.52[a]
Town/village	213	68.1	8.04±4.00	4.02±1.45[b]
	81	25.9	7.83±3.74	4.33±1.80[c]
χ^2/p			χ^2=2.572/p=0.276	χ^2=23.188/ p=0.000**, a>c>b

[1]Two non-normally distributed independent groups were compared using Z: Mann-Whitney U Test [2]Three non-normally distributed independent groups were compared using X^2: Kruskal-Wallis Test, CAS: Coronavirus (COVID-19) Anxiety Scale, MMAS-8: Morisky Medication Adherence Scale; *:p<0.05; **:p<0.01

As seen in Table 2, 45.0% of the participants had a disease duration of 1-10 years, the treatment modality of 53.0% consisted of diet, oral antidiabetics and insulin treatment, 36.4% had been using oral antidiabetic medications for 11-20 years, and 38.6% had been using insulin for 6-10 years. DM-related complications developed in 36.4% of the participants, 62.9% attended health follow-ups regularly, 87.2% adhered to their medication treatment, and 68.1% did not adhere to their diet treatment. It was found that the COVID-19 pandemic prevented 82.4% of the participants from attending their health follow-ups, and the blood sugar levels of 59.1% were affected due to the COVID-19 pandemic. It was learned that 48.6% of the participants had been COVID-19 positive, and 66.5% had been in contact with a COVID-19 patient (Table 2).

The participants whose disease duration was 31-40 years, those whose treatment modality involved diet, oral antidiabetics and insulin, those whose oral antidiabetic medication use duration was 31-40 years, those with an insulin use duration of 21-30 years, those who had experienced DM-related complications, those who attended their health follow-ups regularly, those who adhered to their medication treatment, those who adhered to their diet treatment, those whose attendance to health follow-ups was not prevented due to COVID-19, those whose blood sugar levels were affected due to

COVID-19, and those who had been COVID-19-positive had significantly higher mean MMAS-8 scores ($p<0.05$) (Table 2). There was no significant difference in the mean MMAS-8 scores of the participants based on their COVID-19 contact status ($p>0.05$) (Table 2).

The participants whose treatment modality included diet, oral antibiotics and insulin, those who adhered to their medication and diet treatment, and those who had not been COVID-19 positive had significantly higher mean CAS scores ($p<0.05$). No significant relationship was found between the other disease-related characteristics of the participants and their mean CAS scores (Table 2).

Table 2. Distributions of the mean CAS and MMAS-8 Scores of the Type 2 DM Patients Based on their Sociodemographic Characteristics (n=313)

Sociodemographic Characteristics	**n**	**%**	**CAS X±SD**	**MMAS-8 X±SD**
DM disease duration[2]				
1-10 years	141	45.0	7.58±3.57	3.79±1.46[a]
11-20 years	116	37.1	7.91±3.90	4.00±1.56[b]
21-30 years	42	13.4	8.85±4.39	4.73±1.46[c]
31-40 years	14	4.5	8.00±4.67	5.14±1.83[d]
χ^2/p			χ^2=2.298, p=0.513	χ^2=18.397, p=0.000**, d>c>b>a
DM treatment modality[2]				
Oral antidiabetic	3	1.0	10.33±5.85[a]	4.00±1.73[a]
Diet and oral antidiabetic	144	46.0	7.22±3.63[b]	3.76±1.54[b]
Diet, oral antidiabetic and insulin	166	53.0	8.43±3.96[c]	4.31±1.53[c]
χ^2/p			χ^2=7.480, p=0.024*, a>c>b	χ^2=11.715, p=0.003*, c>a>b
Duration of oral antidiabetic use[2]				
1-5 years	6	17.9	7.75±3.41	3.78±1.38[a]
6-10 years	7	27.8	7.66±3.85	3.81±1.52[b]
11-20 years	14	36.4	7.78±3.79	4.00±1.56[c]
21-30 years	3	13.7	8.93±4.37	4.79±1.48[d]
31-40 years	3	4.2	7.69±4.71	5.00±1.82[e]
χ^2/p			χ^2=0.541, p=0.627	χ^2=9.985 , p=0.001**, e>d>c>b>a
Duration of insulin use[2]				
1-5 years	3	19.9	8.84±4.06	3.96±1.35[a]
6-10 years	4	38.6	8.46±3.79	4.21±1.46[b]
11-20 years	5	33.1	8.20±3.63	4.32±1.59[c]
21-30 years	4	8.4	8.28±5.75	5.57±1.55[d]
χ^2/p			χ^2=, p=0.910	χ^2=, p=0.019* , d>c>b>a
Has developed DM-related complications[1]				
Yes	114	36.4	8.07±4.48	4.68±1.57
No	199	63.6	7.79±3.48	3.70±1.44
z/p			z=-0.001, p=0.999	z=-5.364, p=0.000**
Attends follow-ups regularly[1]				
Yes	197	62.9	7.41±4.03	5.05±1.57
No	116	37.1	8.18±3.75	3.47±1.22
z/p			z=-1.752, p=0.080	z=-8.394, p=0.000**

Table 2. Continued.

Sociodemographic Characteristics	n	%	CAS X±SD	MMAS-8 X±SD
Adheres to medication treatment[1]				
Yes	273	87.2	8.09±3.83	5.97±1.36
No	40	12.8	6.55±3.91	3.78±1.38
z/p			z=-2.136, p=0.033*	z=-7.498, p=0.000**
Adheres to diet treatment[1]				
Yes	100	31.9	8.64±3.83	4.53±1.55
No	213	68.1	7.54±3.84	3.05±0.97
			z=-2.528, p=0.011*	z=-8.221, p=0.000**
COVID-19 pandemic prevented attendance to follow-ups[1]				
Yes	258	82.4	7.96±3.80	4.20±1.45
No	55	17.6	4.67±1.84	4.83±1.80
z/p			z=-0.819, p=0.413	z=-2.615, p=0.009**
COVID-19 pandemic affected blood sugar levels[1]				
Yes	185	59.1	8.01±3.89	4.79±1.43
No	128	40.9	7.81±3.86	3.43±1.32
z/p			z=-2.136 , p=0.569	z=-7.498, p=0.000**
Has been COVID-19-positive[1]				
Yes	152	48.6	7.38±3.56	4.50±1.45
No	161	51.4	8.38±4.08	4.12±1.60
z/p			z=-2.110, p=0.035*	z=-2.412, p=0.016*
Has had contact with a COVID-19 patient[1]				
Yes	208	66.5	7.68±4.01	4.43±1.47
No	105	33.5	8.31±3.54	4.10±1.64
z/p			z=-1.637, p=0.102	z=-1.856, p=0.063

Min: Minimum, **Max:** Maximum, CAS: Coronavirus (COVID-19) Anxiety Scale, MMAS-8: Morisky Medication Adherence Scale, [1]Two non-normally distributed independent groups were compared using Z: Mann-Whitney U Test, [2]Three non-normally distributed independent groups were compared using X^2: Kruskal-Wallis Test; *:p<0.05; **:p<0.01

As seen in Table 3, the mean CAS and MMAS-8 scores of the participants were 7.89±3.87 and 4.06±1.56, respectively. In our study, the treatment adherence levels of 77.3% of the participants were low with a mean score of 3.35±0.92, while the treatment adherence levels of 22.7% were moderate with a mean score of 6.47±0.50 (Table 3).

Table 3. Mean CAS and MMAS-8 Scores of the Type 2 Diabetes Patients (n=313)

	n	%	X̄±SD	Min	Max	Cronbach's alpha
Mean CAS score (Min: 0, Max: 20)	313	100.0	7.89±3.87	0.0	20.0	0.73
Mean MMAS-8 score of all patients (Min: 0, Max: 8)	313	100.0	4.06±1.56	1.0	7	0.72
Patients with low adherence, <6	242	77.3	3.35±0.92	1	5	
Patients with medium adherence, 6-7 71 22.7	71	22.7	6.47±0.50	6	7	

Min: Minimum, Max: Maximum, X̄: Arithmetic mean, SD: Standard deviation, CAS: Coronavirus (COVID-19) Anxiety Scale, MMAS-8: Morisky Medication Adherence Scale

According to the sociodemographic characteristics and mean treatment adherence levels of the participants shown in Table 4, the treatment adherence levels of the participants had weak positive relationships to their age and place of residence, a weak negative relationship to their education status (p=0.000), and a very weak positive relationship to their income status (p<0.05) (Table 4). Moreover, the treatment adherence levels of the participants had weak positive relationships with their disease durations and their durations of oral antidiabetic medication use, very weak positive relationships to their treatment modality and duration of insulin use, and a very weak negative relationship to their status of having experienced DM-related complications (p<0.05). The status of the participants to consider COVID-19 as an obstacle to treatment management was weakly and negatively associated with their treatment adherence levels (p=0.016), while there was a very weak negative relationship between their mean CAS and MMAS-8 scores (p=0.036) (Table 4).

Table 4. Correlations between the Mean CAS and MMAS-8 Scores of the Type 2 DM Patients

Patient Characteristics	MMAS-8	
	r	p
Age	0.305	0.000**
Education status	-0.285	0.000**
Income status	0.150	0.008**
Place of residence	0.233	0.000**
DM disease duration	0.231	0.000**
DM treatment modality	0.192	0.001**
Oral antidiabetic medication use duration	0.223	0.000**
Insulin use duration	0.166	0.033*
Status of having experienced DM-related complications	-0.304	0.000**
Prevention of treatment management due to COVID-19	0.148	0.009**
Status of having been COVID-19-positive	-0.137	0.016*
CAS	-0.119	0.036*

*Spearman's Correlation, DM: Diabetes Mellitus, CAS: Coronavirus (COVID-19) Anxiety Scale, MMAS-8: Morisky Medication Adherence Scale; *:p<0.05; **:p<0.01

4. Discussion

The COVID-19 pandemic not only continues to show its effects worldwide but also increases the hospitalization rates of especially individuals with chronic diseases like DM and leads them to experience death anxiety, fear, and concerns [7, 8, 14, 32, 33]. Studies conducted with COVID-19 patients have reported the prevalence of DM in these patients in the range of 5-36% [8,34,35]. It has been stated that the COVID-19 pandemic increases the anxiety levels and complication frequencies of DM patients with multiple psychosocial problems and affects their treatment adherence negatively [23, 32, 36, 37]. In the COVID-19 pandemic period, significant factors associated with anxiety and treatment adherence in Type 2 DM patients include worsened glycemic control, quarantine measures, inability to find medications, the inadequacy of vaccines, catching COVID-19, and fear of death. Therefore, the effects of the anxiety created by the COVID-19 pandemic in the treatment and disease processes of Type 2 DM patients on their DM treatment adherence are discussed here along with the reports of other studies in the literature.

In our study, the mean Coronavirus Anxiety Scale (CAS) score of the Type 2 DM patients was found as 7.89±3.87. Şişman et al. reported the mean anxiety score of DM patients as 7.5±4.3 [15]. Singhai et al. stated that DM patients experienced anxiety in the management of their treatment processes when they were infected with COVID-19 due to their infection status and the portrayal of diabetic individuals as a risk group on the media [32]. Bozkurt et al., (2021), in their study in which they investigated the perceived stress level and health anxiety in patients with diabetes mellitus and hypertension during the COVID-19 pandemic, had similar results with our study findings. Patients had higher levels of anxiety, depression and health anxiety compared to healthy individuals [38]. Unfortunately, the pandemic process increases the stress, anxiety and fears of patients and leads to negative health behaviors [13, 15, 39]. Considering that the numbers of cases and mortalities in the COVID-19 pandemic period are increasing day by day, preventing DM patients from experiencing high levels of anxiety, fear and stress will distract them from having thoughts about their possibility of dying. It is thought that it is important to support the management of anxiety and stress in DM patients in the pandemic period and provide a holistic approach by establishing multidisciplinary clinics that offer treatment management for DM patients.

In this study, the mean MMAS-8 score of all participants was found as 4.06±1.56, which indicated low treatment adherence levels in general. The increased probability of getting infected at hospitals due to the COVID-19 pandemic has prevented many patients from entering hospital environments for their follow-ups and treatments [13]. Studies in the literature that have been conducted with DM patients in the COVID-19 pandemic period have stated that the medication and treatment adherence levels of patients have been disrupted, their glycemic indices have worsened, and this situation would increase the disease burden of DM [4, 23, 36, 40,41]. It is considered that if DM patients have low levels of treatment adherence, they will not be able to obtain the optimal benefits expected from diets and medications. According to these results, it is seen as an important issue in the COVID-19 pandemic period to alleviate the anxieties of DM patients and increase their treatment adherence in terms of preventing complications and reducing their mortality rates.

In our study, it was determined that 87.2% of the participants adhered to their medication treatment, but 68.1% did not adhere to their diet treatment, and the COVID-19 prevented 82.4% of the participants from attending their follow-ups. It was found that the mean MMAS-8 scores of those who adhered to their medication and diet treatments were higher. While 59.1% of the participants stated that the COVID-19 pandemic affected their blood sugar levels, those who reported such an effect had a higher mean MMAS-8 score (Table 2). It has been seen in the literature that similar results to those in our study have been reported, the vast majority of patients have difficulty in keeping their blood sugar

levels under control [42], and they experience deterioration in their glycemic control (high fasting blood sugar) [43]. Additionally, it has been emphasized that although individuals state that they adhere to their diet treatments in the pandemic period, they have difficulty in this matter, and their diet treatment adherence rates are low [6, 42, 44]. In DM, adherence to medication and diet treatments is an important issue in reducing their complications and mortalities and increasing their quality of life [42]. It was found in this study that the participants who attended their follow-ups regularly had higher treatment adherence levels. The low treatment adherence levels of the participants who did not attend their follow-ups regularly could be related to the possibility that most of these patients were afraid of going to the hospital during the pandemic period, they could not keep up with their new treatments and medications, their medications and treatment methods were affected, and they had difficulties in adjusting their medication doses. The higher treatment adherence levels of DM patients who attend their follow-ups regularly in comparison to those who do not is an expected result. As long as the pandemic period goes on, patients should be constantly informed about their regular attendance to follow-ups, as well as new developments in medications and treatments.

In this study, in the comparisons of the treatment adherence levels of the participants based on their sociodemographic characteristics, it was found that the participants who were 65 years old or older, those who had higher education degrees, those who were single, those who were not working, those who had good income levels, and those who were living in cities had higher treatment adherence levels ($p<0.05$) (Table 1). However, because MMAS-8 scores under 6 are interpreted as low adherence, the result in our study was not on the desired level. As the result in our study, some other studies in the literature have reported that sex, age and marital status are influential on treatment adherence [15, 41, 44]. These results led us to consider that as most patients in our study were middle-aged or older than 65 years old, they were afraid of getting infected with COVID-19, and their treatment adherence levels were better because of this. It was also considered that because the vast majority of the participants were women, married and housewives, they were unable to utilize diabetes education programs, their knowledge levels were low, this lowered their treatment adherence levels, and thus, the single participants showed better treatment adherence.

It was found in our study that the participants who did not develop complications due to DM had lower treatment adherence levels, and the COVID-19 pandemic prevented most participants from attending health follow-ups (Table 2). Similar results have been reported in the literature, and accordingly, the COVID-19 pandemic increases the stress and anxiety levels and complication rates of DM patients, and as a consequence, it affects treatment adherence negatively [23,32,36]. These results indicated that the participants who did not develop DM-related complications could have been less aware of the outcomes of such complications, or their awareness about complications might not have developed, and their treatment adherence levels were insufficient as a result. It is thought that the patients who had developed COVID-19 infection and those who had ongoing complications were afraid of the disease, infections in general, and death, and because of this, they tried to adhere to their treatment to avoid getting infected again.

In this study, the participants whose DM disease duration was 31-40 years, those whose insulin use duration was 21-30 years, and those whose oral antidiabetic medication use duration was 31-40 years had higher treatment adherence levels (Table 2). While some studies in the literature provided findings that were in agreement with our results [17, 45], there were other studies that did not support our results and stated that as the disease duration of DM patients increases, their treatment adherence decreases [25, 27, 46]. In light of these results, it may be thought that DM patients accept their disease and treatments better as their disease duration increases, they develop better-coping strategies throughout this process, and therefore, their treatment adherence levels increase.

The participants of our study who stated that they adhered to their medication and diet treatments had higher CAS scores. It was also observed that the participants who had been COVID-19-positive had higher anxiety levels than those who had not been COVID-19-positive (Table 2). Previous studies have found that in the COVID-19 pandemic period, DM patients have high levels of concern about getting the disease and getting sick, they are afraid of dying, and this situation could lead them to experience anxiety [16, 42]. Based on these results, it is believed that DM patients with high COVID-19-related anxiety levels show better adherence to their medication treatments. Although a substantial ratio of the world's population has been vaccinated, the pandemic still poses a great risk for individuals with chronic diseases like DM. Therefore, the necessary precautions should be taken to enable individuals with chronic diseases to attend their follow-ups regularly.

In our study, a negative significant relationship was identified between the mean CAS and MMAS-8 scores of the participants ($p<0.05$). Studies in the literature carried out with DM patients have provided similar results and revealed that the anxiety and stress levels of these patients are high, their eating behaviors are negative, and their blood sugar levels and body mass indices increase [15, 47].

5. Conclusions and recommendations

In our study, it was determined that as the anxiety levels of the Type 2 DM patients increased, their treatment adherence levels decreased. It is seen that although vaccination efforts are in place in the ongoing COVID-19 pandemic period, most individuals who have chronic diseases are afraid of going to the hospital, this may affect their treatment adherence negatively, and it is important to lower the anxiety levels and increase the treatment adherence levels of patients of chronic diseases in cases like epidemics and pandemics. As long as the COVID-19 pandemic continues, it is recommended to establish diabetes support desks at hospitals, family health centers and public health centers where healthcare services are provided to reduce the anxiety levels and increase the treatment adherence of DM patients, who are in the high-risk group, enabling follow up on patients online at home by activating telehealth services, and provide the necessary information and psychosocial support that will reduce the concerns of patients.

Limitations of the Research

The sample of this study consisted of DM patients visiting the internal medicine outpatient clinic of a State Hospital in Turkey, and the results do not represent all DM patients in Turkey. In addition, whether the patients have psychiatric disorders is limited to the patient file and patient statement. The difficulties in the low number of patients with DM coming to the outpatient clinic due to the COVID-19 pandemic and the difficulty of working in accordance with mask, distance and hygiene conditions can be counted among the limitations.

Source of funding

There was no funding for this study.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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Ethical statement

Ethics committee approval was gained from the Ethics Committee for Non-Interventional Clinical Studies at Selcuk University (Decision Number:2020/25) and the Scientific Research Platform of the Ministry of Health (Protocol number: 2020-12-08T11_10_22).

Conflict of interest:

The authors declare that they have no confict of interest.

Authors' Contributions:
Concept – S.Ş., A.Y.K.; Design- S.Ş., A.Y.K; Supervision- S.Ş., A.Y.K; Resource- S.Ş., A.Y.K; Materials- S.Ş., A.Y.K; Data Collection and/orProcessing–S.Ş., A.Y.K., Z.B.T; Analysis and/or Interpretation- S.Ş., A.Y.K.; Literature Search– S.Ş., A.Y.K.; Writing– S.Ş., A.Y.K.; Critical Reviews– S.Ş., A.Y.K.; Other- S.Ş., A.Y.K.

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Research Article

INTESTINAL PARASITE INFECTIONS FREQUENCY AND ASSOCIATED RISK FACTORS IN INHABITANTS OF THE CITY OF YAOUNDÉ, CAMEROON

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Abstract: *Intestinal parasite infections are still prevalent in developing countries and in Cameroon where over 90% of the population is at high risk. To assess the distribution of intestinal parasitic infections and risk factors in the city of Yaoundé, both household and parasitological surveys were conducted from October to December 2019 among inhabitants of lowlands aged 15 years and over. Stools samples were collected and screened for intestinal parasite presence using Kato Katz and Formol-Ether methods. Sociodemographic status, prevention measures against intestinal parasitic diseases, and practices with increased exposition to risky environments were then recorded.*
A total of 229 participants (142 females: 62.0%; 87 males: 38.0%) were enrolled in the study, and 24.02% (55/229) were found infected by helminthes (ten species) and/or protozoans (one species). Participant infection rates and risk varied by parasite species and socio-demographic factors. Global risk analysis showed that age (OR ranges: 3.78-15.96), anti-parasitic drug consumption (OR: 2.53), eating behavior, hygiene (OR: 22.4), occupation (OR ranges: 1.92-3.53), and type of toilets (OR: 3.4) were strongly associated with risk of infection by intestinal parasites. The risk increased in the 15-30 years age group for Ascaris lumbricoïdes, Trichuris trichiura, and Schistosoma mansoni, unpredictably in those washing their hands before meals for A. lumbricoïdes and Hymenolepis nana, in respondents using antiparasitic drugs as auto-medication for H. nana and in those using traditional toilets for A. lumbricoïdes. However, other variables with high OR values (>5.0) might be a potential risk factor for the occurrence of specific parasite infections. The study suggests the need for household sensitization and community actions including integrated environmental management as a complementary strategy to reduce intestinal parasite transmission in the city of Yaoundé.

Keywords*: Intestinal-parasites, Infection-risk, inhabitants, Yaoundé, Cameroon.*

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1. Introduction

Intestinal parasitic infections caused by helminthes and protozoans affect around 3.5 billion people across the world [1]. These diseases of global health concern i.e. ascariasis, hookworm infection, trichuriasis and amoebiasis are among the main public health problems in developing countries particularly sub-Saharan Africa countries, where poor housing, inadequate water supplies, open defecation, poor waste management contribute to their transmission and persistence. The high density of the population in cities and close contact between people also constitute hot spots for the rapid emergence and spread of such diseases [2]. Although a significant reduction of these diseases' burden has been reported during the last decades, several factors closely linked to unplanned urbanization in Africa are maintaining the diseases present in urban settings. Lack of resources for the implementation of good wastewater management and landscape profiles in some locations from low and middle-income countries are also driven factors of these infections, particularly among school-age children, people with poor personal hygiene, and food service workers [3- 5]. Although intestinal parasite infections are not often associated with clinical signs and symptoms, some parasite infections may cause serious damage and occasionally the death of their hosts [6]. The high number and diversity of potential carriers of these parasites make them difficult to eradicate and control [7]. For the control of these infections in school-age children, WHO recommends preventive chemotherapy with albendazole/mebendazole against Soil Transmitted Helminthes (STH) and praziquantel against schistosomiasis [8]. Preventive chemotherapy primarily aims at reducing worm loads and associated morbidity [9]. However, this chemotherapy does not protect from re-infection [10], and due to an increased risk of infection observed among adults with low protective immunity, the global epidemiology of this disease and its social significance need to be also investigated for sustainable control and elimination [11]. Thus, it is necessary to complement preventive chemotherapy with other measures including wastewater management, sanitation, and hygiene (WASH), as well as social mobilization [12]. In Cameroon, around 16.1 million inhabitants are at risk and 10 million are infected with helminth parasites [13], notably *Ascaris lumbricoides*, hookworm, *and Trichuris trichiura* [14]. Thus, up to 10 million people are deprived of access to safe water sources, basic health services, essential medications, and suitable sanitation and living standards in rural areas as well as in main city of the country [15]. It is therefore important to check whether current practices and attitudes of the people living in the lowlands increase the risk of infection by intestinal parasites in the city of Yaoundé, Centre Region of Cameroon.

2. Material and Methods

2.1. Study sites and population

The study took place in seven administrative subdivisions of the capital of Cameroon, Yaoundé (3°51'N; 11°30'E). The city area belongs to the Mfoundi administrative division and covers ~ 200 Km^2 with an estimate of nearly 3 million inhabitants in 2020 [16]. The river Mfoundi and its tributaries form the hydrograph network. The selection of sampling locations was based on their distribution in the different subdivisions, and the presence of lowland areas, streams, and/or market gardening activities. They were Nkolondom and Etoa Meki (Yaoundé I), Tsinga and Cité verte (Yaoundé II), Efoulan and Ngoa Ekelle (Yaoundé III), Ekounou and Nkodengui (Yaoundé IV), Essos (Yaoundé V), Mvog Betsi and Etoug Ebe (Yaoundé VI), Nkolbisson and Oyom Abang (Yaoundé VII). Participants were asymptomatic people above 15 years old living in the seven selected subdivisions, representing about 55% of the total population.

2.2. Household investigation and ethical considerations

A cross-sectional study was carried out from October to December 2019, based on household surveys which included interviews and stool samples. A non-random sampling method was applied using a combination of a convenient selection of households and "quota sampling" of representative age groups of subjects per household. The minimum household size was randomly set at 30 per subdivision, with at least one participant enrolled per household. Therefore, the “minimal effective population size” was 210 participants across the seven study subdivisions of Yaounde, representing 1.3 per 10.000 inhabitants of the targeted population. The interview consisted of a pretested questionnaire applied to participants either in English, French, or the local language for 30 minutes. Each questionnaire was made up of combined questions and included sociodemographic data (sex, age, level of education, family size, occupation), preventive measures against IPD (sources of drinking water, hand washing before meals, automedicated drugs consumption, treatment of drinking water and proper food handling) and daily practices (market gardening and livestock activities, eating with hands, types of toilets and direct contact with soils/rivers). Participants were given containers for stool sample collection. Participants received advice on when to collect tools samples and how to store them. Stool samples were collected the next day between 8:00 to 10:00 am and were immediately stored at +4°C and transported to the laboratory for standard parasitological analysis. The research protocol has received approval from the Centre Regional Ethical Committee of Cameroon under the ethical clearance document N°/200-1/CRERSHC/2019 signed on the 8th February 2019. Administrative authorities and household heads provided their clearances for the study at the levels of subdivision and community, respectively. All the participants signed a consent form to participate after being informed of the purpose and objectives of the study.

2.3. Laboratory analysis

Parasites in stool samples were detected after microscopic examination using Kato-Katz (KK) method [17] and the Formalin-Ether Concentration (FEC) technique [18]. A slide was "positive" or "negative" based on the crosschecking examination of 41.7 mg of fresh material per sample mounted with distilled water for KK thick smears and with lugol's iodine for FEC thick smears. The combination of FE method along with the standard KK method increases the sensitivity of the diagnosis [19]. A qualified technician checked for the presence of intestinal parasites (protozoans and helminthes) in both sets of thick smears under a light microscope at 100X and 400 X magnifications.

2.4. Data analysis

The "Quota method" to determine the lowest sample size proposed for the analysis of the questionnaire in Cameroon i.e. 64 (15-30 years), 53 (31-50 years), and 21 (more than 50 years). The total number of parasites (eggs or larvae) was the overall parasite load (N) in stools expressed as egg per gram of stool was given following the WHO formula i.e. N=nx24, with n as the number of parasites counted in thick smear (41.7 mg of the pellet). The parasite intensity assessment was by "median", "arithmetic mean" and "geometric mean" using Excel 2016 package. The "median" was the middle number in a given sequence of numbers ranked by order from lowest to highest and the "arithmetic mean" as the sum of individual density divided by the total of individuals. The "geometric mean", was the nth root of the product obtained by multiplying each individual parasite density of the set of data, where "n" is the total number of individuals. Medcalc® and SPSS software calculated confidence intervals and Odd ratio rates. Assuming the "normal distribution” of our study participants, we applied parametric tests like Pearson’s Chi-square and ANOVA to compare the infection rates and mean parasite densities among parameters or variables, respectively. Data were considered significant at a rate of $P<0.05$. Whereas, odd ratios (OR) were calculated to estimate the risk of infection among groups in the

study population. Values of OR>1.0 were indicative of a positive association with an increased risk of infection by intestinal parasites. Factors associated with increased risk of infection were those showing significant p-values and ORs.

3. Results

3.1. Socio-demographic profiles of respondents

Profiles of the 229 respondents included demographic parameters, preventive measures against IPD and daily practices were summarized (Table 1). The average number of people per household was 2.0 and families with up to 5 individuals were more represented (74.7%). The age varied from 15 to 82 years (mean ± SD: 33.96±15.58) and included three age groups: youths (15-30 years), active adults (31-50 years), and old people (>50 years). Female participants represented 62.0% (n=142) and males 38.0% (n=87). Almost 56% of respondents were from the informal sector. Proper food handling (85.6%), hand washing before meals (62.5%), drinking of potable water (58.1%), and treatment of drinking water (54.1%) were mainly adopted by respondents as preventive measures against intestinal parasite infections. On the practices, over 60% had direct contact with traditional toilets, contaminated soils, and water.

3.2. Overall parasite infection rates and risk association

Different parasite stages (eggs, larvae, or cysts) representing at least 11 species were recorded in stool samples. They included 10 helminthes (*Ascaris lumbricoides*, *Trichuris trichiura*, *Hymenolepis nana*, *Necator americanus*, *Paragonimus westermanii*, *Schistosoma mansoni*, *Schistosoma sp*., *Taenia sp*., *Trichostrongylus sp*. and *Enterobius vermicularis*) and one protozoan (*Balantidium coli*). The global infection rate was 24.02% (55/229), i.e. 23.58% (54/229) for helminthes and 0.44% (1/229) for *Balantidium* protozoan. The single infection rate was 20.52% (47/229) and the co-infection rate reached 3.49% (8/229), mainly by *A. lumbricoïdes/H. nana*, *A. lumbricoïdes/T. trichiura* and *S. mansoni/H. nana* (37.5% each), *A. lumbricoïdes/N. americanus* (12.5%) and *A. lumbricoïdes/H. nana/T. trichiura* (12.5%). Global risk analysis of investigated factors did not show any significantly increased risk of intestinal parasite infection according to sex (p=0.356, OR: 0.75), level of education (p=0.128, OR ranges: 1.48-3.18), family size (p=0.235, OR ranges: 1.27-2.42) and household preventive measures and practices (p values: 0.137-0.414, OR ranges: 0.23-2.53). Though significant variations on the overall infection rates were recorded across age, anti-parasitic drug consumption, eating behavior, occupation, and type of toilets, OR values revealed increased infection risk only in 15-30 years age groups (OR ranges: 3.78-15.96), in those practicing antiparasitic auto-medication (OR: 2.53) and in civil servant groups (OR ranges: 1.92-3.53) (Table 1).

3.3. Infection risk by parasite species

The trends of infection risk also varied according to parasite species detected (Table 2). The risk has increased significantly for *A. lumbricoïdes* among the 15-30 years age group (18.2% prevalence, OR: 5.9), unexpectedly among those washing their hands before meals (11.2% prevalence, OR: 22.4), and in those using traditional toilets (10.1% prevalence, OR: 3.4). For *T. trichiura* (6.8% prevalence, OR: 23.4) and *Schistosoma mansoni* (18.2% prevalence, OR: 10.2) infections, only 15-30 years age group was the riskiest factor. *Hymenolepis nana* infections were more often associated with respondents practicing hand washing before eating (18.2% prevalence, OR: 39.0) and antiparasitic auto-medication (14.8% prevalence, OR: 4.7). Other factors with high OR values might stand up at increased risk of infection, notable sex for *S. mansoni*, *E. vermicularis* and *B. coli* (ORs: 4.94) and agricultural activities (market gardening and livestock) for *P. westermanii* (OR: 7.82) and *Trichostrongylus* sp (OR: 7.70).

Table 1. Parasite infection and risk ratio range by sociodemographic factors and household practices

Factors/groups		Participants (%)	NP	Infection Rate % (± 95% CI)	P	OR (95% CI)
Age range (years)	15-30	44 (19.21)	26	59.09 (38.6-86.58)	<0.001*	0.59-9.05 (NC)
	31-50	138 (60.3)	19	13.77 (8.29-21.5)		1
	> 50	47 (20.52)	10	21.28 (10.2-39.13)		
Gender	Male	87 (37.99)	18	20.69 (12.26-32.7)	0.356	0.75 (0.39-1.40)
	Female	142 (62.01)	37	26.06 (18.35-35.92)		1
Levels of education	Primary	44 (19.21)	12	27.27 (14.09-47.64)	0.128	1.48-3.18 (NC)
	Secondary	138 (60.3)	37	26.81 (18.88-36.96)		1
	University	47 (20.52)	6	12.77 (4.68-27.79)		
Occupation	Student	77 (33.63)	22	28.57 (17.91-43.26)	0.015*	0.52-3.55 (NC)
	Civil servant	23 (10.04)	10	43.47 (20.85-79.96)		1
	Informal sector	129 (56.33)	23	17.83 (11.3-26.75)		
Family size (number per household)	<5	58 (25.33)	17	29.31 (17.07-46.93)	0.235	1.27-2.42 (NC)
	05-10	130 (56.77)	32	24.62 (16.84-34.75)		1
	>10	41 (17.90)	6	14.63 (5.37-31.85)		
Type of toilets	Traditional	148 (64.63)	28	18.92 (12.57-27.34)	0.015*	0.47 (0.25-0.87)
	Modern	81 (35.37)	27	33.33 (21.97-48.5)		1
Sources of drinking water	Tap/Mineral	133 (58.08)	36	27.07 (18.96-37.47)	0.203	1.50 (0.80-2.82)
	Spring	96 (41.92)	19	19.79 (11.92-30.91)		1
Treatment of drinking water	Filtration	31 (13.54)	4	12.90 (3.52-33.04)	0.593	0.92a (0.50-1.70)
	Boiling	7 (3.06)	0	0		1
	Decantation	3 (1.31)	0	0		
	Biodisc	3 (1.31)	0	0		
	Chloration	58 (25.33)	11	18.97 (9.47-33.93)		
	SODIS	22 (9.60)	14	63.64 (34.79-106.77)		
	None	105 (45.85)	26	24.76 (16.18-36.28)		
Eating with hands	Yes	186 (81.22)	34	18.28 (12.66-25.54)	< 0.001*	0.23 (0.11-0.47)
	No	43 (18.78)	21	48.84 (30.23-74.65)		1
Hand washing before meals	Yes	143 (62.45)	39	27.27 (19.39-37.28)	0.137	1.64 (0.85-1.40)
	No	86 (37.55)	16	18.60 (10.63-30.21)		1
Proper food handling (wash vegetables and fruits)	Yes	196 (85.59)	45	22.96 (16.75-30.72)	0.361	0.69 (0.31-1.56)
	No	33 (14.41)	10	30.30 (14.53-55.73)		1
Direct contact with soils/rivers	Yes	146 (63.76)	37	25.34 (18.35-34.41)	0.534	1.23 (0.65-2.34)
	No	83 (36.24)	18	21.69 (12.85-34.27)		1
Market gardening & Livestock activities	Yes	64 (27.95)	13	20.31 (10.82-34.73)	0.414	0.75 (0.37-1.51)
	No	165 (72.05)	42	25.45 (18.35-34.41)		1
Regular deworming (at least twice a year)	Yes	58 (25.33)	11	18.97 (9.47-33.93)	0.297	0.68 (0.32-1.43)
	No	171 (74.67)	44	25.73 (18.7-34.54)		1
Auto medicated drugs consumption	Albendazole	36 (15.72)	12	33.33 (17.22-58.23)	0.032*	2.53a (1.34-4.79)
	Mebendazole	60 (26.20)	18	30.00 (17.78-47.41)		1
	Metronidazole	19 (8.30)	7	36.84 (14.81-75.91)		
	None	114 (49.78)	18	15.79 (9.36-24.95)		

NP= number of a positive case of infection, CI= confidence interval, OR= Odd ratios ;a: comparison is done between treated and non-treated; *:p<0.05;**:p<0.01

Table 2. Odd ratios of parasite species according to risk factors

	Age	Gender	Level of education	Occupation	Family size	Type of toilets	Source of drinking water	Treatment of drinking water	Eating with hands	Hand washing before meals	Proper food handling	Direct contact with soils/ rivers	Market gardening & Livestock activities	Regular deworming (at least twice a year)	Auto medicated drugs consumption
Ascaris lumbricoides	**0.55-5.91****	0.52	0.22-0.84	0.57-1.13	0.37-3.43	**9.02****	1.22	0.49a	1.67	**22.39****	1.19	0.71	0.57	0.98	0.95-1.64a
Trichuris trichiura	**0.07-23.36****	1.09	0.78-3.27	0.15-0.48	**0.96-9.56****	0.81	1.07	1.28a	0.34	6.87	0.24	0.85	0.23	0.73	0.17-2.05a
Necator americanus	1.04-3.27	1.63	0.61-1.74	0.92-1.82	0.32-11.55	2.78	0.72	4.30a	1.18	3.06	0.86	0.56	0.51	0.56	0.32-1.66a
Hymenolepis nana	0.49-2.57	0.70	0.49-2.56	0.40-0.73	0.82-1.30	1.56	3.41	0.58a	0.96	**39.01****	0.67	0.44	0.43	0.67	**0.27-4.67a****
Schistosoma mansoni	**1.02-10.22****	4.94	0.62-3.21	1.30-2.10	0.22-0.83	0.18	2.18	0.28a	0.70	1.82	0.51	1.72	0.85	0.97	0.15-0.62a
Schistosoma sp	1.03-1.07	0.53	1.03-1.07	0.30-1.82	0.74-0.83	0.18	2.18	2.56a	0.70	1.82	0.51	0.19	7.82	0.57	0.53-5.77a
Paragonimus westermanii	0.31-9.55	4.94	0.11-3.11	0.92-5.51	0.71-0.96	0.18	2.18	0.28a	0.70	1.82	0.51	1.72	0.85	0.97	0.32-1.66a
Trichostrongylus sp	0.34-9.55	0.54	1.03-1.07	0.92-5.51	0.11-0.74	0.18	0.24	0.28a	0.07	0.20	0.51	1.72	7.70	0.98	0.32-1.66a
Enterobius vermicularis	0.31-9.55	4.94	1.03-1.07	0.30-1.82	0.71-0.96	1.66	2.18	0.28a	0.70	1.82	0.51	1.72	0.85	0.97	0.11-1.66a
Taenia sp	1.04-3.27	1.64	0.61-1.74	0.92-1.82	0.44-1.61	0.54	0.72	0.85a	0.23	3.06	0.86	0.56	2.60	15.18	0.32-9.78a
Balantidium coli	0.35-3.11	4.94	1.03-1.07	0.30-1.82	0.71-0.96	1.66	2.18	2.56a	0.70	1.82	0.51	1.72	0.85	0.97	0.32-1.66a

a: factor with OR estimates adjusted between 2 groups (treated vs. non-treated); *:p<0.05;**:p<0.01 OR associated with significant infection rates

The overall arithmetic means parasite density was 1472.29 ± 6658.07 epg, ranging from 264.00 to 2,940.00 ppg. There were also variations according to parasite species and participant profiles. The following species *A. lumbricoides* (4,114.5 ± 12,331.92epg), *T. trichiura* (470.0±318.67epg), and *S. mansoni* (426.0±590.99epg) recorded the highest densities of parasite stages, while *N. americanus, Schistosoma sp, P. westermani, Trichostrongylus sp, E. vermicularis* and *B. coli* did not exceed 24.0ppg in samples. Moreover, the parasite density trend was not consistent with the prevalence status of participants. The mean density was high in youths (15-30 years) and old participants (>50 years), among male participants, and as expected in those using traditional toilets, drinking untreated water, eating with hands, or in absence of regular deworming (Table 3). Surprisingly, factors known to be effective against intestinal parasite infections (i.e. hand washing before meals, limited contact with soils/water) were found associated with high mean parasite densities. Therefore, we completed the estimation of parasite density using geometric mean and median as adjusted estimators. There was no consistency between arithmetic and geometric means of parasite density, geometric mean and median estimates showing alleviated discrepancies across investigated factors and species, compared to the arithmetic trends of mean parasite density. The extent of the dispersion of parasite densities (maximum-minimum) was 2,676 with arithmetic mean, 4.4 and 11.5 times higher than the median (612) and geometric mean (232.16), respectively.

Table 3. Variations of mean and median values of parasite density associated with sociodemographic factors and practices of participants

Factors/groups		**Arithmetic mean epg ($\bar{X}$ ± SD)**	**Geometric mean epg**	**Median epg**
Age range (years)	15-30	2,136.00 (±9,335.01)	165.03	120
	31-50	382.74 (±454.91)	134.17	96
	> 50	1,816.80 (±4,426.38)	191.55	72
Gender	Male	2,940.00 (±11,219.13)	139.55	96
	Female	758.27 (±2,335.75)	180.98	168
Levels of education	Primary	504.00 (±426.18)	273.04	576
	Secondary	2,160.00 (±8,568.38)	159.14	120
	University	411.20 (±555.33)	145.12	96
Occupation	Student	313.09 (±510.86)	99.92	60
	Civil servant	1,692.00(±4,449.69)	219.69	168
	Informal sector	2,485.56 (±9,900.59)	239.59	216
Family size (number per household)	<5	1,358.12 (±3,385.42)	286.28	576
	5-10	1,675.50 (±8,430.16)	109.38	96
	>10	712.00 (±682.82)	332.08	660
Type of toilets	Traditional	2,124.00 (±8,974.59)	218.63	204
	Modern	796.44 (±2,738.04)	125.11	96
Sources of drinking water	Tap/Mineral	907.2 (±2,834.67)	150.11	96
	Spring	1,943.2 (±8,682.78)	180.96	132
Treatment of drinking water	Filtration	342.00 (±525.58)	132.89	108
	Boiling	0	0	0
	Decantation	0	0	0
	Biodisc	0	0	0
	Chloration	384.00 (±547.39)	116.46	72
	SODIS	348.00 (±432.28)	153.78	168
	None	2,712 (±9,616.17)	208.55	144
Eating with hands	Yes	2,192.47 (±8,426.53)	206.89	204
	No	306.28 (±470.11)	116.63	96
Hand washing before meals	Yes	1,517.87 (±6,780.50)	165.69	120
	No	264.00 (±271.53)	181.20	264
Proper food handling (wash vegetables and fruits)	Yes	1,432.53 (±7,092.19)	177.46	144
	No	1,651.20 (±4,475.38)	123.83	148

Table 3. continued

Factors/groups		Arithmetic mean epg ($\bar{X}$ ± SD)	Geometric mean epg	Median epg
Direct contact with soils/rivers	Yes	733,62 (±8,167.89)	171.00	144
	No	2,912.00 (± 6,779.03)	139.95	72
Market gardening & Livestock activities	Yes	439.38 (± 10,652.06)	162.35	120
	No	1,758.29 (±6,717.88)	150.49	96
Regular deworming (at least twice a year)	Yes	274.10 (±416.72)	107.08	72
	No	2,104.67 (±8,192.36)	209.65	192
Auto medicated drugs consumption	Albendazole	1,604.00 (±4,027.54)	320.75	420
	Mebendazole	290.67 (±430.73)	111.40	72
	Metronidazole	675.43 (±659.23)	298.31	672
	None	2,876.00 (±11,231.18)	127.48	96

epg= number of eggs per gram of stool; SD: standard deviation

4. Discussion

Following Hippocrates, several centuries before, addressing human health in relation to its living environments is increasing worldwide through various integrated approaches or concepts [19]. Among them, the "One Health" concept, as an integrated approach that recognizes this fundamental relationship between the health of people, animals, plants, and the environment, is complementing in-country and regional actions for the control and elimination of various diseases including intestinal parasitic soil/water-borne diseases. Our study aimed at providing probable responses on whether there is a linkage between intestinal parasitic infections among humans and their living conditions in the lowlands of Yaoundé, the capital city of Cameroun. The environments of study locations were dominated by flooding areas, rivers, and wells usually used for domestic duties and agriculture during the study period lasting from October to December. These environments situated in lowlands are covered by market gardens where perishable crops such as lettuce (*Letica sativa*), tomatoes (*Lycopersicon esculenta*), parsley, and bitter leaf (*Vernonia amygdalina*) amongst other vegetables are cultivated for household consumption and neighboring markets. In a negative way, these lands are also among the sources of vulnerability to intestinal parasitic infections addressed in this paper, along with sociodemographic status, preventive measures taken by people (regular deworming, WASH principles, and personal hygiene), and daily duties (i.e. market gardening, livestock). Our main findings indicated a high prevalence of intestinal parasite infections among study participants (~24%), especially caused by the dwarf tapeworm (*Hymenolepis nana*), *Ascaris lumbricoïdes* roundworm, and *Schistosoma mansoni*. This parasitological profile was similar to what was previously observed in many regions of Cameroon as well in humans [20] as in environment samples [21]. In fact, it was shown that the environment and the behaviour influenced the rate of infection among local communities [22, 23]. Thus, some occupations (i.e. tea pickers, miners) and various factors including humid tropical climate, lack of access to potable water, poor hygiene, illiteracy, and poverty increase the vulnerability to intestinal parasite infections [24, 25]. In study locations, this vulnerability was significantly associated with youths of 15-30 years age group, poor hygiene and sanitation standards (hand washing before meals, type of toilets), improper use of anti-parasitic drug prophylaxis, and occupation, principally for specific intestinal parasitic diseases, i.e. hymenolepiasis, ascariasis, and *Schistosoma mansoni* infection. These outcomes follow the findings from other regions of Cameroun [26, 27] and the WHO's concerns on school and preschool-age children, and adults involved in occupations like tea pickers, miners [28]. Otherwise,

some factors like sources of drinking water, direct contact with soils/rivers and family size displayed high OR values, and might be increasingly addressed in future studies as a potential risk for intestinal infections in targeted sites. In this paper, we also estimated the parasite load as the intensity of infection using the arithmetic mean, geometric mean, and median. However, the trend of arithmetic means estimates showed significant variations compared with geometric mean and median estimates. These latest estimates (geometric mean and median) mitigated variations of parasite intensity among sex, age, level of education, and other factors. These significant discrepancies between the arithmetic mean and geometric mean estimates have been highlighted by Ojja [29]. Some authors trying to explain the rightful use of the arithmetic mean instead of geometric mean and/or median suggest that it overestimates the distribution of data while geometric mean or median allows an appropriate quantification of the distribution as the well realistic extent of values [30]. The size of our positive sample (less than 100) might also affect the accuracy of parasite density estimates regardless of the mode of calculation. Addressing all biases and sampling constraints might improve the outcomes of research studies on the relationships between intestinal parasitic infections, host reservoirs, and environments.

5. Conclusion

The main finding of this research provides further evidence of the endemicity of intestinal parasite infections in Yaoundé, the capital city of Cameroon. Prevalence of such intestinal parasite infections was high (~ 24%) with increased risk associated with living conditions, poor sanitation, and hygiene standards in lowlands. Globally, the vulnerability to infection by roundworms, whipworms, and flukes increased for respondents from 15-30 years old, as well as those washing hands before meals, using antiparasitic drugs as auto-medication, and traditional toilets. However, our study showed some limitations (low sample size, sampling method, cross-sectional study) that might mitigate the significance and accuracy of findings, or not allow to point out other risk factors of intestinal parasite infections in study locations. Thus, the study suggests the need for household sensitization and community actions including integrated environmental management as a complementary strategy to reduce intestinal parasite transmission in the city of Yaoundé.

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Ethical statement

The Centre Regional Ethical Committee of Cameroon approved the research protocol by the ethical clearance document N°/200-1/CRERSHC/2019 signed on the 8th February 2019.

Conflict of interest

The authors declare not to have any conflict of interest.

Author's contributions

All the authors mentioned in this paper have significantly contributed to this research. They contributed to setting up the study design, performing the laboratory analyses, and collaborating on the written and proofreading parts of the final document.

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Research Article

PROGNOSTIC VALUE OF DYNAMIC THIOL-DISULFIDE HOMEOSTASIS IN PREDICTING HOSPITAL MORTALITY IN HYPOXEMIC RESPIRATORY FAILURE

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Abstract: *Hypoxemic respiratory failure (HRF) is a PaO_2 < 60 mmHg with normal or subnormal $PaCO_2$. The gas exchange is impaired at the level of the alveolo-capillary membrane. HRF is associated with a high mortality rate in hospitals, and there is no diagnostic laboratory test to predict this mortality. This study evaluates the possibility of predicting mortality in HRF patients with dynamic thiol-disulfide homeostasis parameters, which are indicators of oxidation state. Sixty-two patients with HRF and 40 healthy individuals in the control group were included in the study. Dynamic thiol-disulfide parameters were studied from the serum of all participants. Total and native thiol levels were significantly lower in the patients than in the control group (p <0.05). Disulfide levels were higher in patients who died than in survivors (p <0.01). The logistic regression analysis determined that the rise in disulfide values increased the mortality risk by 1.57 times. Progressive hypoxemia increases oxidation. Serum disulfide level is a valuable parameter in predicting mortality in hypoxemia.*

Keywords*: Hypoxemia; thiol-disulfide; oxidative stress; mortality*

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1. Introduction

Hypoxemic respiratory failure (HRF), also referred to as type I respiratory failure, is a clinical picture of the respiratory system's oxygenation function failing [1]. HRF can be seen in almost all lung diseases, usually involving fluid accumulation or collapse in the alveoli, and many extrapulmonary disorders such as obesity and heart failure [2]. Recently, the importance of HRF has increased due to the effects of the disease associated with SARS-CoV-2 infection (coronavirus disease 2019; COVID-19) in the lungs [3]. Acute HRF is among the most common causes of hospital mortality, with an approximately 30% rate [4]. Nowadays, the diagnosis of HRF is made by clinical findings, arterial blood gas tests, and chest radiography. Various scores such as APACHE II are currently used for the severity of such diseases, and there is no single laboratory parameter routinely used to predict mortality [5].

Insufficient oxygenation can result in hypoxia in the lung and other tissues [6]. There are conflicting studies in the literature between hypoxia and oxidative stress. Cell culture and experimental animal studies show both the increase and decrease of reactive oxygen species (ROS) in hypoxia [7, 8].

Thiols are organic compounds containing the sulfhydryl group. These compounds have general antioxidant properties [9]. During oxidation, intramolecular and intermolecular disulfide bonds are

formed between two sulfhydryl groups, and since this is a reversible reaction, it is called the dynamic thiol-disulfide homeostasis [9]. In addition, it can also be an index for oxidant-antioxidant states in many pathological conditions, such as heart disease, diabetes, cancer, and neurological diseases [10].

This study aimed to investigate the relationship between hypoxemia and oxidative stress based on the dynamic thiol-disulfide balance. Also, we aimed to determine whether dynamic thiol-disulfide homeostasis parameters effectively predict mortality in patients diagnosed with HRF.

2. Material and Methods

2.1. Study population

This cross-sectional study included 62 HRF with chronic obstructive pulmonary disease (COPD) patients admitted to the Kırşehir Training and Research Hospital emergency department and 40 healthy individuals who were admitted to the emergency department and had no health problems. Those using antioxidant drugs, chronic liver disease, malignancies, or active smokers were excluded from the study. The diagnosis of HRF was made based on clinical findings, chest radiography, and arterial blood gas test measurements. Fourteen of the 62 HRF patients died soon after being admitted to the hospital; ~~3~~ three from sepsis, six from cardiac arrest, and five from pulmonary disease; ~~48~~ forty-eight patients survived. All participants provided written informed consent. The investigation conforms to the principles outlined in the Declaration of Helsinki.

2.2. Ethical Consideration

The study was approved by the Ethics Committee of Ahi Evran University Faculty of Medicine (Ethical committee approval number and date: 2018-03/32, 13/02/2018).

2.3. Laboratory Parameters

Venous blood samples were collected from all participants into anticoagulant-free serum tubes and tubes containing K2EDTA at the first admission. Serum tubes were centrifuged at 2000 x g for 10 minutes. Routine biochemistry tests were performed immediately from a portion of the serum collected, and the remaining serum was transferred to microcentrifuge tubes and stored at −80 °C.

Routine biochemistry tests, including glucose, urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), and C-reactive protein (CRP), were measured in a Cobas 501 (Roche Diagnostics®, Germany) autoanalyzer. Complete blood count parameters from the blood samples collected in tubes with K_2EDTA have been studied on the Sysmex XN-1000 (Sysmex Corporation, Kobe, Japan) device. Blood samples collected from the radial or femoral artery to dry lithium heparin injectors were immediately analyzed for pH, O_2 saturation, PaO_2 (partial pressure of oxygen), $PaCO_2$ (partial pressure of carbon dioxide), and HCO_3 (bicarbonate) parameters using the RAPIDLab® 348EX (Siemens Healthcare GmbH, Germany) instrument at room temperature.

The parameters of thiol-disulfide homeostasis were measured as previously described by Erel and Neseliolu [11]. Total thiol and native thiol tests were run with commercial kits (Rel Assay Diagnostics, Gaziantep, Turkey) using the Cobas 501 (Roche Diagnostics®, Germany) biochemistry autoanalyzer. Disulfide levels were calculated as follows:

$$[total\ thiol\ values - native\ thiol\ values]/2 \quad (1)$$

2.4. Statistical Analysis

All statistical analyses were performed using SPSS software (version 21.0, SPSS Inc., Chicago, IL, USA) and Excel (Microsoft Turkey). The normality of variables was determined by Kolmogorov-Smirnov and Shapiro-Wilks tests. Results were presented as mean ± standard deviation or median (at

the 25th and 75th percentiles) for continuous variables and frequency for categorical variables. To compare two groups, an unpaired t-test or Mann-Whitney U-test was used for continuous variables, a χ^2 test was used for categorical data, and Pearson's / Spearman's test was used for correlation analysis. One-way analysis of variance (ANOVA) was used to compare more than two normally distributed groups. Bonferroni comparison was made as a post hoc test after the ANOVA test. The Kruskal-Wallis test was performed to compare more than two groups that were not normally distributed. Dunn's nonparametric comparison was performed as a post hoc test after the Kruskal-Wallis test. A linear regression model was used to examine the independent effects of different predictors. Logistic regression analysis was used to find other predictors of mortality in the study. In this analysis, variables were chosen using the backward elimination method. The receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic value for mortality of variables found to contribute to the logistic regression model significantly. Values of $p < 0.05$ were considered statistically significant.

3. Results

The demographic characteristics and laboratory findings of the study group are summarized in Table 1. There was no statistically significant difference in demographic characteristics between the groups.

Table 1. Demographic characteristics and laboratory results of the groups.

Parameters	Deceased (n = 14)	Survivor (n = 48)	Control (n = 40)	p-value
Age, years	71.5 ± 13.1	68.5 ± 10.8	66.7 ± 7.3	0.292
Sex, male %	57.1	70.8	67.5	0.628
BMI, kg/m^2	27.5 ± 6.4	27.5 ± 6.7	26.7 ± 3.8	0.783
Hypertension, %	42.9	50.0	47.5	0.892
Diabetes mellitus, %	42.9	27.1	27.5	0.493
Glucose, mg/dL	127 (96-193)	124 (104-145)	109 (98-183)	0.662
Urea, mg/dL	66 (46-111)	49 (35-69)	49 (37-58)	0.247
Creatinine, mg/dL	1.43 (0.90-1.88)	0.89 (0.77-1.11)	0.90 (0.74-1.23)	0.113
ALT, IU/L	11 (6-21)	15 (9-23)	15 (8-21)	0.322
AST, IU/L	17 (11-32)	22 (14-28)	19 (12-28)	0.811
CRP, mg/L	10.3 (5.52-13.4) *†	1.49 (0.53-4.31)	1.04 (0.41-2.55)	**<0.001**
Leukocyte, x10^{3}µL	9.80 ± 4.7	9.24 ± 4.3	9.68 ± 4.0	0.860
Total thiol, µmol/L	296 ± 61*†	309 ± 56†	424 ± 57	**<0.001**
Native thiol, µmol/L	254 ± 56*†	274 ± 54†	381 ± 58	**<0.001**
Disulfide, µmol/L	21.8 ± 3.8*†	17.4 ± 4.1	17.9 ± 3.0	**0.001**
O_2 Sat, %	66.6 ± 9.9	71.6 ± 8.2	-	0.061[a]
pH	7.37 ± 0.05	7.35 ± 0.05	-	0.213[a]
$PaCO_2$, mmHg	40.0 (37.2-42.0)	40.5 (34.0-44.8)	-	0.760[b]
PaO_2, mmHg	43.2 ± 8.3	43.6 ± 8.8	-	0.863[a]
HCO_3, mEq/L	24.2 ± 2.8	24.6 ± 3.4	-	0.736[a]

Note: AST, aspartate transaminase; ALT, alanine transaminase; BMI, body mass index; CRP, C-reactive protein; HCO_3, bicarbonate; O_2 Sat, oxygen saturation; PaO_2, partial pressure of oxygen; $PaCO_2$, partial pressure of carbon dioxide.
[a,b]: p values were obtained via unpaired t-test and Mann-Whitney U-test, respectively. *p<0.05 versus Survivor,†p<0.05 Control

There was a statistically significant difference in CRP levels between the patients who were deceased and survived and the control group; CRP levels were approximately ten times higher in patients deceased than others (p<0.001, Table 1). Other biochemical tests in the three groups were statistically

similar. There were statistically significant differences in thiol-disulfide homeostasis parameters between the groups. Both total and natural thiol levels were significantly lower in surviving patients and deceased, both from each other and in the control group. In contrast, disulfide levels were significantly higher only in those who were deceased (p=0.001, Table 1, Figure 1). Mean leukocyte count and blood gas parameter values in the three groups were statistically similar.

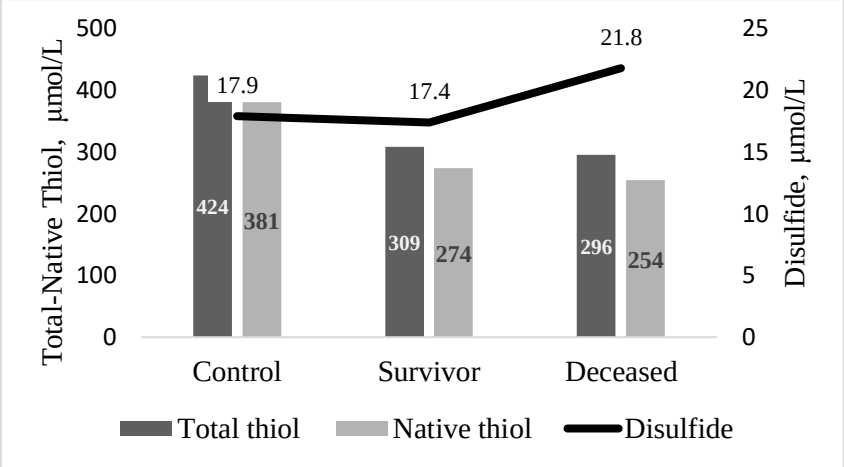

Fig. 1 Average disulfide values in control, survivor, and deceased groups

We also evaluated the correlations of laboratory findings of deceased patients. The correlation between CRP, an important marker for inflammation, and disulfide levels were not significant (r = -0.180, p = 0.538). There was an inverse correlation between disulfide and O_2 saturation levels, an indicator of hypoxemia (r = -0.632, p = 0.015; Figure 2). In the linear regression analysis for disulfide and oxygen saturation in the deceased group, it was found that oxygen saturation was responsible for approximately 40% (r^2 = 0.339) of the increase in serum disulfide levels. There was no statistically significant relationship between other parameters.

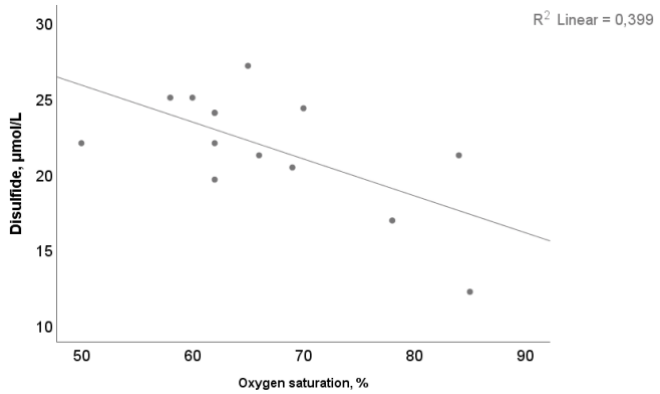

Fig. 2 Scatter plot showing disulfide levels and oxygen saturation in the deceased group.

Table 2 shows the logistic regression analysis to determine the variables that predict mortality. According to the logistic regression analysis results, an increase in total thiol level decreased the mortality probability by 0.98 times, and an increase in disulfide and CRP levels increased the mortality probability by 1.57 and 1.19 times, respectively. There was no statistically significant prediction of the effect of gender on mortality.

Table 2. Logistic regression analysis to estimate the probability of death.

Risk Factor	OR (95% C.I.)	p-value
Total thiol (μmol/L)	0.98 (0.96–0.99)	0.044*
Disulfide (μmol/L)	1.57 (1.18–2.08)	0.002**
CRP, (mg/L)	1.19 (1.04–1.35)	0.011*
Gender (1)	0.19 (0.03–1.24)	0.083

CRP, C-reactive protein; * :p<0.05; **: p<0.01

ROC analysis was performed to determine whether CRP, total thiol, and disulfide variables had a cut-off value in predicting mortality in patients with HRF. As there was no statistically significant cut-off value of total thiol values on death, the area between the reference line and the line of total thiol values was not statistically significant (AUC: 0.537, p = 0.674). In the ROC analysis, cut-off values of 4.18 mg/dL for CRP and 19.5 μmol/L for disulfide were found in predicting mortality, respectively (Figure 3).

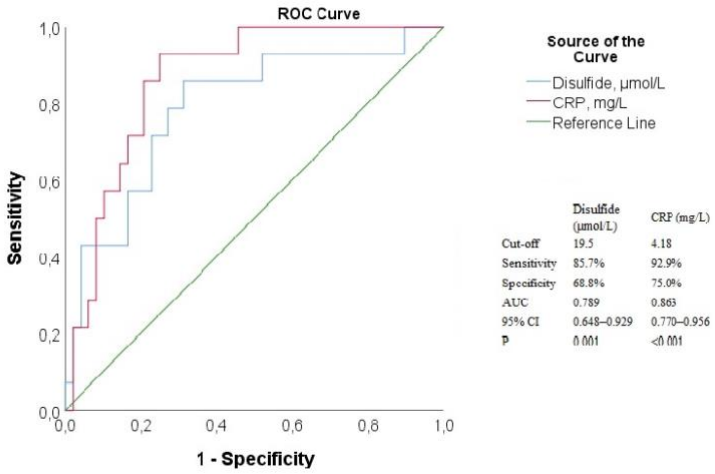

Fig. 3 ROC curve for disulfide and CRP values

4. Discussion

In this study, we found that due to the oxidative stress caused by hypoxemia, the dynamic thiol-disulfide balance was preserved in survivors in patients with HRF, but the balance shifted towards disulfide in patients who died. We found that the disulfide parameter is more valuable than other routine laboratory tests in predicting mortality.

During normal cellular metabolism in aerobic respiration organisms, ROS and reactive nitrogen species (RNS) are released, which can be harmful to the organism [12, 13]. At the same time, these species deliberately produce these compounds at low levels for use in many physiological processes, such as the killing of pathogens, autophagy, apoptosis, and some signaling pathways [14]. Organisms have developed various antioxidant defense systems to keep ROS under control and prevent damage to themselves, including non-enzymatic peptides containing thiol, such as glutathione, and enzymatic antioxidants, such as catalase and superoxide dismutase (SOD). Thus, an oxidant-antioxidant balance is achieved in the body [9, 15]. In any case, if this balance shifts in favor of ROS increase, oxidative damage occurs. Oxidative damage is associated with many diseases, such as cardiovascular, neurodegenerative, metabolic, and inflammatory diseases [16]. An increase in ROS production under hypoxemic conditions has been found in various experimental studies. Among these studies, there are

studies in the literature that show that both the direct ROS itself and the number of oxidation products it causes and the antioxidants decrease against it [17-21]. The increase in ROS in hypoxia is thought to be the signaling function required by the cells to respond to hypoxia [22].

The levels of various compounds and enzyme activities are measured to assess the oxidant-antioxidant levels in the body. One of these measurements is thiol-disulfide homeostasis [10]. In case of ROS increase, thiols are oxidized to disulfides and the equilibrium shifts towards disulfide. If the ROS increase is relatively small and short-lived, the antioxidant responses can be activated to reduce excess ROS and restore equilibrium. However, when the ROS increase is at high levels and persistent (in cases of chronic oxidative stress), antioxidant responses are insufficient, and restoration cannot be achieved [23]. In our study, there was a slight increase in serum disulfide levels in HRF patients than in the control group, while there was a decrease in total and native thiols, suggesting that oxidation is at controllable levels. We found that the increase in hypoxia is responsible for the increase in disulfide levels. It was observed that oxygen saturation decreased, and disulfide levels increased in patients who died (Figure 2). The high disulfide values of the deceased patients indicate that the oxidation was severe in those individuals and that the antioxidant thiols were insufficient to prevent oxidant damage. In addition, since CRP is a good marker for inflammation, we examined whether there is a relationship between CRP and disulfide levels. However, we could not find a relationship. It suggests that inflammation did not contribute to disulfide levels in patients who deceased.

The hospital mortality rate from acute HRF is about 30% [4], and the leading causes of death are sepsis, pulmonary dysfunction, and neurological dysfunction [24]. In the current study, 14 of the patients (23%) died after admission to the emergency department. In our study, when biochemical tests, blood gas, and dynamic thiol-disulfide parameters were compared between those who are deceased and those who survived, there were only significant increases in disulfide and CRP levels but no significant differences in all the remaining parameters. These results show that routine parameters and blood gases may not be so beneficial in predicting the mortality of these patients. On the other hand, serum disulfide levels are significant in predicting mortality in these patients.

Our study has some limitations, in that it was conducted in a single center, and the study group was relatively small in numbers. In addition, the underlying primer disease and comorbidities of the patients that caused HRF may also have affected disulfide levels and mortality.

5. Conclusion

In HRF, ROS increases due to hypoxia and progressive hypoxemia, oxidation level, and mortality risk. Our study demonstrated that the routine biochemical and blood gas parameters used in predicting the mortality of HRF patients were insufficient. However, we found that the serum disulfide parameter predicted mortality better in these patients.

We believe that the findings we obtained from our study will shed light on further studies. Antioxidant supplements that cause an increase in blood thiol levels, such as glutathione, can be given to patients with hypoxemic respiratory failure who are admitted to the emergency department with high disulfide levels. In this way, it can be investigated whether it has a positive effect on the mortality of patients.

Ethics approval

The study was approved by the Ethics Committee of Ahi Evran University Faculty of Medicine (Ethical committee approval number and date: 2018-03/32, 13/02/2018). The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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Author contributions

B. I: Conceptualization, writing - Original Draft preparation, Methodology, Formal analysis
D. Z. K: Conceptualization, Methodology, Investigation
H. M. .C: Conceptualization, Methodology, Writing - Original Draft preparation
Z. M. E: Writing- Reviewing and Editing, Visualization
B. C: Investigation
S. E: Investigation
K.G: Data curation, Formal analysis

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Research Article

EFFECTS OF RESTRICTION MEASURES ON MORBIDITY AND MORTALITY IMPLEMENTED DURING COVID-19 PANDEMIC IN TURKEY: A RESEARCH THROUGH NATIONAL DATA INCLUDING ONE YEAR

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Abstract: *This research is aimed to determine the effects of restriction measures implemented in Turkey during the COVID 19 pandemic by detecting variations in the "number of cases per day", "test positivity rate per day", and "number of death per day" according to different restriction periods. In order to be able to analyze based on cases declared as standard, the periods of restriction measures between November 18, 2020, and November 17, 2021, were included in the research. The data of the Ministry of Health was used as the source. When making a statistical assessment for the "number of cases per day" and the "test positivity rate per day", we evaluated each restriction period to include the first 10 days after the end of this period. When comparing the "death numbers per day", we evaluated each restriction period to include the daily death numbers for the first 21 days after the end of that period. The highest means were seen for all three parameters examined during the "revised local decision-making phase". These mean are 57,396 for the number of cases per day, 18.4 for test positivity rate per day, and 351 for the number of deaths per day. This period is the only period in which the means for "number of cases" and "number of deaths" are higher than the first period, which is the reference period, and for these parameters, a statistically significant difference is detected with the reference period ($p<0.001$). There is a decrease in the means for all three parameters examined during "lockdown periods" and after this period that is the "gradual normalization period". Restriction measures have played a role in reducing the mortality and morbidity associated with COVID-19. The increase in morbidity and mortality during periods when epidemic management is partially decentralized can provide evidence-based data for assessments of the effects of decentralization.*

Keywords: *restriction measures, COVID-19, Turkey, decentralization*

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1. Introduction

COVID-19 pandemic has deeply affected Turkey as well as worldwide [1]. Non-pharmaceutical interventions (NPI) are widely been used in Turkey during struggling with the pandemic [2, 3]. Non-pharmaceutical interventions (NPI) are defined as public health measures that aim to control of transmission in the community by the ECDC (European Centre for Disease Prevention and Control) [4]. NPI contains individual measures such as washing hands and using mask; environmental measures such as ventilation indoors; and population-based measures including restrictions of movements. Furthermore, testing and contract tracing are another essentials items of NPI [4].

In this pandemic, the development of an effective vaccine has been relatively short compared to its counterparts in history. However, there is a significant time gap between the onset of the epidemic and the onset of widespread vaccination. Despite significant efforts, immunization rates are far from

achieving mass immunity [5]. On the other hand, it is still not possible to talk about the existence of effective treatment agents [6]. Due to all these factors, NPI emerges as the main tool set in the fight against the pandemic.

Different studies have shown that effectiveness of restriction measures including social movement restrictions which are one of the important components of NPI during the COVID-19 pandemic. Studies conducted in China, the country where the epidemic started, have shown that restriction measures are effective tools to suppress the spread of the disease [7]. The effectiveness of restriction measures in suppressing the epidemic has been demonstrated in the example of a developing country such as Nigeria and a developed country such as the UK [8, 9]. In a study examining the data of 34 countries, it was found that restriction measures in the early period of the epidemic were associated with a decrease in incidence [10].

Travel restrictions, limitation of the gathering of people, closure of primary schools, closure of universities, rules related to general social distance, shutting down public spaces such as cafes, restaurants, bars, shopping malls, and curfew are examples of implementation of restriction measures [11, 12]. Various restriction periods have occurred in Turkey throughout the periods including different restrictions of movement practices [2, 13]. Monitoring and evaluating the effectiveness of restriction measurements will contribute to more effective management of the pandemic.

This study aimed to determine the effects of restriction measures implemented in Turkey by detecting variations in the number of cases per day, test positivity rate per day, and the number of death per day according to different restriction periods.

2. Methods

2.1. Scope of the assessment

After November 25, 2020, the number of cases continued to be announced based on the standardized definition by the Ministry of Health of Turkey throughout the pandemic [1]. In this study, the number of daily cases reported since November 25 2020 was evaluated in order to ensure data standardization. Since the restriction period covering 25 November, 2020 is the period starting with 18 November 2020, the restriction period starting with 18 November was the first period examined within the scope of this research. In order to be able to analyze a one-year period, the period of restriction measures between November 18, 2020, and November 17, 2021, were included in the research.

The number of cases per day, test positivity rate per day, and mortality rate per day were achieved by the website of the Ministry of Health of Turkey[1].

2.2. Definition of restriction periods

We have defined restriction periods according to implementations of the Ministry of Internal Affairs of Turkey [2]. For restriction measures periods up to 1 June 2021, in naming these restriction periods, we used the officially announced names and the names in a review article for restriction practices in Turkey [2, 13].

The implementation dates of restriction periods are “18.11.2020-30.11.2020” for the “national partial curfews”, “01.12.2020-28.02.2021” for the “national extended curfews”, “01.03.2021-29.03.2021” for the “local decision-making phase”, “30.03.2021-13.04.2021” for the “revised local decision-making phase”, “14.04.2021-28.04.2021” for the “partial lockdown”, “29.04.2021-16.05.2021” for the “full lockdown”, “17.05.2021-31.05.2021” for the “gradual normalization” [2, 13].

The second phase of gradual normalization was begun on 01.06.2021. Period including “01.06.2021-31.08.2021” was named as “2nd phase of gradual normalization/summer 2021”. In order to reveal the seasonal variation pattern, we defined the period that started after September 1 as a separate

period, although there was no change in this date in terms of restriction practices. Therefore, we have named "autumn 2021" the last period we have investigated.

2.3. Assessment of the number of cases per day and test positivity rate per day

In general, the incubation period for COVID-19 ranges from 2-14 days. The mean incubation time was 5.84 days (99% confidence interval: 4.8-6.8), and the median incubation time was 4.8 days [14]. According to a study including 14,618 patients from different 114 Belgian hospitals, the median time between symptom onset and diagnosis was 5 days. This time differs according to some descriptive characteristics [15]. In the statistical evaluation process, we took into account the incubation period and the time between the onset of symptoms and the application to the health institution. When making a statistical assessment for the "number of cases per day" and the "test positivity rate per day", we evaluated each restriction period to include the first 10 days after the end of this period. For this reason, the calendar intervals taken as a basis in the statistical assessment follow the calendar intervals related to the restriction applications with a ten days difference.

2.4. Assessment of the number of deaths per day

Centers for Disease Control and Prevention (CDC) says that the median time from onset of illness to acute respiratory distress syndrome (ARDS) was 8–12 days, and the median time from onset of illness to ıntensive care unit admission was 9.5–12 days [16]. World Health Organization (WHO) says that the time between symptom onset and death ranged from about 2 weeks to 8 weeks [17]. According to a study carried out in China and included 1833 deaths, the median interval for symptom onset to death was 17.0 days (12.0–22.0) [18]. We wanted to take into account the incubation period and the time between the onset of symptoms and death while making the statistical evaluation of the death numbers. When making a statistical assessment for the “number of deaths per day”, we evaluated each restriction period to include the first 21 days after the end of this period. For this reason, the calendar intervals taken as a basis in the statistical assessment follow the calendar intervals related to the restriction applications with a 21 days difference. Figure 1 shows the "number of days of restriction periods"

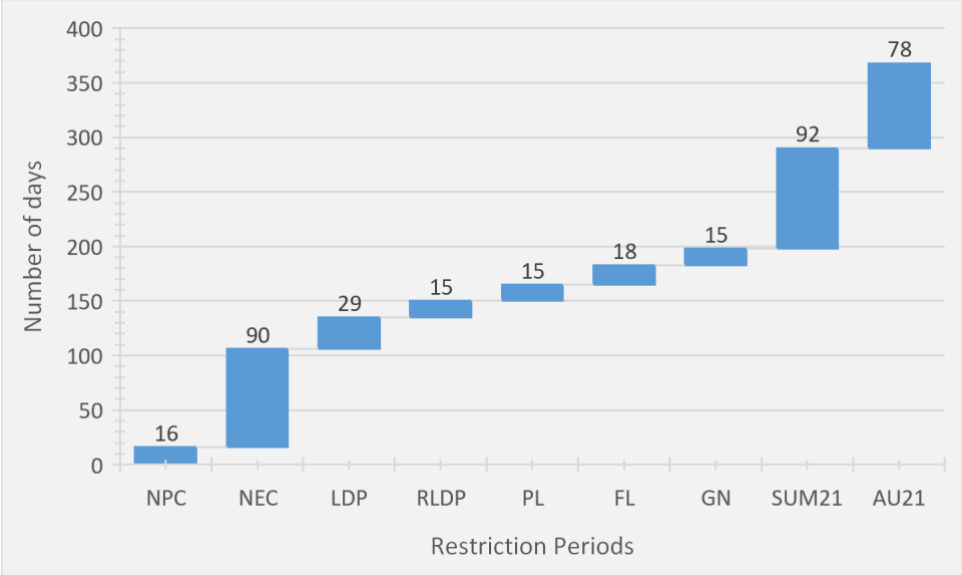

Figure 1. Number of days of statistical assessment periods of restriction periods
(NPC: National partial curfews, NEC: National extended curfews, LDP: Local decision-making phase, RLDP: Revised local decision-making phase, PL: Partial lockdown, FL: Full lockdown, GN: Gradual normalization, SUM21:2nd phase of gradual normalization/summer 2021, AU21: Autumn 2021)

2.5. Statistical analysis

The restriction periods were compared in terms of the number of cases per day, test positivity rate per day, and the number of deaths per day. Analysis of variance was applied in statistical analysis. Dunnett's test was used as a post hoc test. In the bivariate comparison, the first period (national partial curfews) was used as the reference period. $p < 0.05$ was used for statistical significance.

3. Results

Table 1 shows the number of cases per day according to statistical assessment periods of restriction measures. The mean of the number of cases has increased with the "local decision-making phase". We can see the highest mean number of cases per day in the "revised local decision-making phase". The mean number of cases has declined with the "partial lockdown period". The decrease is continued throughout the "full lockdown period" and "gradual normalization period". On the other hand, the number of cases has increased with 2nd phase of gradual normalization and autumn of 2021.

Table 1. Number of cases per day according to statistical assessment periods of restriction measures

Statistical assessment periods of restriction measures (n[a])	Number of cases per day		Mean difference	p
	Mean	Min-max		
National partial curfews (n=16)	30,928	28,351-33,198		
National extended curfews (n=90)	11,894	5,277-3,2106	-19,033	0.000**
Local decision-making phase (n=29)	29,928	13,378-55,941	-999	0.996
Revised local decision-making phase (n=15)	57,396	49,438-63,082	26,468	0.000**
Partial lockdown (n=15)	31,021	18,052-43,301	93	1.000
Full lockdown (n=18)	10,887	7,523-15,191	-20,040	0.000**
Gradual normalization (n=15)	6,731	5,386-8,426	-24,196	0.000**
2th phase of gradual normalization/summer 2021 (n=92)	14,139	4,418-27,356	-16,788	0.000**
Autumn 2021 (n=78)	27,056	21,177-33,860	-3,871	0.154

[a]: number of days included in the statistical assessment, **:p<0.001

Figure 2 is a box plot graphic that shows the number of cases per day according to statistical assessment periods of restriction measures

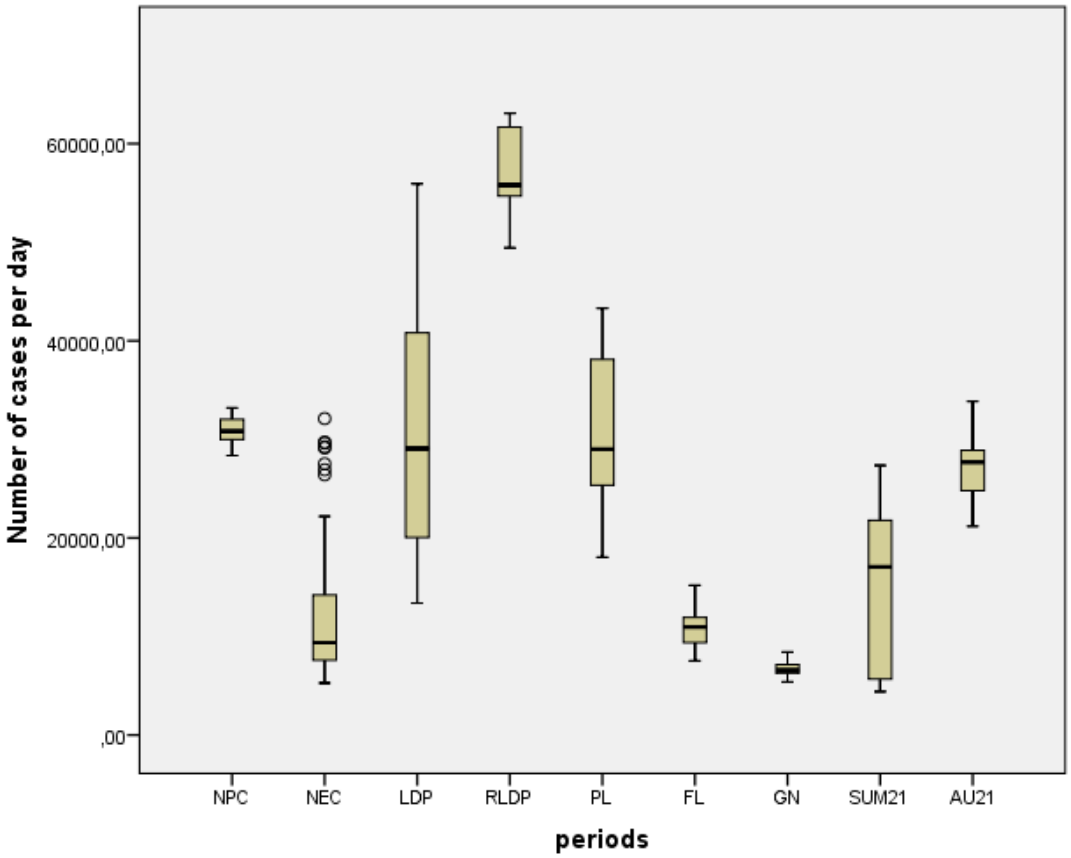

Figure 2. Number of cases per day according to statistical assessment periods of restriction measures. (NPC: National partial curfews, NEC: National extended curfews, LDP: Local decision-making phase, RLDP: Revised local decision-making phase, PL: Partial lockdown, FL: Full lockdown, GN: Gradual normalization, SUM21: 2nd phase of gradual normalization/summer 2021, AU21: Autumn 2021)

Table 2 shows the test positivity rate per day according to statistical assessment periods of restriction measures. The mean test positivity rate has increased with the "local decision-making phase". We can see the highest mean test positivity rate in the "revised local decision-making phase". The mean test positivity rate has decreased with the "partial lockdown". The decrease is continued throughout the “full lockdown period” and the “gradual normalization period”. On the other hand, the test positivity rate per day has increased with 2nd phase of gradual normalization and autumn 2021.

Table 2. Test positivity rate per day according to statistical assessment periods of restriction measures

Statistical assessment periods of restriction measures (n[b])	**Test positivity rate per day**		**Mean difference**	**p**
	Mean	**Min-max**		
National partial curfews (n=16)	16.9	14.7-17.8		
National extended curfews (n=90)	7.3	3.5-15.4	-9.5	0.000**
Local decision-making phase (n=29)	13.5	9.6-18.3	-3.3	0.000**
Revised local decision-making phase (n=15)	18.4	16.3-20.2	1.5	0.230
Partial lockdown (n=15)	11.9	7.8-15.3	-4.9	0.000**
Full lockdown (n=18)	5.1	3.4-7.7	-11.8	0.000**
Gradual normalization (n=15)	3.1	2.6-3.8	-13.9	0.000**
2th phase of gradual normalization/summer 2021 (n=92)	5.4	2.0-10.2	-11.5	0.000**
Autumn 2021 (n=78)	7.7	6.1-9.5	-9.3	0.000**

[b]: number of days included in the statistical assessment; **:p<0.001

Figure 3 is a box plot graphic that shows the test positivity rate per day according to statistical assessment periods of restriction measures.

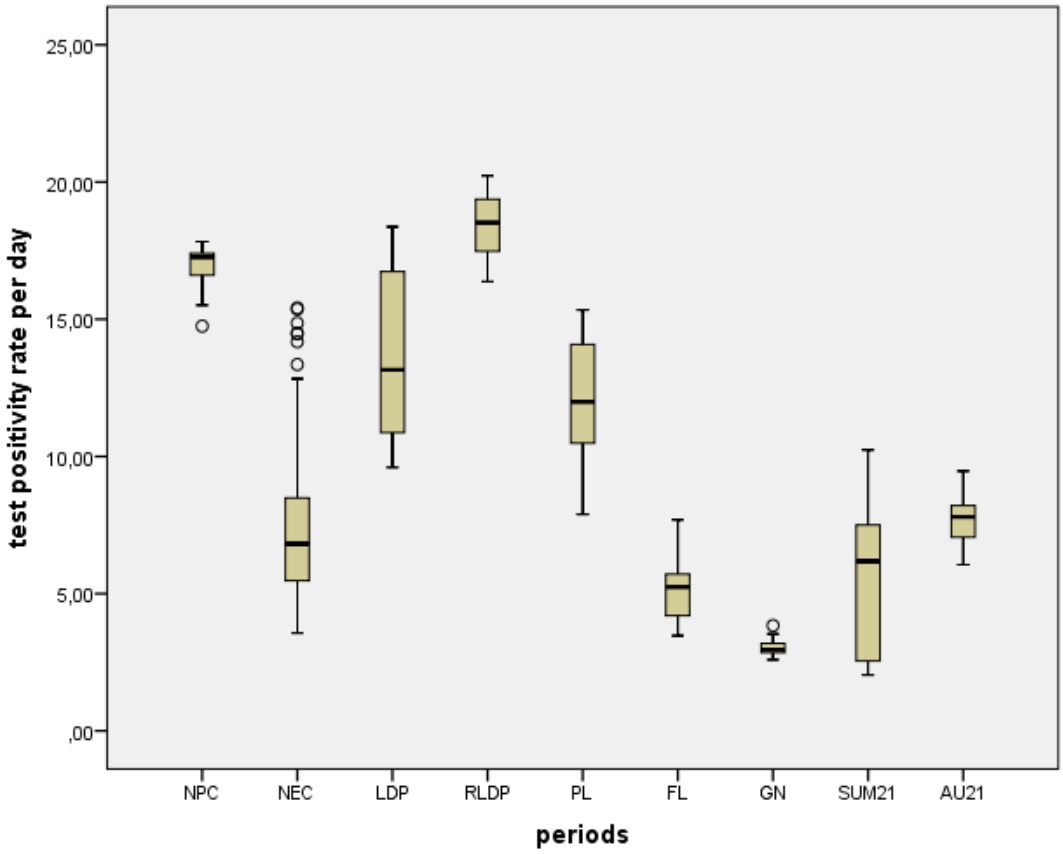

Figure 3. Test positivity rate per day according to statistical assessment periods of restriction measures. (NPC: National partial curfews, NEC: National extended curfews, LDP: Local decision-making phase, RLDP: Revised local decision-making phase, PL: Partial lockdown, FL: Full lockdown, GN: Gradual normalization, SUM21: 2nd phase of gradual normalization/summer 2021, AU21: Autumn 2021)

Table 3 shows the number of deaths per day according to statistical assessment periods of restriction measures. This means the number of deaths per day has increased with the "local decision-making phase". We see the highest mean number of deaths per day in the "revised local decision-making phase". The mean number of deaths per day has decreased with the "partial lockdown". Decreasing has continued further periods. We have seen the lowest mean during the period of gradual normalization. Unfortunately, the mean number of deaths has increased with 2nd phase of gradual normalization.

Table 3. Number of deaths per day according to statistical assessment periods of restriction measures

Periods of restriction (n[c])	Number of deaths per day		Mean difference	p
	Mean	Min-max		
National partial curfews (n=27)	210	168-254		
National extended curfews (n=90)	130	62-259	-80.2	0.000**
Local decision-making phase (n=29)	214	117-341	3.7	1.000
Revised local decision-making phase (n=15)	351	336-394	140.3	0.000**
Partial lockdown (n=15)	259	203-356	49.1	0.057
Full lockdown (n=18)	153	92-231	-57.8	0.009*
Gradual normalization (n=15)	71	51-96	-138.9	0.000**
2nd phase of gradual normalization/summer 2021 (n=92)	139	35-290	-70.9	0.000**
Autumn 2021 (n=78)	209	175-248	-0.8	1.000

[c]: number of days included in the statistical assessment; *:p<0.01; **:p<0.001

Figure 4 is a box plot graphic that shows the number of deaths per day according to statistical assessment periods of restriction measures.

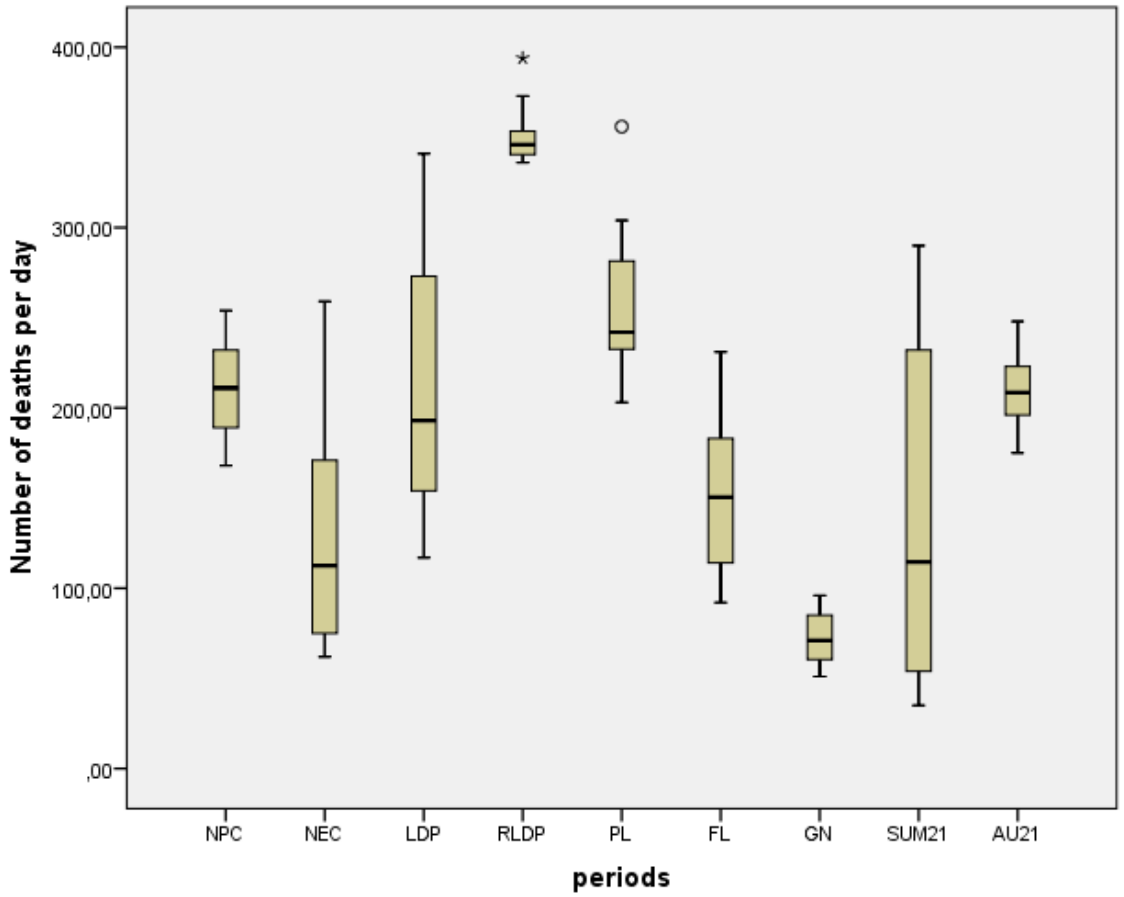

Figure 4. number of deaths per day according to statistical assessment periods of restriction measures. (NPC: National partial curfews, NEC: National extended curfews, LDP: Local decision-making phase, RLDP: Revised local decision-making phase, PL: Partial lockdown, FL: Full lockdown, GN: Gradual normalization, SUM21: 2nd phase of gradual normalization/summer 2021, AU21: Autumn 2021)

4. Discussion

Various restriction measures have been implemented in Turkey since the beginning of the pandemic. The first restriction measures started in March 2020, when the first case was seen in Turkey. In June 2020, the start of the "new normal" period was declared, and the restrictions were greatly relaxed [19]. Parallel to the course of the epidemic, the scope of restriction measures in Turkey, as well as in the whole world, has undergone various changes over time. Depending on these changes, the periods of restriction measures were named with different names [13, 19, 20].

With the implementation of new restriction measures in the autumn of 2020, a series of restriction periods that will last until the summer of 2021 has begun. The first restriction period of the autumn semester has started with the new measures that are implemented on November 18, 2020 (National partial curfews). Restrictions were increased in the "National extended curfews" period. In the next period, local public authorities were authorized to implement the measures (local decision-making phase). The next period continued with some revisions to the measures (revised local decision-making

phase). Later, "partial lockdown" was declared on April 14, and "full lockdown" was announced on April 29 [2, 13, 19].

Because this research covers a one-year evaluation, the last taken into account restriction measurement implementation day is 17 November 2021. Therefore, the last date is taken into account for the number of cases and the test positivity rate in the statistical evaluation is 27 November 2021. The last date taken into account for the number of deaths in the statistical evaluation is 8 December 2021. The date of the first Omicron Virant case in Turkey is stated as 12 December 2021 [21]. Various variants have been seen since the beginning of the pandemic. The latest variant was Omicron [22]. It is known that the Omicron variant spreads more easily than the original virus and the Delta variant [23]. The fact that the data included in this study included the periods before the Omicron variant appeared, provided the opportunity to make standard comparisons.

It is noteworthy that the highest values for all three parameters examined within the scope of this research were observed in the "revised local decision-making phase". Among the reasons for the increase in this period may be the partial relaxation of the measures. However, disruptions in the decision-making processes of local public authorities regarding the implementation of the measures may also be among the potential causes. It is generally suggested that the effectiveness of the health system is also correlated breadth of scope of the local authority's decision-making power [24]. On the other hand, it is mentioned that the effects of decentralization on health systems are complicated, and there are factors related positive and negative impacts of decentralization [25]. The effects on the health outcomes of the period in which the decisions regarding the restriction measures were decentralized in Turkey can be considered as an example of the possible consequences of decentralization. Experiences in pandemic management can provide evidence-based data for discussions on health policy.

The lowest mean for the "number of cases per day" and "test positivity rate" parameters are seen in the "gradual normalization" and "full lockdown" periods. The lowest mean for the "number of deaths per day" is in the "gradual normalization" period. These results show the effectiveness of restriction measures. A study aimed to investigate NPI that includes 175 countries have shown that restriction measurement was effective for reducing cases [26]. In different studies, the effectiveness of restriction measures in suppressing the epidemic has been demonstrated [27-29].

It has been shown that restriction measures can be effective in limiting mobilization. A study including Australia, Japan, Hong Kong, and Singapore has shown that the largest declines in mobility were seen in places that enforced mitigation policies. Furthermore, this study emphasizes that the increase in the number of cases is observed despite the existence of the stay-at-home rule due to the inability of migrant workers to be adequately quarantined [30]. The fact that the restriction measures for Turkey did not include people who have to continue to work may have been a factor that reduced the effectiveness of the measures[31].

In this study, the statistical analysis includes numbers for the first 10 days of the next restriction period for "number of cases", and "test positivity rate". Statistical analysis includes numbers for the first 21 days of the next restriction period for the "number of deaths". However, the periods based on the statistical assessment may not exactly reflect the implementation dates of the restrictions. For example, for all three parameters examined, the means in the "gradual normalization" period are lower than in the "full lockdown" period. This result may indicate that the effects of the restriction periods continue in the next period.

4.1. Limitations

Restriction measures aim to flatten the curve by decreasing R-value. We did not use the change in R-value to evaluate the effects of restrictions in this study. This point is a limitation of our assessment.

The intertwining of the measures applied in different restriction periods makes it difficult to compare different types of measures. A limitation is that the effectiveness of different restraint measures was not compared in this study.

The different PCR testing policies applied at different times of the epidemic may be a factor that makes standard comparison difficult.

COVID-19 vaccination in Turkey started on January 13, 2021[32]. On November 17, 2021, the last day to be evaluated within the scope of this study, the rate of those who received two doses of vaccine, which was accepted as the initial protocol for Turkey, was 59%[33]. Another limitation of the study is that vaccination status was not taken into account.

5. Conclusions

Restriction measures have played a role in reducing the mortality and morbidity associated with COVID-19. The experience of the COVID-19 pandemic shows that public health interventions continue to function as effective tools in limiting the effects of the epidemic. On the other hand, the increase in the number of cases during periods when epidemic management is partially decentralized can provide evidence-based data for assessments of the effects of decentralization.

Ethical Consideration

Ethics committee application was not made because the research was conducted based on publicly available and, anonymized data sources that were produced by the Ministry of Health of Turkey.

Conflict of Interest

The author declares no conflict of interest.

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Research Article

THE RELATIONS BETWEEN FEAR OF COVID-19, ANXIETY OF DEATH, AND MEANING OF LIFE AMONG NURSING STUDENTS

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Abstract: *Aim of the study was to determine the effects of socio-demographic factors on fear of COVID-19, death anxiety, and meaning of life among nursing students, and to explain the relations between fear of COVID-19, death anxiety, and meaning of life. The study was conducted with 262 students on 7-27 October 2020 in a descriptive-correlational and cross-sectional design. According to the correlation analysis, a moderate and positive relationship was detected between the Fear of COVID-19 Scale (CFS) and Turkish Death Anxiety Scale (TDAS) total score and subscale scores. The mean age of the students who participated in the study was found to be 20.63±2.31, 64.1% were female. It was found that 29% of the students had sleep problems during this period, 7.6% were diagnosed with COVID-19, and 85.9% of them had their close friends and relatives diagnosed with COVID-19. The majority of the students (n=16) who were diagnosed with COVID-19 passed this process under quarantine at home without treatment, 59.2% of them stated that someone in their close circle had a positive COVID-19 test, and 31.7% lost a relative due to COVID-19. The model that was created in the multiple linear regression analysis which was made to determine the effects of TDAS and the Meaning of Life Questionnaire (MLQ) on CFS was found to be statistically significant (F:54.91, p<0.001). In this respect, it was also found that death anxiety and meaning of life were statistically significant (R^2=0.29) as the determinants of fear of COVID-19 (explanatory power). It was determined in the study that, as the fear of COVID-19 increased, death anxiety also increased. However, it was also found that the meaning attached to life did not change, and the meaning of life and death anxiety were significant determinants of the fear of COVID-19.*

Keywords: *Fear of Covid-19, death anxiety, the meaning of life, nursing students*

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1. Introduction

The Coronavirus Disease (COVID-19), which originated in the city of Wuhan in China, is considered to be the biggest public health crisis that appeared so far[1,2]. The disease spread to many countries within a short time period, and turned into a global epidemic; therefore, the WHO declared it a pandemic on March 11, 2020[3]. The first COVID-19 case was confirmed on March 11, 2020, in Turkey, followed by a rapid increase in the number of cases and deaths. Some restrictions have been introduced since then, as is the case in many other countries. One of these was the closure of all schools, including universities, for 3 weeks. With the rapid spread of the pandemic, this period was later extended. The distance education system was started with the closure of schools. Although a decreased number of cases and deaths were detected in the summer months, an increase was observed again as of September, which continued to increase. In this way, education continued online at universities[4]. The

increased case count and deaths affected all healthcare workers, especially nurses because nurses are exposed to a heavy workload because of providing care to hospitalized patients, and also, the risk of being infected by the disease increases. With its deadly and highly contagious effects, COVID-19 has caused many psychological problems such as fear and death anxiety in the whole society, especially among healthcare workers[2,5-7].

Death anxiety is among the inherent human feelings. The uncertainty of death has always aroused fear in human beings [8,9]. Although death anxiety is a feeling that affects people under normal conditions, it can be argued that this effect is more than ever causing fear under the current pandemic conditions [10]. Fear is an adaptive feeling enabling those actions are taken to deal with a potential threat condition. Too much or too little fear can harm both individuals and society [11]. It was reported in a previous study that fear of COVID-19 has a positive relation with death anxiety [12]. It was determined in another study that the perceived risk of COVID-19 increased death anxiety [13].In another study that was conducted with security forces, it was emphasized that such individuals experienced high death anxiety during the COVID-19 pandemic[14]. Although COVID-19 has mortal effects on older adults, younger people are also affected negatively. A positive relation was found between perceived stress and death anxiety during the COVID-19 pandemic in a study that was conducted with young people [7].

Another variable that was associated with death anxiety and fear is the meaning of life, which is defined as the understanding and adaptation of an individual to himself and the outside world, namely, the ability to understand life [15]. It was reported in a study that investigated the relations between the meaning of life and fear of COVID-19 that there were negative relations between these two variables [16]. In another study, it was shown that high meaning of life levels in individuals was associated with lower COVID-19 stress [17]. A negative relation was reported in a study that was conducted with young individuals between death anxiety and meaning in life[18]. However, some sociodemographic factors were also reported to be associated with fear of COVID-19, death anxiety, and the meaning of life[19-21].In light of all these data, no study was detected in the literature investigating the triple relation of fear of COVID-19 with death anxiety and the meaning of life. It is already known that the COVID-19 pandemic has had many psychological effects on nursing students[22-24]. Nursing students may face fear and death anxiety because they were confined to their homes and were disconnected from social life with the distance online classes and because they were the nurses of the future. The fact that the pandemic is continuing and its uncertainty might have affected future nurse candidates negatively in this respect. For this reason, the purpose of the study was to determine the effects of socio-demographic factors on the fear of COVID-19, death anxiety, and the meaning of life of nursing students, and to explain the relations among fear of COVID-19, death anxiety, and the meaning of life.

2. Materials and Methods

2.1. Participants

The descriptive-correlational and cross-sectional study design was used in the present study. The study was conducted with the students of Dicle University Ataturk Faculty of Health Sciences Nursing Department between 7 and 27 October 2020. The alpha value was 0.05 and the sample size was calculated as 134 to obtain 95% power with an effect size of 0.3 by using the G*Power Program version 3.1.9.7 [26]. The Convenience Sampling Method was used to determine the sampling. The data of the study were collected online with the help of a web-based (Google Forms) questionnaire that was prepared by the researchers. The online questionnaire that was prepared for all students was sent to social networks (WhatsApp, Facebook, etc.) to increase the representation power of the universe, and they were asked to fill them out. A total of 262 out of 464 students enrolled in the high school completed the questionnaire. Informed consent was obtained from the students by making necessary explanations

about the study in the introduction part of the online questionnaire. The students participated in the study by confirming the sentence "I agree to participate in the study". The response time took an average of 15-20 minutes.

2.2. Inclusion Criteria;

The students of Dicle University, Atatürk High School of Health Nursing Department who volunteered to participate in the study were included in the study. Those who did not want to participate in the study were excluded.

2.3. Instruments

The Personal Information Form, Fear of COVID-19 Scale(CFS), Turkish Death Anxiety Scale (TDAS), and Meaning of Life Questionnaire(MLQ) were used to collect the data.

Personal Information Form: This form was created by the researchers by scanning the literature [27-29]. The form included essential individual characteristics such as age, gender, class, marital status, economic status of the individuals, information on illness/health status, smoking and alcohol use status, illness, family history of chronic illness as well as questions that contain information on COVID-19, such as catching COVID-19, receiving treatment, the status of relatives catching COVID-19, and the presence of close acquaintances who died due to COVID-19.

Fear of COVID-19 Scale(CFS): The Turkish adaptation, validity, and reliability study of the scale that was developed by Ahorsu et al. was conducted by Satici et al. (2020). The applicable age range of the scale is wide and can be used for university students and adults. All items on the scale that consists of 7 questions are scored positively. The questions were scored between 1 and 5 (1- I strongly disagree…5- I strongly agree) by using a 5-point Likert-type scaling. There is no reverse-scored item on the scale. A score between 7 and 35 is received on the scale. A high score indicates a "high" level of fear of the COVID-19 pandemic. The Cronbach Alpha value was found to be α=.82in the Turkish validity and reliability study of the scale [30, 31]. The Cronbach Alpha value of the scale was found to beα=.87 in this study.

Turkish Death Anxiety Scale (TDAS): It is a 20-item scale that was developed by Sarıkaya and Baloğlu (2016), and has three sub-dimensions as Ambiguity of Death, Exposure to Death, and Agony of Death. TDAS items were prepared in a 5-point Likert form. Each item is given zero points for the answer "never", 1 for the answer "rarely", 2 for the answer "sometimes", 3 for the answer "often", and 4 for the answer "always". The scale is scored between 0 and 80, and high scores indicate high death anxiety. Scores between 0 and 29 indicate low death anxiety, scores between 30-59 indicate moderate death anxiety and scores between 60-80 indicate high death anxiety. The Cronbach Alpha Internal Consistency Coefficient was calculated to determine the reliability of the scale, and the Cronbach's Alpha value for the 'uncertainty of death factor' was found to be 0.94, 0.92 for the 'thinking about death and witnessing factor', and 0.76 for the 'pain factor' [32]. The total Cronbach Alpha value of the scale was determined to be α=.96 in this study.

Meaning of Life Questionnaire(MLQ): The scale was developed by Steger et al. (2006), and its adaptation into the Turkish language was conducted by Akın and Taş (2015). MLQ consists of 10 items. The scale provides a 7-point Likert-type measurement (1=It is completely accurate for me, and 7=It is not true at all). Item 9 is reverse-coded. The scale consists of two sub-dimensions, present meaning and searched meaning. The internal consistency reliability coefficients of the MLQ were found to be 0.77 for the present meaning subscale and 0.83 for the searched meaning subscale. The test-retest reliability coefficients obtained with an interval of four weeks were found as 0.89 for the present meaning subscale, and 0.92 for the searched meaning subscale [33,34]. A low score indicates a higher meaning of life. The Cronbach Alpha Value of the scale was determined to be α=.76 in the present study.

2.4. Data Analysis

The study data were analyzed with the SPSS 25.0 Program (SPSS Inc., Chicago, IL, USA). The mean, standard deviation, minimum, maximum, numbers, and percentages were used in the analyses of the descriptive data. It was examined whether the scales had a normal distribution in each group by calculating the mean total scores. The Kurtosis, Skewness, and Shapiro-Wilk were used in normality tests, and it was found that the scale scores had a normal distribution. The Students test and ANOVA test were used to analyze the sociodemographic variables. Pearson Correlation was used in examining the relations between the scales, Spearman Correlation was used in studying the relations between non-normally distributed numerical variables, and linear Regression Analysis was used to examine the effects of the scales on the dependent variable. Also, Cronbach's Alpha Coefficient was calculated in the internal consistency analysis of the scales. All findings were evaluated at a $p<0.05$ significance level.

3. Results

The sociodemographic characteristics of the students who participated in the study are given in Table 1. The mean age of the students who participated in the study was found to be 20.63±2.31, 64.1% were female, 32.4% were in the first year, 32.1% were in the second year, and 97.7% were single. It was also found that 73.7% of them had nuclear families. It was determined that 93.9% of them were not working, 69.1% perceived their economic status as moderate, the average number of people living at home was 6.49±2.30, and 17.6% of the students had family members over the age of 65 at home. When their sociodemographic characteristics were compared with the total score averages of the scale, a significant difference was found between the groups in terms of gender, grade, and working status according to the total score averages of CFS and TDAS. It was determined in the Student's t-test that the total mean scores of CFS and TDAS of the women were statistically higher than those of men. When the differences between the groups were examined in terms of the grades they studied with the SchefeTest, it was seen that the mean scores of CFS of the students in the 2nd and 3rd grades were higher than those of the 1st-grade students, and the students in the 4th grade had a significantly higher TDAS total score than those in the 1st grade. It was seen that the students who did not work in any job had higher CFS total scores than those who worked. A positive and very weak relation was detected between the ages of the students and the total scores of CFS and TDAS, and a negative and very weak relationship between the number of people living at home and the total CFS scores (Table-1).

Table 1. The Comparison of the Sociodemographic and Sociodemographic Data of the Students with Total Score Average of CFS, TDAS, and MLQ

Characteristics	$\bar{X}$ ± SD	Min-Max	CFS	TDAS	MLQ
Age	20.63±2.31	18-39	r: 0.13[a] p:0.02*	r: 0.17[a] p:0.04*	r: -0.68[a] p:0.27
Gender	n	%			
Female[1]	168	64.1	t: 3.82	t: 3.9	t: 0.88
Male[2]	94	35.9	p< 0.001** 1>2[c]	p:0.000** 1>2[c]	p: 0.37
Grade					
Grade[1]	85	32.4	F: 6.27	F: 4.04	F: 0.88
Grade[2]	84	32.1	p:0.000**	p:0.008**	p:0.45
Grade[3]	44	16.8	2>1[c]	4 >1[c]	
Grade [4]	49	18.7	3>1[c]		
Marital status			t: 0.17	t: 1.32	t: -0.37
Married	6	2.3	p: 0.86	p: 0.18	p: 0.70
Single	256	97.7			

Table 1. Continued

Characteristics	X̄ ± SD	Min-Max	CFS	TDAS	MLQ
Family type				F: 0.40	
Nuclear family	193	73.7	F: 0.17	p:0.66	F: 0.54
Extended family	56	21.4	p:0.83		p:0.58
Separated family	13	5			
Economic status					
Good	12	4.6	F: 1.32	F: 2.48	F: 2.23
Moderate	181	69.1	p:0.26	p:0.08	p:0.10
Poor	69	26.3			
Working status			t: -3.93	t: -0.76	t: -1.68
Working[1]	16	6.1	p:0.000**	p: 0.44	p: 0.09
Not Working [2]	246	93.9	2>1[c]		
Number of people living at home	6.49±2.30	2-15	r: -0.17[b] p:0.005**	r: -0.57 p: 0.35	r: -0.41 p:0.50
Presence of people over the age of 65 at home					
Yes	46	17.6	t: 0.58	t: 1.05	t: 1.57
No	216	82.4	p:0.56	p:0.29	p:0.11

[a]Spearman Correlation; [b]Pearson Correlation ; [c]Scheffe Test ; *p<0.05; **p<0.01

The health status and health-related variables of the students who participated in the present study in the pandemic period are given in Table 2. Although 92% of the students did not have any chronic diseases, it was found that 56.9% had chronic diseases in a family member living in the same house. The medical diagnoses of asthma, bronchitis, diabetes and Mediterranean Fever were detected in the students, respectively. It was also found that 2.3% of them had a psychological disorder, and when the diagnoses of these psychological disorders were examined, almost all of them were diagnosed with anxiety disorder. It was found that 29% of the students had sleep problems during this period, 7.6% were diagnosed with COVID-19, and 85.9% of them had their close friends and relatives diagnosed with COVID-19. The majority of the students (n=16) who were diagnosed with COVID-19 passed this process under quarantine at home without treatment, 59.2% of them stated that someone in their close circle had a positive COVID-19 test, and 31.7% lost a relative due to COVID-19. It was determined that 85.1% of them did not smoke, and the majority of the smokers stated that their smoking did not change in the pandemic period. When the alcohol use of the students during the pandemic period was evaluated, it was found that 96.6% did not use alcohol, 1.5% quit, and 1.1% reduced its amount. Also, 42.7% of the students were affected by the epidemic psychologically, and 69.8% of them found their health status the same as before the pandemic period.

Significant differences were detected between the groups in terms of total mean scores of CFS in the analysis of variance made according to the change in perception of the students who participated in the study with the diagnosis of COVID-19 in terms of being psychologically affected by the pandemic, and the perception of the health status before the pandemic. It was determined that the CFS total scores of the students who were not diagnosed with COVID-19 had higher CFS scores compared to those who were diagnosed with COVID-19, and those who stated that they were psychologically affected much by the pandemic had higher CFS scores compared to those who stated that they were not affected at all or were partially affected, and those who found their current health status worse compared to the pre-pandemic period had higher CFS scores than those who perceived it the same ($p<0.05$). Significant differences were detected between the groups in terms of total CFS score averages according to the presence of chronic disease in family members who lived in the same house, presence of an individual diagnosed with COVID-19 in the family or close circle, alcohol use during the pandemic, being affected psychologically by the pandemic, and the change in perception of the health status before the pandemic. It was determined that those who perceived their current health status as worse had significantly higher TDAS scores than those who perceived the same, and those who had a chronic

disease in their family members who lived in the same house had significantly higher TDAS scores than those with relatives who did not have a chronic disease, the students who had close relatives with the diagnosis of COVID-19 had significantly higher TDAS scores than those who had friends with the diagnosis of COVID-19, those who did not drink alcohol during the pandemic had higher TDAS scores than those who reduced alcohol use, those who were psychologically affected much during the pandemic period had higher TDAS scores than those who were affected partially or not at all compared to the pre-pandemic period ($p<0.05$). No relations were detected between the groups between the mean scores of the students' sociodemographic - health variables, numerical variables, and MLQ total scores ($p>0.05$, Table 2).

Table 2. The Comparison of the Health Variables of the Students during the Pandemic Period and their CFS, TDAS, and MLQ Total Scores According to These Variables

Characteristics	N	%	CFS	TDAS	MLQ
Presence of chronic diseases					
Yes	21	8	t: 1.29	t: 0.03	t: 0.48
No	241	92	p: 0.19	p: 0.97	p: 0.96
Presence of chronic diseases in people living in the same house					
Yes[1]	149	56.9	t: 1.91	t: 2.68	t: 1.46
No[2]	113	43.1	p: 0.057	p: 0.008** 1>2	p: 0.14
Presence of psychological disease					
Yes	6	2.3	t: 0.64	t: 1.77	t: -0.48
No	256	97.7	p: 0.51	p: 0.07	p: 0.96
Sleep problems					
Yes	76	29	t: 0.88	t: 0.92	t: 1.48
No	189	71	p: 0.37	p: 0.35	p: 0.13
COVID-19 diagnosis status					
Yes[1]	20	7.6	t: -3.35	t: -0.17	t: - 0.38
No[2]	242	92.4	p: 0.002** 2>1	p: 0.86	p: 0.69
COVID-19 diagnosis status of family or relatives					
No[1]	37	14.1	F: 2.08	F: 2.99	F: 0.36
Yes. there were people who had the diagnosis[2]	45	17.2	p:0.10	p: 0.032* 3>4	p:0.7
There were people who had the diagnosis in relatives[3]	155	59.2			
there were people who had the diagnosis in friends[4]	25	9.5			
Loss due to COVID-19					
Yes	83	31.7	t: 1.89	t: 1.28	t: 0.11
No	179	68.3	p: 0.06	p: 0.20	p: 0.90
Smoking during the pandemic					
I am a non-smoker	223	85.1			
I quit	8	3.1	F:1.27	F: 2.30	F: 1.04
I increased smoking	2	0.8	p: 0.27	p: 0.059	p: 0.38
No change	20	7.6			
I decreased smoking	9	3.4			
Alcohol use during the pandemic					
I am not using[1]	253	96.6	F: 0.99	F: 3.12	F: 2.34
I quit[2]	4	1.5	p:0.39	p:0.02* 1>4	p:0.07
No change[3]	2	0.8			
I reduced it[4]	3	1.1			

Table 2. Continued

Characteristics	N	%	CFS	TDAS	MLQ
Being psychologically affected by the pandemic					
Very much[1]	112	42.7	F: 19.39	F14.44	F: 1.01
Partly[2]	138	52.7	P:0.000**	P:0.000**	p:0.13
None[3]	12	4.6	1>2	1>2	
			1>3	1>3	
Present health status compared to pre-pandemic health status					
Better[1]	6	2.3	F: 5.19	F: 5.61	F: 0.51
The same[2]	183	69.8	p: 0.002**	p: 0.000**	p:0.66
Worse[3]	71	27.1	3>2	3>2	
Much worse[4]	2	0.8			

*:p<0.05; **:p<0.01

The total scale and subscale mean scores of the CFS, TDAS, and MLQ, which were used in this study, and the relations between the scales are given in Table 3.

Table 3. The Total and Subscale Mean Scores and Relationships between the Scales

The Scales	$\bar{X}$ ± SD	Min-Max	CFS	TDAS	MLQ
CFS	18.06±6.09	7-35	-	r: 0.54 p:0.000**	r: 0.37 p:0.55
TDAS	34.32±19.36	0-80	r: 0.54 p:0.000**	-	r: 0.70 p:0.25
Ambiguity of Death	17.45±10.39	0-40	r: 0.50 p:0.000**	r: 0.94 p:0.000**	r: 0.09 p:0.11
Exposure to Death	10.77±7.62	0-28	r: 0.49 p:0.000**	r: 0.88 p:0.000**	r: 0.02 p:0.75
Agony of Death	4.00±2.33	0-8	r: 0.47 p:0.000**	r: 0.81* p:0.000**	r: 0.04 p:0.44
MLQ	27.72±8.39	12-70	r: 0.37 p:0.55	r: 0.70 p:0.25	-
Present Meaning	15.53±4.76	6-35	r: 0.78 p:0.20	r: 0.11 p:0.06	r: 0.80 p:0.000**
Searched Meaning	12.19±5.36	5-35	r: -0.12 p:0.85	r: 0.07 p:0.90	r: 0.85 p:0.000**

r:Pearson correlation coefficient; *p<0.05; **p<0.01

According to the Pearson Correlation Analysis, a moderate and positive relationship was detected between CFS and TDAS total score and the subscales; however, no significant relations were found between CFS and MLQ, and TDAS and MLQ. It was found that the model established in the Multiple Linear Regression Analysis, which was made to determine the effects of TDAS and MLQ on CFS, was statistically significant (F:54.91, p<0.001). In this respect, it was also found that the death anxiety and meaning of life were statistically significant (R^2=0.29) as the determinants of fear of COVID-19 (explanatory power). In this model, it was found that death anxiety explained 29% of the fear of COVID-19 (Adjusted R Square = 0.292) (Table-4).

Tablo 4. The effect of TDAS and MLQ on CFS

Dependent Variable	Independent Variable	B	ß	t	p	F	Model (p)	R^2
CFS	Constant	12.187		10.966	0.000**	54.91	0.00	0.29
	TDAS	.172	.546	10.45	0.000**			
	MLQ	-.001	-.001	-.015	0.98			

**p<0.01

4. Discussion

The findings of the present study, which was conducted to determine the effects of socio-demographic factors on the fear of COVID-19, death anxiety, and the meaning of life of nursing students, and also to explain the relations between fear of COVID-19, death anxiety, and the meaning of life, were discussed in the light of the literature data.

It was found that 2.3% of the students who participated in the present study had a psychological disorder, almost all of them were diagnosed with anxiety disorder, and more than half of them had chronic diseases in a family member living in the same house. It was also found that the relatives and/or friends of the majority of the students were diagnosed with COVID-19, one-third of the students lost one of their relatives because of COVID-19, they were affected psychologically by the pandemic, and approximately one-third of them had sleep problems in this period. Fear and anxiety against material-spiritual losses were seen in all individuals as a reaction to the pandemic process [35,36], insomnia, anger, illness, fear of death, inability to be alone, crying, desire to follow the same order, excessive boredom, daintiness, lack of order and attention were increased[12,37], post-traumatic stress disorder was more frequent, especially in individuals who lost a loved one and grieving symptoms were high [38]. The death of a relative, the feeling of loneliness, and the interruption of social support might cause death anxiety in individuals [39]. Briefly; it can be argued that the pandemic process has triggered intense death and loss/loneliness anxiety in individuals.

It was found that the total mean scores in CFS and TDAS were higher in women than in men. It was reported in the literature that the fear of COVID-19[40,41], anxiety[335,36, 42], and death anxiety rates were higher in women [43-46]. Albeit rare, some studies reported that the death anxiety levels of men were higher than those of women [47]. Another study reported that male and female students experienced similar negative emotions because of the pandemic[48]. In previous studies that were conducted during pandemic periods, women were found to perceive the disease as more contagious and mortal, were more protective of their beloved ones [43], worried more about the death of others[46]; and therefore, had higher anxiety levels[49]. Individuals are more interested in the environment in adolescence and make plans for their future such as establishing emotional relations, having a profession, and having an important status in society about their lives. However, the pandemic, closed schools, curfews, reduced job opportunities, and restricted social relations have affected these dreams negatively for adolescents causing them to become more anxious individuals. When the sampling of the study was considered, the reason for their experience more fear of COVID-19 and death anxiety may be related to the fact that they had unfinished jobs to do.

It was found that the mean total CFS score of 2nd and 3rd-grade students who participated in the study was higher than that of the 1st-grade students, the total TDAS score of the 4th graders was higher than that of 1st graders, and the students who did not work in any job had higher CFS total score than the working students. It was reported in previous studies that the COVID-19 fear and death anxiety scores of students were affected by the grade variable[44,50]. De Los Santos *et al.* (2021) reported that the fear of COVID-19 was mostly in the 1st grades, unlike our study. In the same study, they also reported that students were afraid of being ready for clinical practice, being able to provide care to a COVID-19 patient, and finding equipment in the clinic [49].In nursing education, clinical practices were performed in hospitals before the pandemic, and the students who participated in the study estimated that although the clinical practice was performed online at the time when the study was conducted, the senior students guessed that they were more likely to start working after graduation in clinics and intensive care units where the cases were very intense. The students whose graduation was approaching were already worried about the future even before the pandemic, the lack of clinical practices, the students not feeling completely ready for the clinic, and the rate of spread of the pandemic in the city

where the study was conducted was high, the uncertainty of the progression of the pandemic, and the high rates of real death tolls increased as the graduation approached may be argued to have increased the rates of fear of COVID-19 and death anxiety. In the first year, nursing students did not participate in the practice in the hospital because of the pandemic, they did not know the risks of the profession, or they thought that there was a long time for face-to-face practice; therefore, their fear level may be less. Another result of the study was that the students who did not work had more fear of COVID-19 than working students, which can be considered that all their psychological energies related to the disease were invested in anxiety [51]. Because students who work and/or have to work spend their energies on their schools, work, and families, and may be less focused on their fears. On the other hand, they may have faced pandemic conditions and coped with the anxiety of obscurity because they work or have to work.

It was determined in this study that as the age of the students increased, the total scores received in CFS and TDAS increased, and as the number of people living at home increased, the total score received in CFS decreased. It was reported in the literature that the highest level of anxiety is between the ages of 18-24 [12, 49], especially in students who have high anxiety and depression levels [27] and experience high COVID-19 anxiety levels [36]. The fact that the students lived with their families during the distance education process might have triggered the feeling of trust indirectly eliminating the uncertainty because people knew that their families would support them. Also, living lonesome provides an opportunity for the individual to perform spiritual values and rituals and socialize[44]. For this reason, the individual may feel safer as the number of people in the house increases. As can be understood from the number of individuals in the house and the family type of the students who participated in the study, the number of households is usually crowded in the region they live in.

It was determined that the CFS total scores of the students who were not diagnosed with COVID-19 had higher CFS scores compared to those who were diagnosed with COVID-19, and those who stated that they were psychologically affected much by the pandemic had higher CFS scores compared to those who stated that they were not affected at all or were partially affected, and those who found their current health status worse compared to the pre-pandemic period had higher CFS scores than those who perceived it the same ($p<0.05$). Current studies report that the uncertainty of COVID-19 and feelings of fear, unhappiness, hopelessness, and helplessness, which are all caused by the anxiety of illness, cause intense strain on the psychological processes of individuals, and staying at home even increases the feeling of depression, health anxiety, financial anxiety, and loneliness [52,53]. Similarly, it was reported that the increased number of cases causes individuals to perceive an increased level of fear, anxiety, and stress [54]. It was reported in the literature that the presence of COVID-19 in the individual or his/her family causes increased anxiety levels [35]. Especially the individual trying to cope with difficult physical symptoms e.g. shortness of breath and persistent fever, away from all beloved ones, might cause intense anxiety and deterioration of psychological health [55]. However, in this study, the reason why students who were diagnosed with COVID-19 experienced less fear of COVID-19 than those who did not may be associated with the fact that individuals considered they had antibodies against the disease, which were protecting themselves, or individuals who had COVID-19 knew the effects of the disease on themselves, or their anxiety levels might have decreased because they survived.

In the study, it was determined that the students who did not have chronic diseases in the family members living in the same house had higher TDAS scores at significant levels than those who did not have any family members with chronic diseases, those who had close relatives diagnosed with COVID-19 had higher TDAS scores than those whose friends were diagnosed with COVID-19, those who did not drink alcohol during the pandemic had higher TDAS scores than those who reduced alcohol use, those who were affected psychologically much during the pandemic period had higher TDAS scores than those who were affected partially or not at all, and those who perceived their current health status

as worse had significantly higher TDAS scores than those who perceived it to be the same compared to the pre-pandemic period. It was reported in the literature that individuals are concerned about the transmission of the virus to family members whom they particularly consider to be sensitive [49]. Because it is already known that COVID-19 infection is more frequent, has a more severe progression, and mortality rates are higher in individuals with chronic diseases [56,57]. It was also reported that anxiety levels are high in people living with people who had chronic diseases, and the risk of their loved ones is an important predictor of the fear of COVID-19 [11]. University years coincide with the adolescence period of many individuals. Adolescents have high mortality rates, and alcohol use is among the causes of mortality[58]. Individuals who face anxiety because of the COVID-19 pandemic may turn to alcohol as a way of coping [12]. For this reason, death anxiety may be higher in non-alcoholics.

It was also determined in the present study that as the fear of COVID-19 increased, death anxiety also increased. However, the meaning attributed to life did not change, and the meaning of life and death anxiety were significant as the determinants of the fear of COVID-19. In other words, it was found that the death anxiety levels and the meaning given to life explained the fear of COVID-19, which has affected the psychological and physical health of individuals negatively by causing material and moral losses in individuals [3]. The increasing death count, diseases, and sequelae because of COVID-19 have increased the insecurity, fear, uncertainty, and death anxiety in individuals[59,60]. Death anxiety is the feelings, fears, and thoughts about death. In other words, death anxiety is related to the perception of one's death, or the perception of annihilation and/or nihilism. It was reported previously that there are dimensions of death anxiety such as fear of punishment after death, loss of body, fear of loss of identity, anxiety about loss of control, fear of nihilism, fear of death of relatives, the anxiety of being alone in life, the anxiety of uncertainty, and anxiety of feeling pain; and it is affected by variables such as the frequency of facing death and near-death experiences. Although there are different results reported regarding these variables in the literature, it is already known that anxiety levels are high, especially in the members of the profession who face death frequently. The fact that death is an end is an unchangeable fact for people [60,61], and death anxiety plays important role in our lives by making its presence felt in the background continuously [61]. Because people know that they are going to die one day, they look for ways to cope with death anxiety in different ways throughout their lives. On the one hand, people try to establish meaningful relationships to cope with their fear of death, and being aware of death can cause a great sense of fear or meaninglessness in individuals on the other hand[29]. Pandemics can trigger the usual thoughts of death because it has been reported in the literature that fear of COVID-19 increases psychological illnesses such as stress, anxiety, and depression [62].In this respect, it is also known that the fear of death is at the root of these disorders [10]. For this reason, it can be argued that fear of COVID-19 and death anxiety are related to each other.

It was found in the study that as the fear of COVID-19 and death anxiety increased, the meaning attached to life did not change. There were long-term terrorist conflicts in 2016 in the city where the study was conducted, and people witnessed the death of their loved ones and/or relatives, the destruction of their homes, had to migrate to the city, experienced economic problems, and were exposed to stigmatization. Studies show that individuals exhibit intense anxiety and depressive symptoms [63,64].In this respect, the findings suggest that intense anxiety may have overshadowed the meaning of life in these individuals.

Limitations

The present study had several limitations. It was conducted with an online questionnaire using the Convenience Sampling Method. Only the university students that represented the educated population with such access opportunities were able to participate in the study. The lack of a structured face-to-face evaluation was also another limitation. The study was cross-sectional; therefore, the

participants could not be followed, and the change in the findings in the process could not be evaluated either.

5. Conclusion

It was determined in the study that, as the fear of COVID-19 increased, death anxiety also increased. However, it was also found that the meaning attached to life did not change, and the meaning of life and death anxiety were significant determinants of the fear of COVID-19. In other words, it was found that the level of death anxiety and the meaning attached to life explained the fear of COVID-19. The fear of COVID-19, meaning of life, and death anxiety are concepts that affect the life and quality of life of people from all age groups. Ignoring these concepts may mean that some factors that affect many psychological disorders are neglected. It was reported in previous studies that uncertainties are faced during university years regarding the future, and these uncertainties greatly affect fear, meaning of life, and death anxiety, which created a critical period in terms of psychological health development for the future[65]. For this reason, the awareness of students regarding the meaning of death and life can be increased so that they can adopt healthier attitudes towards life and death and evaluate these as a whole. In this way, contributions can be made to them to feel death anxiety at a healthier level and enrich their lives. There is a need for future studies to be conducted in multiple centers with larger samples, which will enable us to understand the level of fear of COVID-19, meaning of life, and death anxiety in many age and disease groups, and will examine the relations with diseases in detail, and will discuss the topic based on phenomenological and treatment approaches.

Ethical statement

The study adhered to the Declaration of Helsinki principles. Written approval was obtained from the R.T. Ministry of Health, General Directorate of Healthcare Services (11.06.2020/2020-06-05T22_29_23), the Non-Interventional Ethics Committee of a university (16.07.2020/255), and Dicle University, Atatürk School of Health Directorate (22.07.2020/70366). Online written consent was obtained from the participants who met the inclusion criteria and who agreed to participate in the study.

Conflict of interest

The authors have no conflict of interest.

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Authors' Contributions

All authors mentioned in the paper made a significant contribution to the research.

G. Y: Conceptualization, Methodology, Formal analysis, Writing - Original draft preparation (%60)

F. G: Conceptualization, Methodology, Resources, Investigation (%40).

All authors read and approved the final manuscript.

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Research Article

ASSOCIATION BETWEEN RISK FACTORS AND COGNITIVE IMPAIRMENT AMONG TYPE II DIABETES MELLITUS PATIENTS

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Abstract: *Diabetes mellitus type II is considered one of the leading causes of illness and mortality over the globe. Diabetic retinopathy, neuropathy, and nephropathy are all effectively screened on a regular basis. Recent research has shown that cognitive deterioration can occur in patients with diabetes and that it can go unnoticed for a long time, implying that routine screening is necessary. An observational cross-sectional study was conducted among 158 patients with a complaint of Type II Diabetes Mellitus aged between 60-79 years of age were found with cognitive impairment on the basis of Mini-mental Score Examination (MMSE) in a tertiary care center. Detailed history along with laboratory and biochemical data were taken from patients after taking written informed consent and approval of the Institutional Ethical committee through the pre-structured questionnaire. Mild cognitive impairment was noted in 88 (55.69%) type II diabetes mellitus patients and Normal cognitive function in 70 (44.30%). Those with Mild Cognitive Impairment had higher HbA1c (6.57 ± 1.27 vs. 6.13 ± 1.22), higher Fasting Blood Sugar (148.34 ± 18.61 vs. 145.25 ± 16.31), Post Prandial Blood Sugar (173.91 ± 42.64 vs. 167.47 ± 38.15) and Tumor Necrosis Factor-α (79.32 ± 8.74 vs. 72.98 ± 6.76), which were statistically significant. The cognitive domains of executive function, naming, attention, language, and memory showed a statistically significant difference between those with Mild cognitive impairment and Normal cognitive function. There were no differences in the mean age, duration of disease, and education level between the groups. The significant prevalence of Mild cognitive impairment in type II diabetes patients emphasizes the value of routine screening of cognitive functions. Further research into the link between cognitive impairment and poor blood glucose control is needed to see if improving blood glucose control can assist in enhancing cognitive functions.*

Keywords: *Cognitive impairment, Type II diabetes mellitus, MMSE, Risk factors, TNF-α*

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1. Introduction

The major risk factors for Type II diabetes mellitus (T2DM), are characterized by relative insulin deficiency and insulin resistance, sedentary lifestyle, and obesity [1]. The prevalence of T2DM is increasing in developing and developed countries because of changes in socioeconomic factors and the increased practice of unhealthy lifestyle habits [2]. T2DM is associated with cognitive impairment and exhibiting worse cognitive ability and more abnormalities on brain imaging than individuals without

diabetes [3,4]. The prevalence is particularly higher for mild cognitive impairment (MCI) in T2DM patients older than 65 years [5]. Multiple long-term epidemiological studies have implicated T2DM as a risk factor for cognitive impairment and dementia in the elderly [6,7].

The causes underlying T2DM patients' cognitive impairment and brain anatomical abnormalities are still unknown. Several risk factors for Mild cognitive impairment in T2DM patients have been identified, including vascular risk factors, macrovascular diseases, microvascular complications, poor glycaemic control, increased insulin level, increased oxidative stress, accumulation of amyloid-beta peptide and tau hyperphosphorylation, and decreased nerve growth factor [3, 7, 8]. However, the significance of such impairment is generally overlooked in favour of other T2DM consequences; there are no specific tools for avoiding or correcting cognitive deficiencies in diabetic patients [9]. Given that early-stage therapies for cognitive impairment are somewhat effective [10], it's crucial to understand the features of MCI in T2DM patients and to discover the most efficient diagnostic indicators for Mild cognitive impairment in these patients.

The aim of the current study was to determine the characteristics of cognitive impairment in T2DM patients in this age range, as well as to identify potential risk factors and biomarkers based on the demographic and clinical parameters of the patients. This knowledge could aid efforts to detecting MCI in T2DM patients early on.

2. Materials and Methods

The present study was conducted among 158 patients with the complaint of T2DM aged between 60-79 years of age who were found with cognitive impairment on the basis of MMSE score in Rajeev Gandhi Centre for Diabetes & Endocrinology and Department of Physiology on patients of Type II Diabetes Mellitus attending Diabetes clinic in Jawaharlal Nehru Medical College hospital, Aligarh Muslim University after approval from Institutional ethical committee dated 17.11.2011. Detailed history along with laboratory and biochemical data were taken from patients after taking written informed consent through the pre-structured questionnaire. The study was extracted by the thesis done for the fulfillment of a Master's Degree (MD) in Physiology after ethical approval of the Institutional Ethical Committee Ethics Committee, Faculty of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University dated 17.11.2011.

Tumour Necrosis Factor-alpha (pg/ml) (TNF-α) ELISA in vitro of enzyme-linked immunosorbent assay kit (Gen-Probe Diaclone) was used for the quantitative measurement of human TNF-α in serum of selected study subjects. The test was performed in the departmental laboratory of the Department of Biochemistry, Jawahar Lal Nehru Medical College, Aligarh Muslim University, Aligarh, India.

Only T2DM patients aged 60-79 years were included on the basis of diagnosis of diabetes from revised American Diabetic Association Criteria i.e. fasting plasma glucose >126 mg/dl (> 6.1 mmol/1) and 2 hours postprandial plasma glucose >200 mg/dl (>11.1 mmol/1) along with those given written informed consent were included in the study. Any systemic condition other than T2DM related to neuropathy (malnutrition, alcoholic neuropathy, renal failure), known case of chronic depression, psychiatric illness, neuropathies associated with exogenous toxic agents, metals or drugs, and pregnant women with HRT were excluded from the study.

The data were collected and entered in MS excel 2010. Different statistical analyses will be performed using R software version 4.0.2. The one-sample Kolmogorov – Smirnov test will be employed to determine whether the data sets differed from a normal distribution or not. Normally distributed data were analysed using parametric tests and non-normally distributed data were analysed using non-parametric tests. Descriptive statistics were calculated for qualitative and categorical variables. Graphical representation of the variable was shown to understand the results clearly. An Independent T-test or student t-test was applied to measure the mean difference between the two groups.

The correlation was estimated to measure the strength of the relationship between two or more quantitative variables.

3. Results

Table 1 illustrates the demographic profile of the study subjects. The age of the subjects are categorized into two groups .i.e. 60-67 years and 68-79 years. It is found that subjects are maximum from 60-67 years (53.8%) followed by 68-79 years (46.2%). The BMI of the study subjects are maximum >25 (46.8%) followed by 18.5-24.9 (30.4%) and <18.5 (22.8%). The Mini-Mental Score Examination (MMSE) is maximum in 18-23 (55.7%) followed by 24-30 (44.3%).

Table 1. Distribution of Demographic Profile of study subjects

Variables	Categories	n	%
Age Groups	60-67 years	85	53.8
	68-79 years	73	46.2
Body Mass Index	<18.5	36	22.8
	18.5-24.9	48	30.4
	>25	74	46.8
Mini-Mental Score Examination	18-23	88	55.7
	24-30	70	44.3

Figure 1 shows the demographic profile of the study subjects. The age of the subjects are categorized into two groups .i.e. 60-67 years and 68-79 years. It is found that subjects are maximum from 60-67 years (53.8%) followed by 68-79 years (46.2%). The BMI of the study subjects are maximum >25 (46.8%) followed by 18.5-24.9 (30.4%) and <18.5 (22.8%). The Mini-Mental Score Examination (MMSE) is maximum in 18-23 (55.7%) followed by 24-30 (44.3%).

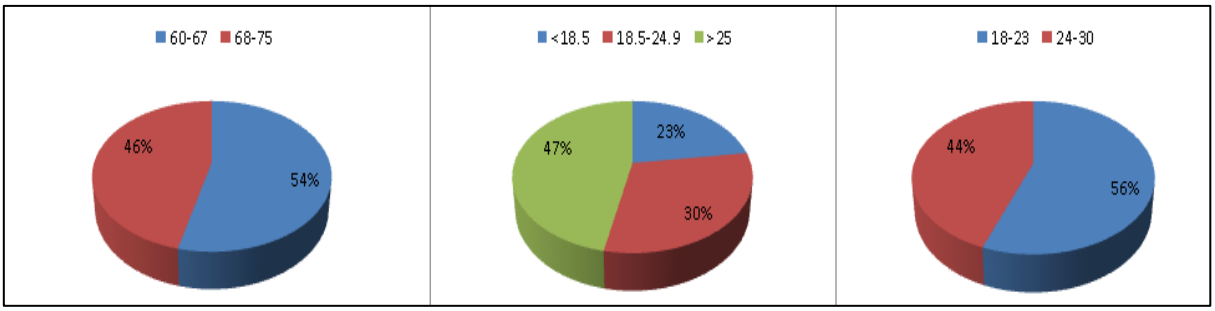

Figure 1. Graphical Representation of Age-groups, Body Mass Index and Mini-Mental State Exam score

Table 2 illustrates the MMSE of the study subjects. The MMSE of the subjects are categorized into five sub-categories .i.e. Orientation, Registration, Attention & Calculation, Recall and Language. It is found that subjects in Orientation were maximum in 8th and 9th score which is 33.5% and 27.2% respectively. In Registration, score is maximum in 2nd (77.8% followed by 3rd score (13.9%). In Attention & calculation, all study subjects is in 3rd score (100%). In Recall, all study subjects is in 1st score (100%). In Language, maximum score is 7 (98.7%) followed by 8th and 9th score in MMSE which was 0.6% in each scores.

Table 2. Distribution of Mini-mental Score Examination (MMSE) scores at different categories among subjects

Variables	Categories	n	%
Orientation	7.0	40	25.3
	8.0	53	33.5
	9.0	43	27.2
	10.0	22	13.9
Registration	1.0	13	8.2
	2.0	123	77.8
	3.0	22	13.9
Attention & Calculation	3	158	100.0
Recall	1	158	100.0
Language	7	156	98.7
	8	1	0.6
	9	1	0.6

Table 3 illustrates the minimum value, maximum value, mean and standard deviation of various socio-demographic variables and clinical parameters. Total 158 study subjects are in this study. The mean age of subjects is 69.48 years with 4.75 standard deviation, the mean weight of subjects is 62.61 kg with 10.34 standard deviation, the mean height of subjects is 1.58m with 0.08m variability, the mean BMI of subjects is 27.16 with 4.59 standard deviation, the mean blood sugar (fasting) of subjects is 156.62 with 17.40 variability, the mean blood sugar (postprandial) of subjects is 243.37 with 30.18 variability, the mean TMF-α of subjects is 62.51 with 13.25 variability, the mean HbsA1C of subjects is 8.44 with 1.25 variability. The mean total score (MMSE) among the study subjects is 23.30 with standard deviation of 2.66 in the study.

Table 3. Description of socio-demographic and clinical parameters

Descriptive Statistics	N	Minimum	Maximum	Mean	S.D.
Age (yrs)	158	61.0	75.0	69.85	4.76
Weight (kg)	158	45.05	84.20	62.62	10.35
Height (m)	158	1.4	1.7	1.58	0.083
Body Mass Index	158	19.03	34.90	27.17	4.59
Blood Sugar (Fasting) (mg/100ml)	158	129.90	187.08	156.62	17.40
Blood Sugar (Post prandial) (mg/100ml)	158	198.78	293.74	243.38	30.19
Tumour Necrosis Factor-alpha (pg/ml)	158	34.71	93.43	62.52	13.26
Hemoglobin A1C (%)	158	7.48	10.95	8.44	1.25
Total Score	158	19.0	29.0	23.30	2.67

Table 4 illustrates the mean difference between the various socio-demographic variables, clinical variables and the Mini-Mental Score Examination (MMSE). It is found that there is statistical significance difference (p-value<0.05) in age, weight, Blood sugar fasting, blood sugar postprandial, tumour necrosis factor-alpha (TNF-α), Haemoglobin A1C (HbsA1C) and Mini-Mental Score Examination **(**MMSE). Furthermore, It is found the statistical insignificant difference (p-value>0.05) between Height, body mass index and Mini-Mental Score Examination (MMSE).

Table 4. Comparison of sociodemographic and clinical parameters with MMSE score

Variables Name	Mini-Mental Score Examination	n	Mean	S.D.	95% CI (LL-UL)		p
Age	18-23	88	66.10	4.76	-3.17	-.19	.027*
	24-30	70	67.78	4.61			
Weight (kg)	18-23	88	64.16	10.0	0.26	6.73	.034
	24-30	70	60.66	10.51			
Height (m)	18-23	88	1.58	0.08	-0.02	.02	.837
	24-30	70	1.58	0.08			
Body Mass Index	18-23	88	24.42	4.38	-0.88	2.02	.437
	24-30	70	23.85	4.85			
Blood Sugar (Fasting) (mg/100ml)	18-23	88	148.34	18.61	-8.59	2.41	.026*
	24-30	70	145.25	16.31			
Blood Sugar (Postprandial) (mg/100ml)	18-23	88	173.91	42.64	-18.28	7.15	.038*
	24-30	70	167.47	38.15			
Tumour Necrosis Factor-alpha (pg/ml)	18-23	88	79.32	8.74	2.24	7.35	.003**
	24-30	70	72.98	6.76			
Hemoglobin A1C (%)	18-23	88	6.57	1.27	-0.64	.148	.032*
	24-30	70	6.13	1.22			

*:p<0.05; **:p<0.01

Table 5 shows the strength of relationship between the various socio-demographic variables, clinical parameters and the Mini-Mental Score Examination (MMSE). It is found that there is weak positive correlation between age, body mass index, blood sugar (postprandial) and MMSE. Moreover, there is negative correlation between the blood sugar fasting and the MMSE. Furthermore, there is positive correlation between TNF-α, HbsA1C and the MMSE.

Table: 5. Correlation of socio-demographic and clinical parameters with total MMSE score

Variables	Statistics	Total Score
Age (yrs)	r	.115
	p	.152
Body Mass Index	r	.055
	p	.023*
Blood Sugar (Fasting) (mg/100ml)	r	-.138
	p	.044*
Blood Sugar (Postprandial) (mg/100ml)	r	.342
	p	.026*
Tumour Necrosis Factor-alpha (pg/ml)	r	.576
	p	.001**
Hemoglobin A1C (%)	r	.638
	p	.023*

r: correlation value; *:p<0.05; **:p<0.01

158 participants having type II DM were included in this study. Eighty eight (55.70%) type II diabetes mellitus patients had Mild cognitive impairment (MMSE score ≤ 23) and 70 (44.30%) type II diabetes mellitus patients had normal cognitive function (MMSE score ≥24). The HbA1c, FBS, PPBS, and TNF-α levels were significantly higher in patients with Mild cognitive impairment [Table 4]. There were statistically significant differences in mean age, weight, blood sugar (fasting), blood sugar (postprandial), TNF-α, and HbA1C between the groups. HbA1c, PPBS, and TNF-α levels showed a positive correlation with the MMSE scores, while FBS showed a negative correlation with MMSE score [Table 5]. Of the domains tested, orientation, registration, attention &calculation, recall, and Language showed a statistically significant difference between those with Normal cognitive function and Mild cognitive impairment [Table 4].

Only 2.6% of those with abnormal results in the Mild cognitive impairment group could name all five terms used for memory tests correctly, whereas 25% of those with normal scores could. Only 10.5% of those with Mild cognitive impairment were able to repeat both of the administered questions, but 53.1% of those with Normal cognitive function were able to do so. The difference in orientation ratings between the groups was just marginally significant. The difference in abstraction scores between the two groups was not statistically significant.

4. Discussion

The current study examined the prevalence of Mild cognitive impairment in type II diabetes patients in North India. Mild cognitive impairment was shown to be prevalent in 54.3% of the people in our study. This is higher than earlier Indian research, which showed a range of 19.5% to 48.0% [11,13]. Earlier studies using the MMSE, trail-making tests, modified MMSE, and other neuropsychological tests such as the digit span test, digit symbol substitution test, and others were found to be less sensitive in detecting Mild cognitive impairment when compared to the current study using the MMSE score test for cognitive functions evaluation.

Patients with cognitive impairment had significantly higher FBS, PPBS, HbA1c, and TNF-α, all of which were negatively associated with MMSE scores in our study. Cognitive impairment was detected in 11.6% of patients with good glycemic management (HbA1c under 7%) and 30.2% of patients with HbA1c 7% or higher in a prior study by Roy et al. [11]. Subjects with glucose levels >125 mg/dl had 1.73 times increased chance of developing neurocognitive impairment, according to Khullar et al. [12,13]. The ACCORD MIND experiment, which included 2977 type II diabetes patients, discovered a statistically significant age-adjusted link between HbA1c level and four cognitive test scores [14]. The HbA1c level has been shown to be inversely related to both the clock in a box and the clock drawing test [15]. As a result, our findings are consistent with previous research suggesting that poor glycemic management in type II diabetes is linked to cognitive deterioration.

While there is a considerable body of evidence relating abnormal blood glucose levels to cognitive impairment, it is unclear whether bettering glycemic control leads to improved cognition. Enhanced HbA1c was linked to improved cognition in non-amnestic areas in the diabetes control and complications study in type 1 diabetes [16]. Improving HbA1c levels in an aged population over a 5-year period was linked to a slower rate of global cognitive deterioration, according to Luchsinger et al. [17].

In previous research, being a woman and having diabetes for a longer period of time were found to be independent risk factors [12]. Our research found no evidence of a gender difference or a link between diabetes duration and gender.

Executive function, name, attention, language, and memory indicated a statistically significant difference between those with Normal cognitive function and those with mild cognitive impairment in the current study. Attention, language, orientation, visual perception, visual movement organisation, and

logical questioning were all found to improve with effective cognitive training in individuals with mild cognitive impairment in a prior study [18]. The relevance of early identification of mild cognitive impairment was highlighted in a study on the outcome of a cognitive training programme in adults with mild cognitive impairment [19].

We used the Oxford Medical Education version of MMSE score, which is relatively easy and quick to perform. The level of education among subjects in both groups was similar.

In conclusion, our research reveals a high prevalence of undiagnosed mild cognitive impairment in type II diabetes patients who visit an outpatient clinic. All glycaemic control indicators and MMSE scores, which represent cognitive function, had a strong negative connection. These findings support the use of a sensitive measure like the MMSE in routine screening of type II diabetes mellitus patients to detect mild cognitive impairment. In the future, studies on the effects of better glycaemic control on cognitive function will be needed to better appreciate the implications of our findings in the long-term management of these patients.

Authors' Contributions:

All authors mentioned in the paper must have significantly contributed to the research. The level of their contribution also must be defined as follows:

Author Name	Conceptualization	Data Collection	Methodology	Analysis & Interpretation	Drafting Manuscript	%
Mir Abdul Munif	√	√	√		√	65%
Laxman Verma			√		√	20%
Malik Faizan Ahmad	√				√	20%
Anas Ahmad Khan			√	√	√	30%
Ankit Singh	√		√	√	√	35%

Ethical statement

The study was extracted by the thesis done for the fulfillment of a Master's Degree (MD) in Physiology after ethical approval of the Institutional Ethical Committee Ethics Committee, Faculty of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University dated 17.11.2011.

Conflicts of interest

The authors declare no potential conflicts of interest related to the research, authorship, and publication of this article.

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Research Article

INVESTIGATION OF THE RELATIONSHIP BETWEEN ANXIETY STATUS OF NURSING STUDENTS AND THEIR COMMITMENT TO THE PROFESSION DURING COVID-19 PANDEMIC

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Abstract: *This study examined the relationship between nursing students' anxiety and professional commitment during the Coronavirus (COVID-19) pandemic process. This research used a descriptive and correlational research design; it was conducted in the fall semester of the 2020-2021 academic year when the pandemic process continued. The research was conducted with 1026 nursing students from two state and two private universities, these students who agreed to participate formed the sample of the research. Sociodemographic characteristics, questions about the COVID-19 Pandemic process, Beck Anxiety Scale, and Nursing Professional Commitment Scale were used to collect data. Data were collected online. The 1st and 4th-year male students' professional commitment average whose grade point average is below 2.00 was low. The anxiety average of female students, students who are in the 2nd year, students whose grade point average is below 2.00, who are between the ages of 17-20, who have a chronic illness who lost an acquaintance due to COVID-19 was found as high. It was found that 20 % of nursing students experienced a moderate and high level of anxiety, and that they experienced decreased professional commitment due to an increase in anxiety level and that there is a weak negative relationship between them. In the pandemic process, as the anxiety of nursing students increased, their professional commitment decreased.*

Keywords: *Nursing Students; COVID-19; Professional Commitment; Anxiety*

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1. Introductıon

COVID-19 is a virus that spread worldwide and a virus that causes severe pneumonia [1]. COVID-19 has been declared a pandemic by the World Health Organisation as of March 11, 2020, with a total of 118 thousand cases in 114 countries and causing 4 thousand 291 casualties [2].

COVID-19caused many problems in many areas, and education is one of them. Higher Education Council (YÖK) has decided to switch to distance education in universities to slow the spread of the virus in Turkey and reduce victimisation in education. Although in theory the distance education has been done, hospital practices for applied courses were not completed. In the nursing profession, which includes applied education and theoretical content, hospital practices have not been performed. This process increased the anxiety areas of nursing students about their profession, one of the problems are the problems experienced in the remote completion of the training[3] and another problem is that nurses, who are at the forefront in patient care, are in the high-risk group during the COVID-19 pandemic [4,5].

It is stated that while healthcare workers are increasingly infected with coronavirus due to stress and long working hours, there is also an increase in physical, mental, and emotional exhaustion levels [4,6,7]. In addition to all this, the fact that healthcare workers experience the risk of infecting their families also causes anxiety [4,8]. It is known that nursing students who witnessed what happened during the COVID-19 pandemic and experienced the pandemic process experienced symptoms of anxiety [3,9]. These situations which cause anxiety may affect nursing students' commitment to the profession. Commitment to the profession is defined as the time, and effort individuals spend in order to do their profession in a better manner and to improve themselves (more so in the technical sense) [10]. It is stated that commitment to the profession is affected by factors such as education level, age, burnout, job satisfaction [11]. Nurses in close contact with patients with COVID-19 or with suspected illness face many challenges and risks such as pathogen exposure, long working hours, psychological problems, fatigue, occupational burnout, physical or psychological violence [12]. In addition, the cancellation of employees' leave, the frequent coverage of news in verbal and written media about healthcare workers who lost their lives during the pandemic may affect the professional commitment of nursing students who have had difficulties during their education.

Commitment to the profession is important in achieving professional status as a member of the healthcare team in the future, providing qualified service to the community, and having a strong professional identity [13]. Commitment to the profession is an important criterion for nurses to make an effort while conducting this profession throughout their lives, to be willing to improve themselves, and to be determined to continue their profession [11].

Based on this, this research aimed to identify the relationship between the anxiety experienced by nursing students during the pandemic process, which is an anxiety-inducing situation, and the commitment to the profession; in addition, this research aimed to identify variables that affect anxiety and the professional commitment.

Research Questions:

1. Do nursing students' levels of anxiety, and professional commitment differ according to their sociodemographic characteristics?
2. Do the levels of anxiety and professional commitment of nursing students differ according to their experiences regarding the COVID-19 pandemic process?
3. Do nursing students' levels of professional commitment differ according to the anxiety degree experienced during the COVID-19 pandemic process?
4. Is there a relationship between the anxiety experienced by nursing students regarding the COVID-19 pandemic process and their professional commitment?

2. Materials and Methods

2.1. Type of the Research

This is descriptive and correlational research conducted to examine the relationship between nursing students' anxiety levels and professional commitment during the COVID-19 pandemic process and to determine the influencing factors.

2.2. Time and Place of the Research

The research population consists of students enrolled in two different foundations -two-state two private universities- in the fall semester of the 2020-2021 academic year. In the research, we tried to reach the whole universe without using any sampling method. A total of 1026 students who volunteered to participate in the research were included in the sample.

2.3. Data collection tools

2.3.1 General Information Form*:*

The General Information Form used in the research was prepared by the researchers and includes questions about the student's introductory characteristics.

2.3.2 Beck Anxiety Scale

The scale was developed by Beck et al. (1988) and Turkish validity and reliability study of the scale was conducted by Ulusoy (1993)[14]. Each item is scored between 0 and 3, and high scores from the scale indicate a high anxiety level. Scores between 0-17 obtained from the scale indicate low, 18-24 indicate moderate, 25 points and above indicate a high anxiety level. In the research, the Cronbach alpha coefficient of the scale was calculated as 0.92.

2.3.3 The Nursing Professional Commitment Scale

The scale was developed by Lu et al. (2000), and its validity and reliability studies in Turkish were conducted by Cetinkaya et al. (2015). The scale is a four-point likert-type scale with 26-items and three sub-scale[15]. The Nursing Professional Commitment Scale includes the following sub-dimensions; continuing to become a member of the profession (8 items), belief in goals and values (5 items), and willingness to make an effort (13 items); potential answers range from "strongly disagree (1)" to "strongly agree (4)". In the scale, items 14,15,16,17,18,19,20,21,25 are reverse oriented. An increase in the score obtained from the scale indicates that nurses' commitment to the profession is high [15]. The Cronbach alpha coefficient of the scale was calculated as 0.67 in the research. The data were collected online by considering the pandemic process, using the information form and scales.

2.4. Data Analysis

Descriptive statistical methods (mean, median, frequency, percentage) were used while evaluating the research data. The suitability of the quantitative data to normal distribution was tested with the Kolmogorov Smirnov test, and it was determined that the quantitative data did not show a normal distribution. Mann-Whitney U test and Kruskal-Wallis test were used for comparisons of quantitative variables.

Ethical Dimension of the Research: Written permission has been obtained from the Turkish Ministry of Health (approval dd.2020-07-01; No.T14_51_23). Ethics committee approval was obtained from the Ethics Committee of the Maltepe University (approval dd. 10.07.2020; No.220/08-06).

3. Results

It was found that 33.7% of the students within the scope of the research study at a state university, 82.3% are women, 98.6% are single, 56.2% are between the ages of 17-20, 92.6% are not working, the grade point average of 35.5% is between 2.50-2.99, 30.3% are in year 2, 84.1% chose to be a nurse willingly, 78.0% still want to become a nurse, 86,4% do not think that they chose the wrong profession, 68.9% want to work during the pandemic process voluntarily, 81.2% experience anxiety during the pandemic process, 91.1% do not have a chronic illness, 80.6% do not experience a physical or mental problem during the pandemic process, 76.2% have a relative or acquaintance diagnosed with coronavirus 19, 76.3% have a relative or acquaintance who was diagnosed with coronavirus 19 and recovered, 69.6% do not have a relative or acquaintance who lost their lives due to coronavirus 19 (Table 1).

Table 1. Distribution of student characteristics

Characteristics	n	%
University of Education		
Foundation 1	153	14.9
Foundation 2	243	23.7
State 1	284	27.7
State 2	346	33.7
Gender		
Women	844	82.3
Man	182	17.7
Marital status		
Married	14	1.4
Single	1012	98.6
Age		
Between 17-20	578	56.3
21 and above	448	43.7
Employment Status		
Working	76	7.4
Not working	950	92.6
Grade Point Average (42 students did not answer this question)		
2.00 and below	25	2.4
Between 2.01-2.49	108	10.5
Between 2.50-2.99	364	35.5
Between 3.00-3.49	361	35.2
3.50 and above	126	12.3
Year		
1	224	21.8
2	311	30.3
3	290	28.3
4	201	19.6
The status of willingly choosing to be a nurse		
Yes	863	84.1
No	163	15.9
The current status of wanting to be a nurse		
Yes	800	7.0
No	40	3.9
Undecided	186	18.1
The status of thinking you chose the wrong profession		
Yes	140	13.6
No	886	86.4
The status of wanting to work voluntarily during the pandemic process		
Yes	707	68.9
No	319	31.1
The status of experiencing anxiety during the pandemic		
Yes	833	81.2
No	193	18.8
The status of having a chronic illness		
Yes	91	8.9
No	935	91.1
Experiencing a physical or mental health problem during the Coronavirus pandemic process		
Yes	199	19.4
No	827	80.6
The status of having a relative or acquaintance diagnosed with Coronavirus		
Yes	783	76,3
No	243	23.7
The status of having lost a relative or acquaintance due to Coronavirus		
Yes	312	30.4
No	714	69.6

It was found that female students between the ages of 17-20 have higher score averages on the Nursing Professional Commitment Scale and on Beck Anxiety Scale. It was determined that Nursing Professional Commitment Scale score averages of students whose grade point average is 2.00 and below are lower than students whose grade point average is between 3.00-3.49 and 3,50 and above and have a higher Beck Anxiety Scale total point average it was determined that Nursing Professional Commitment Scale score average of students who are in the 2nd year are higher than students who are in other years and it is due to 3rd and 4th year students' having a higher Beck Anxiety Scale (Table 2).

Table 2. Distribution of sociodemographic variables that affect students' levels of professional commitment and anxiety

Groups		n	Nursing Professional Commitment Scale Median	Beck Anxiety Scale Median
Gender	Women	844	90.00	8.00
	Men	182	87.00	4.00
		U	63287.5	56588.5
		P	p:0.000 **	p:0.000**
Marital Status	Married	14	92.00	4.00
	Single	1012	89.00	7.00
		U	6321.5	6881.5
		P	p:0.488	p:0.854
Age	Between 17-20	578	90.00	8.00
	21 years old and above	448	88.50	6.00
		U	118567.5	117523.5
		P	p:0.020*	p:0.011*
Employment Status	Yes	76	91.00	7.00
	No	950	89.00	7.00
		U	35205.5	35500.0
		P	p:0.719	p:0.809
Grade Point Average	2.00 and below	25	88.00	9.00
	Between 2.00-2.49	108	89.00	8.00
	Between 2.50-2.99	364	88.50	7.00
	Between 3.00-3.49	361	91.00	7.00
	3.50 and above	126	91.00	7.00
		H	23.200	4.685
		P	p:0.000**	p:0.321
Year	1	224	88.50	7.00
	2	311	91.00	9.00
	3	290	89.00	8.00
	4	201	88.00	5.00
		H	9.884	22.187
		P	p:0.020*	p:0.000**

U: Mann Whitney U test; H:Kruskall Wallis H Test; post hoc pairwise Mann-Whitney analyses; *:p<0.05; **:p<0.01

While the Nursing Professional Commitment score average of students who chose to become a nurse willingly is higher, their Beck Anxiety Scale score average is lower. While the total score average of the Nursing Professional Commitment Scale score of students who currently want to become nurses and students who do not think they chose the wrong profession is higher, their Beck Anxiety Scale score average is lower. We observed that the total score average of the Nursing Professional Commitment Scale of students who want to work voluntarily during the pandemic process is higher, their Beck Anxiety Scale score average is lower (Table 3). We observed that the Beck Anxiety Scale score average of those who experience anxiety during the pandemic, those who have a chronic illness, those who have a relative or acquaintance diagnosed with covid19, those who lost a relative or an acquaintance due to covid 19 is higher (Table 3).

Table 3. Distribution of variables related to the covid-19 pandemic process that affect the professional commitment and anxiety levels of students

Groups	n	Nursing Professional Commitment Scale Median	Beck Anxiety Scale Median
The status of willingly choosing to be a nurse			
Yes	863	91.00	7.00
No	163	75.00	10.00
	U	27135.0	60405.5
	P	p:0.000**	p:0.040*
The current status of wanting to be a nurse			
Yes	800	92.00	7.00
No	40	63.50	16.50
Undecided	186	77.00	9.00
	H	279.5	9917.5
	P	p:0.000**	p:0.000**
The status of thinking you chose the wrong profession			
Yes	140	70.00	12.00
No	886	91.00	7.00
	U	13240.0	42874.0
	P	p:0.000**	p:0.000**
The status of wanting to work voluntarily during the pandemic process			
Yes	707	91.00	7.00
No	319	85.00	8.00
	U	76441.0	99508.0
	P	p:0.000**	p:0.003**
The status of experiencing anxiety during the pandemic			
Yes	833	90.00	8.00
No	193	89.00	4.00
	U	79102.0	58794.0
	P	p:0.729	p:0.000**
The status of having a chronic illness			
Yes	91	90.00	13.00
No	935	89.00	7.00
	U	42081.0	29630.5
	P	p:0.864	p:0.000**
The status of having a relative or acquaintance diagnosed with Coronavirus			
Yes	783	89.00	8.00
No	243	91.00	5.00
	U	89432.0	77780.5
	P	p:0.157	p:0.000**
The status of having lost a relative or acquaintance due to Coronavirus			
Yes	312	89.00	9.00
No	714	90.00	6.00
	U	105437.5	88205.0
	P	p:0.173	p:0.001**

U: Mann Whitney U test;H:Kruskall Wallis H Test, post hoc pairwise Mann-Whitney analyses; *:p<0.05; **:p<0.01

The total score average of the Nursing Professional Commitment Scale of students with a low level of anxiety is found to be significant and higher than students with a high level of anxiety (p:0.000) (Table 4). The total score average of Nursing Professional Commitment Scale of students with a low level of anxiety (6.29±4.93) is found as 90.00; anxiety score average of those with a moderate anxiety level (20.93±1.93), have a total score of professional commitment of 88.00, and students with a high

level of anxiety score average (31.44±7.03) have a total professional commitment score average of 82.00 (Table 4).

Table 4. Comparison of students' professional commitment scale scores according to their anxiety levels

	Avg.±Ss.		**n**	**Median**	**Nursing Professional Commitment Scale Total Score Average**
Beck Anxiety Scale	10.18±9.41	Low (0-17)	817(%79.63)	5.00	90.00
		Moderate (18-24)	121(%11.8)	21.00	88.00
		High (≥25)	88(%8.6)	29.00	82.00
			H		23.347
			P		p:0.000**

H:Kruskall Wallis H Test; post hoc pairwise Mann-Whitney analyses; *:p<0.05; **:p<0.01

A weak negative correlation was found between the average scores of the Beck Anxiety Scale and Nursing Professional Commitment Scale. As the Beck Anxiety score average increased, the total score average of Nursing Professional Commitment decreased (Table 5).

Table 5. The relationship between Students' Beck Anxiety Scale and Professional Commitment Scale

	Beck Anxiety Scale r(p)	**Nursing Professional Commitment Scale** r(p)
Beck Anxiety Scale	1	-0.157 (p:0.000**)
Nursing Professional Commitment Scale	-0.157 (p:0.000**)	1

r: Spearman's rho; **:p<0.01

4. Discussion

This study is important in terms of taking measures by evaluating the reflection of the anxiety levels of nursing students, who are the healthcare professionals of the future, on their professional commitment during the pandemic process, preventing negativities in the health institutions they will work in and increasing the quality of patient care.

In this study, the average scores of professional commitment and anxiety of female students were found to be significantly higher than the average of male students (Table 2). A study by Turk et al. (2018) conducted to examine nursing students' profession preferences concluded that female students preferred the nursing profession more than males, and students chose the profession with the motivation of helping others [16]. On the other hand, male students' professional commitment and anxiety levels were found to be below. A study emphasised that male nurses are inadequate than female nurses in nursing care attitudes and behaviours [17]. A study conducted by Maaravi and Heller in the UK in 2020, with 407 individuals found that women experienced more anxiety during the pandemic process [18]. Studies conducted by Colgecen and Colgecen (2020) evaluating the level of anxiety experienced during the pandemic process, the state-trait anxiety levels of women were found to be significantly higher than men [8]. The results of the study are similar to the results of this study. In our research, the fact that female students have chosen the nursing profession willingly can be shown as the reason for their higher commitment to the profession than males. An important finding in the study is that the grade point

average makes a difference in professional commitment and anxiety. Students with a grade point average of 2.00 and below have lower mean scores on the Nursing Professional Commitment Scale than students whose grade point averages are between 3.00-3.49 and 3.50 and higher; In contrast, the total score average of Beck Anxiety Scale is higher (Table 2). This data suggests that the pandemic process caused a decrease in the roles and responsibilities expected from the student, such as the students' desire to learn and take an active role in learning. Students with low-grade average experience professional anxiety from not having enough professional knowledge and skills during the pandemic process. Therefore, we think that their professional commitment is low.

In this research, the 1st and 4th-year students' commitment and anxiety were lower than 2nd and 3rd-year students. The literature states that although the transition from being a student to professional life is a pleasing experience, beginning to work, working independently, and taking responsibility is worrisome [19]. A study by Kurtuncu and Kurt (2020) on the problems faced by nursing students during the COVID-19 pandemic, found that 1st and 4th year nursing students are worried about the efficiency of the lessons with the distance education system and that 4th year students think that giving practice-based lessons remotely is insufficient[3]. The reason 1st-year students think that their vocational education is insufficient may be due to the fact that they didn't have the opportunity to receive training in clinics, and this might be the reason their commitment to the profession is lower compared to the 2nd and 3rd-year students. The fact that 4th-year students witnessed the negative working conditions created by the pandemic process and that they will start their professional lives under such conditions may have affected their professional commitment. Unlike the results of our research, the Nursing Professional Commitment Scale score average of 2nd-year students and their Beck Anxiety Scale score average is higher compared to 1st,3rd and 4th-year students (Table 2). Continuing nursing education online during the pandemic period and not being able to do hospital practices increased students' anxiety. The reason why 2nd-year students' professional commitment levels are high, which is to say their professional commitment is not affected, maybe due to the thought that both theoretical and practical education will be completed when the conditions are appropriate. However, the fact that 4th-year students will start their profession, and they have a feeling of inadequacy due to online education may have led to this result. In a study, Turk et al. conducted before the pandemic (2018) using the care behaviours scale, the difference between the average scores obtained from the knowledge and skills, respect, and commitment sub-dimensions of the scale was found to be significant [16]. As a result of our study, we found that with the increase in grade level, the average score of commitment to the profession increased and the average scores of anxiety decreased. The reduction in nursing students' anxiety may be due to the increase in theoretical knowledge and experience that comes with grade-level advancement.

Choosing the profession willingly is important for students to be more successful in working life and have higher professional satisfaction. Provided that university students who chose to become a nurse do not like the profession, do not accept the profession, and continue their education solely based on the motivation that finding a job will be easy will cause many negativities for the profession whose field of work is human [20]. Based on this idea, the students who chose the nursing profession willingly, who state that they made the right choice in profession, who want to work voluntarily during the pandemic process have a high level of professional commitment and a low level of anxiety score (Table 3). The study of Peksoy et al. (2020) which examined the perception of professionalism and the commitment to professional values, found scores of professionalism in the profession of fourth-year students with a special interest in nursing are high and significant [21]. The findings of these studies support our study. Although the pandemic process causes difficulties in nursing education, students with low anxiety have a high professional commitment level. Also, to be willing to work voluntarily during the pandemic process is pleasing and promising for the advancement of the nursing profession. The results of a study conducted before the pandemic differ from the results of our study; the study examined the areas in

which students are most anxious. Catching a disease related to their profession (77%) ranked first, and the study suggested that students love and adopt nursing during their education [22]. Our research revealed that students who chose the nursing profession willingly, students who agreed to work as a nurse during the pandemic, even though they knew that they had a high risk of getting infected with COVID-19, have a low level of anxiety and a high level of commitment to the profession. It can be said that students choosing the profession willingly means they have positive or negative information about the profession and that their commitment to the profession is high because they are interested in the education they receive. These positive developments can be explained by the acceptance of nursing as a professional profession and the increase in its prestige in recent years.

The Beck Anxiety Scale average score of students who stated that they experienced anxiety during the pandemic was found to be higher and significant compared to those who stated that they did not experience anxiety (p:0.000) (Table 3). We found that the students' professional commitment scores stated that their anxiety increased during the pandemic did not differ. In our research, the pandemic process was considered a factor that causes anxiety, so we did not investigate other causes of anxiety. However, the continuation of theoretical and practical training online, restrictions students experienced related to the system, having difficulties in following lessons, and the announcement made by the International Nurses Association (ICN) that thousands of nurses were infected by COVID-19 and that hundreds of nurses died [23] may have caused students who will start this profession to experience anxiety. A study revealed that students used the expressions that "I can not focus on my study because the school is closed, I am not able to go to the clinic so I can't learn by practicing one-on-one "and "I can not focus on studying because I am psychologically affected" [3]. Being infected or being with people who are COVID-19 positive is also a condition that increases mental effects [4]. The fact that students expressed their anxiety in this process indicates that they cannot effectively cope with the pandemic process they are in. Another significant result of our research is that students with chronic illness have a high level of anxiety. We found that the anxiety experienced by students with chronic illness does not affect professional commitment. It is known that the presence of chronic diseases in the early period increases the risk of getting infected with SARS-CoV-2 [24]. This situation can cause anxiety in students with chronic illnesses since the COVID-19 virus spreads rapidly; there is no treatment, drug, or vaccine so far.

Similarly, a study conducted by Cao et al. (2020) reports that the reason for the students to experience stress and to delay their academic studies is that their relatives are infected and the risk of being infected [25]. Individuals with poor health and a history of chronic disease reported that they experienced the psychological effects of the epidemic more and the severity of stress, anxiety, and depression are higher during the COVID-19 process [26]. In ensuring the continuity of professional commitment, students with risky chronic diseases in terms of COVID-19 prognosis should be closely followed up and controlled. Students with chronic illnesses are psychologically affected. Initiating support programs to increase psychological resilience in universities can reduce anxiety during the pandemic process.

Students who were diagnosed with COVID-19 and students who lost a relative due to coronavirus-19 have low professional commitment scores and higher anxiety score average(Table 3). The anxious individual feels the dangers of the present moment and the future, and questions their life intensely. If nursing students who will do the profession in the future witness the loss of their relatives and witness the increase in anxiety for a long time, it may create changes in their commitment to the nursing profession. Similar to the results of our study, a study by Dogan and Duzel (2020) conducted to examine fear-anxiety levels in COVID-19 reported that participants are afraid of their family/acquaintances getting infected by the virus; this fear ranked first with a very high rate [27]. Kurtuncu and Kurt (2020) conducted a study on the problems nursing students experienced during the

COVID-19 pandemic, in the study students said "some people around me got infected with the COVID-19 virus [3]. I am always at risk of getting infected. I live with my grandmother, and I meet the needs of the family." The study of participants was evaluated according to their state and anxiety levels according to having a relative diagnosed with COVID-19 infection; unlike the results of our research, there is no significant difference between groups [8]. The reason for this was stated in the same study; it was due to the low number of people who were diagnosed with COVID-19 infection in their relatives. The presence of infected individuals in their immediate surroundings during the pandemic process can be a factor that increases the level of anxiety. Considering both the anxiety of losing a relative and the risk of contamination with the immediate surroundings, including oneself, can affect the level of anxiety. We examined whether students' anxiety levels affect their commitment to the profession and found that the commitment to the profession of students with low anxiety levels was higher than those with high anxiety levels (Table 4). A study by Donmez and Karakus (2019) on newly graduated nurses found that nurses' commitment to the profession is moderate and that job security, working conditions, and team communication are important elements in commitment to the profession [27]. We conducted our research during the pandemic period. We can say the increase in the busy working hours of healthcare workers, being infected with coronavirus, and witnessing an increase in physical, mental, and emotional exhaustion levels cause anxiety in students. There are studies revealing that individuals' anxiety levels have increased in studies conducted in different samples with the COVID-19 outbreak [8,28]. Another study with similar results to our study Okuyan et al. (2020) examined the health anxiety levels of nursing students during the pandemic process and found that their health anxiety levels are high, they feel overwhelmed and anxious and experience the fear of virus contamination and death [9]. The literature reports that the fear of COVID-19 has negative effects on psychology, stress, anxiety, work-family conflict, and substance use [29]. Another study found that about 24.9% of students experienced anxiety due to the COVID-19 pandemic [1]. Similarly, in this study, we found that 20% of the students experienced moderate and high anxiety levels (Table 4). The studies conducted show similarities with the results of our study. A significant result of the research is that due to the increase in the anxiety score averages of the students, their Nursing Professional Commitment average scores decrease and there is a weak negative relationship between them (Table 5). The anxiety individuals experience during the pandemic process may cause serious problems such as a decrease in commitment to the profession, experiencing problems in the transition from being a student to working life, inadequate connection with the profession, reluctance to continue to the profession, and the inability to achieve organisational commitment [30]. A study conducted by Flinkman et al. (2008) revealed that especially young nurses and newly graduated nurses have a higher tendency to quit the profession[31]. Our study, which has a very high sample and was carried out in four different institutions, shows an important problem of the COVID-19 pandemic process reflected on nursing students. To prevent these problems, the insufficiencies of nursing students should be completed before they graduate. In this context, suggestions for nursing education in the COVID-19 pandemic have been developed. One of the suggestions to determine ways to ensure self-confidence, motivation, and self-expression skills in the education process, is to ensure the functionality and improvement of all these processes and establish the necessary systems. Another suggestion is that nursing schools and the health institutions that employ nursing graduates can contribute to the things to be done in the upcoming period and strengthen their efforts by maintaining their communication in cooperation [32]. In line with the approaches, students' anxiety levels can be reduced, and their commitment to the profession can be positive. Because nurses' professional commitment begins to develop during their primary education and continues as a professional socialisation process that contributes to the internalisation of professional values. As a result, professional commitment, patient safety, and perceived patient care quality increase in nurses [33]. During the pandemic process, there may be some consequences of students' starting duty without

being sufficiently prepared to fulfill their roles and responsibilities. This might result in students' being indifferent to the profession and showing inappropriate behaviours towards the group they serve. Problems that may arise can be avoided by addressing and supporting the variables effective for anxiety and professional commitment in the research at an early stage.

Limitations of the Study: The study is limited to nursing students studying at two-state and two foundation universities and agreeing to participate in the research.

5. Conclusion

As a result of the study which was conducted during the pandemic period in Turkey in four different universities, we found that 20% of nursing students experience a moderate to a high level of anxiety, the commitment to the profession decreases due to an increase in the level of anxiety and that there is a weak negative relationship between them. It is a result that should be taken into consideration that as the anxiety of nursing students increases during the pandemic process, their professional commitment decreases.

Our research results serve as a guide to health institutions in which the new graduate nurses will work. It is recommended to develop professional competencies by creating in-service training programs when nursing candidates start working in health institutions. The causes of individual anxiety in students should also be addressed, and support should be provided in their relationships with the profession. Since the pandemic affects the whole world, the results of this research will guide the educational planning of national and international nursing schools and help students prepare better for working life.

The pandemic process has created a sense of anxiety in nursing students, who will practice the nursing profession in the future, and their professional commitment has decreased in line with the anxiety levels. It is recommended that psychosocial support be provided against anxiety throughout the education process and regarding professional commitment which plays a key role in healthcare quality, professional competence be provided in both educational establishments and medical institutions.

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Ethical Dimension of the Research:

Written permission has been obtained from the Turkish Ministry of Health. Ethics committee approval was obtained from the Ethics Committee of the Maltepe University (approval dd. 10.07.2020; No.220/08-06). Written permission has been obtained from the relevant institutions to conduct the study. The research was carried out in accordance with the principles of the Helsinki Declaration.

The compliance to the Research and Publication Ethics:

This study was carried out by the rules of research and publication ethics.

Declaration of Conflicting Interests:

The authors declare that there is no conflict of interest.

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Study design: SA,HK,AY,FA

Data collection and/or analysis: SA,HK,AY,FA

Preparation of the article: SA, HK, AY, FA All authors read and approved the final manuscript.

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Research Article

ASSOCIATION BETWEEN PSYCHOLOGICAL UPSET AND IRRITABLE BOWEL SYNDROME AMONG NURSING STUDENTS AT KSA

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Abstract: *Irritable bowel syndrome (IBS) is a fairly common disorder that occurs in the general population. IBS is a functional bowel disorder associated with decreased work productivity. The aim of this study is to investigate the relationship between psychological upset and irritable bowel syndrome among nursing students at the Hafr Albatin University king Saudi Arabia. A descriptive cross-sectional research design on 223 student nurses from Hafr Al Batin university. One tool is divided into three main parts; demographic data, student's psychological upset, and irritable bowel syndrome manifestations sheet. According to the results of the study there is a statistically significant correlation between students' psychological stiffness and manifestations of irritable bowel syndrome (p <0.001). Also, there are statistically significant relationships were found between psychological stiffness levels and students' Socio-demographic characteristics in the items related to sleeping hours, and the condition of the colon or manifestations of irritable bowel syndrome during exposure to psychological stress((p <0.001). This study recommends that students need to receive regular; periodic in-service psychological adaptation program that contains methods of coping with study stress, especially during exams period which indirectly added stressor to students' psychological upset. There is an obvious need for designed exam counseling preparation. Further studies are needed to study the factors that influence university students' psychological and physiological well-being during the study & exam period rather than stressors.*

Keywords*: Association, psychological upset, irritable bowel syndrome, nursing students*

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1. Introduction

Irritable bowel syndrome (IBS) is a fairly common disorder that occurs in the general population. IBS is a functional bowel disorder associated with decreased work productivity. Diminished quality of life, and increased healthcare costs [1]. IBS is a chronic biopsychological disorder that is “characterized by altered bowel habits with abdominal discomfort or pain with the absence of organic pathology". Besides the motility defect and distorted visceral perception of sensation, IBS is associated with several gastrointestinal and extra-intestinal manifestations [2].

Patients with IBS suffer disturbances in their social and professional life and feel ashamed of their symptoms. They often change their eating habits and frequently resort to healthcare services in a useless search for effective medical care [3].

Several clinical studies and reports from different researchers have shown that among patients seeking medical attention for IBS, 70-90%may have psychiatric co-morbidity, most commonly mood disorders, anxiety disorders, and somatization disorders [4]. The relationship between IBS and other functional bowel syndromes to psychiatric disorders remains uncertain.

Psychiatric disturbance among persons with IBS might represent a reaction to stress in the form of chronic gastrointestinal illness, but this possibility seems to have been excluded by the findings of lesser rates of psychiatric illness among patients with inflammatory bowel disorder [5]. IBS induces an occupational hazard as it affects the performance of patients at work. This was reported in a study from Canada where IBS became the second leading cause of absenteeism after the common cold. [2,6] conducted studies among medical, science, and engineering students in China reported that medical students had a much higher risk of functional bowel disorders (FBD) than science and engineering students. In 2012 among medical students at the University of Western Ontario, Canada; they found that the prevalence of IBS among preclinical and clerkship students was 19.1% and 22.0%, respectively [7]. According to our best knowledge, no one studied IBS among healthcare workers in our region especially since they were suffering a lot in their job; so that is why this study was done.

It is characterized by abdominal pain or discomfort with changed bowel habits but without any organic damage to the intestine (tumor or inflammation) [8,9]. The etiology of IBS is uncertain, and studies have documented that psychological, social, and biological factors can play a role**.** IBS creates an incredible cost for both patients and the health care system [10,11]. It is one of the commonest disorders diagnosed by gastroenterologists [12]. There is a large part of the population suffering from IBS while only some seek health care in the absence of curative therapy. The prevalence of IBS usually varies significantly between countries and depends on the diagnostic criteria used [13]. A study conducted among secondary school male students in Al-Jouf Province, Saudi Arabia, showed that the prevalence was 8.9 and9.2% according to Manning and Rome II Criteria, respectively.

Regarding university students, the prevalence of IBS was found to be 5.7% in one of the Korean colleges. Medical students are under constant stress; the duration it takes to complete their studies, numerous exams, difficult shifts, and the responsibility of managing patients may cause much stress. The role of stress can partly justify the high prevalence of IBS seen among medical students [14]. In 2012, Chu et al. conducted a study among medical, science, and engineering students in China. They reported that medical students had a much higher risk of functional bowel disorders (FBD) than science and engineering students. Another study was conducted in 2012 among medical students at the University of Western Ontario, Canada [15]. found that the prevalence of IBS among preclinical and clerkship students was 19.1 and 22.0%, respectively.

The best way to identify IBS is by understanding its criteria [16]. Some causes of IBS are psychological, such as stress, anxiety, and depression and some are physiological, such as dysregulation of the brain-gut axis and gut motility. Stress is an external stimulus that affects the physiological and psychological wellbeing of a person, triggering physiological responses IBS is the most common diagnosis made by gastroenterologists, where 12% of IBS patients visit a primary care unit [17]. Stress can be defined as a condition or feeling that is experienced when an individual feels that what is demanded of them is beyond their ability, or when they feel the situation they are beyond their control [18]. Stress is a typical reaction to external stressors e.g., students facing heavy study.

A high prevalence of IBS prevailed among medical students and interns. Female, anxiety, living in school dormitory, emotional stress, and higher educational level (grade) were the predictors of IBS. Screening of medical students for IBS, and psychological problems, and reducing stress by stress management are recommended [7].

1.1. Aim of the study

This study aims to investigate the relationship between psychological upset and irritable bowel syndrome among nurse students at the Hafr Albatin University king Saudi Arabia

1.2. Research Questions

1.2.1. What are the Irritable Bowel Syndrome manifestations among nursing students at selected KSA University?
1.2.2. What is the Psychological stiffness level among nursing students in selected KSA universities?
1.2.3. Is there a Relation between Irritable Bowel Syndrome, Psychological stiffness, and student socio-demographic characteristics?

1.3. Theoretical framework

According to [19]. findings and other support references suggested a significantly moderated academic stress to test anxiety relationship. As noted in **Figure 1**, a significantly stronger positive relationship existed between academic stress and test anxiety for those reporting a high level of perceived other support compared to those reporting a low level of perceived Other support

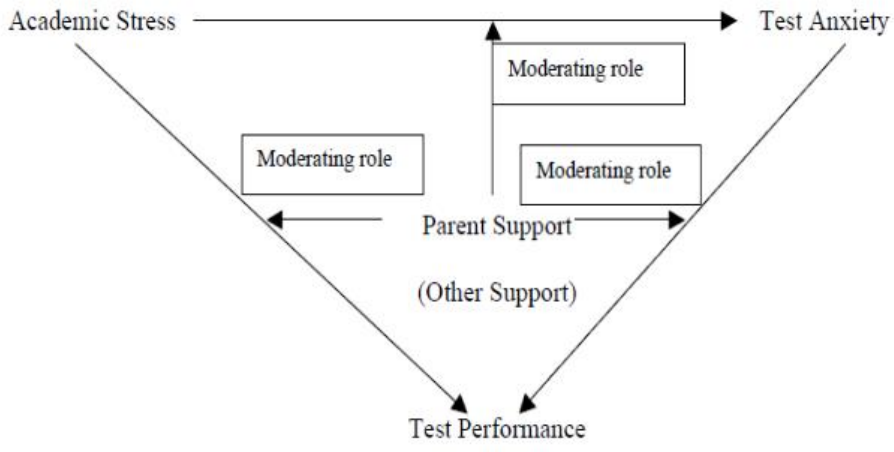

Figure 1. Illustrates academic stress, test anxiety, and performance in high school sample: and the effects of coping strategies and social support [19].

2. Subjects and methods

A descriptive cross-sectional design was utilized in this study at the Nursing Department of Applied Medical Science College, University of Hafr Al-Batin (UHB), KSA on convenience sampling of all available nursing students available during the data collection period (223) students. The inclusion criteria of participants entail their approval to participate in the study.

Tools

One tool was used after the revised literature was divided into 3 main parts as follows:
Part (I): It includes students' Sociodemographic characteristics of nursing students as (age, sex, marital status, and level).
Part (II): It includes psychological upset indicators: it includes 42 selected items adapted from ***AL-Byirag., 2011*** [20] addressing student's psychological upset

Part (III): It includes an irritable Bowel Syndrome manifestation includes 8 items adapted from Ida et al., 2017[21] ***which*** were used to obtain the predictor manifestations of the Irritable Bowel Syndrome.

Scoring system of the patient satisfaction scale

The questions in the psychological upset tool were scored according to Likert Rating Scale as (usually applicable =4, often applicable =3, sometimes applicable =2, Not applicable =1) and the total score of the tool was classified as levels for both stress questions and quality of life questions as considered when it was Low <50%, Moderate 50–<75%, High ≥75%.

Content validity

Validity was used for the modified tool to assure that it covers the objectives. The phase was developed by a Jury of five experts from the Medical-surgical and Psychiatry & Mental Health nursing staff; two Assistant professors of psychiatry & mental health nursing at the College of Nursing, Qassim University, and three Assistant Professors of Medical-Surgical at Nursing college, Hafr Elbatin University. Reliability of the proposed tool was done using Cronbach's alpha test which revealed high reliability (.950).

A pilot study was done on 20 students to approximate the clarity of the tool and then excluded them from the total sample number. The questionnaire sheet was submitted online and then contact the students via their what's-up media and explain the purpose of the study to them and invited them to participate in the study through an online link also the sheet contains a paragraph explaining the study's aim and assuring them that their participation was voluntary and they have the right to withdraw at any time.

3. Statistical analysis

Data were analyzed using the IMB Statistical software Package of Social Sciences (SPSS) Version 20 (Armonk, NY: IBM Corp). Moreover, Quantitative data were described using range (minimum and maximum), mean, and standard deviation using the Chi-square test for categorical variables, to compare between different groups and Fisher's Exact or Monte Carlo correction for chi-square when more than 20% of the cells have expected count less than 5. P-values with $p< 0.05$ are considered statistically significant.

4. Results

Table 1 illustrates a total of 223 students who participated in the study, a nearly two-third quarter (70.4%) of the students less than 22 years old followed by 33.2% of them in the fourth grade. Additionally, most of them (97.3%) are not smokers, more than half of students (62.8%) have smoking in the family, and (51.1%) have enough income monthly the marital status (87.4%) most of them are single. the highest number of participating students (59.6%) had natural sleep comfort and related to the condition of the colon during exposure to psychological stress (61.4%) more than half had Abdominal pain and cramps, and more than half of students (51.1%) slept 6-8 hours a day according to to suffer from irritable bowel disease less than half not suffering.

Table 2 shows less than half of the studied students (46.2%) haven't thought about leaving the nursing profession and college because of the pressure of studying and related to pressure in the nursing profession more than half have this pressure.

As indicated in Table 3 the total score of irritable bowel syndrome manifestations is 17.20±4.57 while the psychological stiffness scale has 114.51±10.23

Table 4 describes there is a moderate level of irritable bowel syndrome manifestations and a scale of psychological stiffens.

Table 5 shows that there are statistical significant findings in the items related to having a smoker in the family, marital status, the nature of sleep, sleeping hours, the condition of the colon during exposure to psychological stress, and taking colon medications

Table 6 showed that there is a statistically significant relationship between the psychological stiffness Scale and student's socio-demographic characteristics mainly in the items related to sleeping hours, and the condition of the colon during exposure to psychological stress

Table 1. Distribution of the studied nursing students according to their socio-demographic characteristics

Socio-demographic characteristics	**(n = 223)**	**%**
Age (years)		
Less than 22 years	157	70.4
More than 22 years	66	29.6
Grade		
First	43	19.3
Second	34	15.2
Third	72	32.3
Fourth	74	33.2
Smoking		
Yes	6	2.7
No	217	97.3
Do you have a smoker in the family?		
Yes	140	62.8
No	83	37.2
Monthly income		
Enough	114	51.1
Not enough	25	11.2
Sometimes	84	37.7
Marital status		
Married	28	12.6
Single	195	87.4
The nature of sleep		
Intermittent	133	59.6
I sleep comfortably	52	23.3
I suffer from insomnia	38	17.0
Sleeping hours		
I sleep less than 6 hours a day	64	28.7
I sleep 6-8 hours a day	114	51.1
I sleep more than 8 hours a day	37	16.6
I suffer from insomnia and the inability to sleep for days	8	3.6
The condition of the colon during exposure to psychological stress		
Persistent diarrhea	30	13.5
Constant constipation	34	15.2
Abdominal pain and cramps	137	61.4
Vomiting and nausea	22	9.9
Do you suffer from irritable bowel disease		
Yes	63	28.3
No	103	46.2
Sometimes	57	25.6
If the answer is yes, how long?		
I do not suffer	103	46.2
Less than one year	23	10.3
1 –3 years	45	20.2
More than 3 years	52	23.3
Are you taking colon medications?		
Yes	8	3.6
No	184	82.5
Sometimes	31	13.9

Table 2. Distribution of the studied nursing students according to their Irritable Bowel Syndrome manifestations (n = 223)

Irritable Bowel Syndrome Scale	N	%
Have you thought about leaving the nursing profession and college because of the pressure of studying?		
Yes	65	29.1
No	103	46.2
Sometimes	55	24.7
Have you ever been under pressure because of the nursing profession?		
Yes	124	55.6
No	52	23.3
Sometimes	47	21.1

Table 3. Distribution of total & Mean scores for IBS manifestations & Psychological stiffness Scale

	Total score	Mean score	% score
Irritable Bowel Syndrome Scale			
Min. – Max.	6.0 – 24.0	1.0 – 4.0	0.0 – 100.0
Mean ± SD.	17.20±4.57	2.87±0.76	62.23±25.38
Psychological stiffness Scale			
Min. – Max.	80.0 – 140.0	1.90 – 3.33	30.16 – 77.78
Mean ± SD.	114.51±10.23	2.73±0.24	57.55±8.12

Table 4. Distribution of the nursing students according to their levels of IBS Manifestations and Psychological Stiffness Scale (n = 223)

	Low <50%		Moderate 50%–75%		High ≥75%	
	N	%	N	%	N	%
Irritable Bowel Syndrome Manifestations	63	28.3	91	40.8	69	30.9
Psychological stiffness Scale	31	13.9	189	84.8	3	1.3

Table 5. Relationship between Irritable Bowel Syndrome Manifestations and student's Socio-demographic characteristics

Sociodemographic characteristics	Irritable Bowel Syndrome Scale						χ^2	p
	Low <50% (n = 63)		Moderate 50%–75% (n = 91)		High≥75% (n = 69)			
	N	%	N	%	N	%		
Age (years)								
Less than 22 years	41	65.1	66	72.5	50	72.5	1.195	0.550
More than 22 years	22	34.9	25	27.5	19	27.5		
Grade								
First	14	22.2	19	20.9	10	14.5	10.941	0.090
Second	12	19.0	11	12.1	11	15.9		
Third	11	17.5	32	35.2	29	42.0		
Fourth	26	41.3	29	31.9	19	27.5		
Smoking								
Yes	0	0.0	5	5.5	1	1.4	3.942 (MC)	0.110
No	63	100.0	86	94.5	68	98.6		
Do you have in smoker in your family?								
Yes	26	41.3	68	74.7	46	66.7	18.478	<0.001*
No	37	58.7	23	25.3	23	33.3		
Monthly income								
Enough	38	60.3	46	50.5	30	43.5	7.753	0.101
Not enough	4	6.3	8	8.8	13	18.8		
Sometimes	21	33.3	37	40.7	26	37.7		

Table 5. Continued.

Sociodemographic characteristics	Irritable Bowel Syndrome Scale						χ^2	p
	Low <50% (n = 63)		Moderate 50%–75% (n = 91)		High≥75% (n = 69)			
	N	%	N	%	N	%		
Marital status								
Married	16	25.4	5	5.5	7	10.1	13.959	0.001**
Single	47	74.6	86	94.5	62	89.9		
The nature of sleep								
Intermittent	39	61.9	55	60.4	39	56.5	21.329	0.001**
I sleep comfortably	22	34.9	21	23.1	9	13.0		
I suffer from insomnia	2	3.2	15	16.5	21	30.4		
Sleeping hours								
I sleep less than 6 hours a day	18	28.6	30	33.0	16	23.2	12.240 (MC)	0.047*
I sleep 6-8 hours a day	38	60.3	45	49.5	31	44.9		
I sleep more than 8 hours a day	7	11.1	14	15.4	16	23.2		
I suffer from insomnia and the inability to sleep for days	0	0.0	2	2.2	6	8.7		
The condition of the colon during exposure to psychological stress								
Persistent diarrhea	15	23.8	8	8.8	7	10.1	37.685	0.001**
Constant constipation	5	7.9	16	17.6	13	18.8		
Abdominal pain and cramps	39	61.9	66	72.5	32	46.4		
Vomiting and nausea	4	6.3	1	1.1	17	24.6		
Do you suffer from irritable bowel disease?								
Yes	10	15.9	32	35.2	21	30.4	17.182	0.002*
No	38	60.3	43	47.3	22	31.9		*
Sometimes	15	23.8	16	17.6	26	37.7		
If the answer is yes, how long?								
I do not suffer	38	60.3	43	47.3	22	31.9	18.874	0.004**
Less than one year	10	15.9	6	6.6	7	10.1		
1 –3 years	9	14.3	18	19.8	18	26.1		
More than 3 years	6	9.5	24	26.4	22	31.9		
Are you taking colon medications?								
Yes	1	1.6	4	4.4	3	4.3	9.718 (MC)	0.034*
No	58	92.1	67	73.6	59	85.5		
Sometimes	4	6.3	20	22.0	7	10.1		

χ^2: Chi-square test; MC: Monte Carlo; *:p<0.05; **:p<0.001

Table 6. Relation between Psychological Stiffness Scale and Socio-demographic characteristics

Socio-demographic characteristics	Psychological stiffness Scale						χ^2	p
	Low <50% (n =31)		Moderate 50%–75% (n = 189)		High≥75% (n = 3)			
	N	%	N	%	N	%		
Age (years)								
Less than 22 year	23	74.2	131	69.3	3	100.0	1.023	0.631
More than 22 year	8	25.8	58	30.7	0	0.0		
Grade								
First	7	22.6	36	19.0	0	0.0	3.662	0.741
Second	5	16.1	28	14.8	1	33.3		
Third	10	32.3	60	31.7	2	66.7		
Fourth	9	29.0	65	34.4	0	0.0		
Smoking								
Yes	0	0.0	5	2.6	1	33.3	5.901	0.120
No	31	100.0	184	97.4	2	66.7		

Table 6. Continued.

Socio-demographic characteristics	Psychological stiffness Scale						χ^2	p
	Low <50% (n =31)		Moderate 50%–75% (n = 189)		High≥75% (n = 3)			
	N	%	N	%	N	%		
Are you have family smokers?								
Yes	19	61.3	120	63.5	1	33.3	1.300	0.620
No	12	38.7	69	36.5	2	66.7		
Monthly income								
Enough	18	58.1	93	49.2	3	100.0	6.946	0.103
Not enough	6	19.4	19	10.1	0	.0		
Sometimes	7	22.6	77	40.7	0	.0		
Marital status								
Married	6	19.4	22	11.6	0	0.0	1.688	0.50
Single	25	80.6	167	88.4	3	100.0		
The nature of sleep								
Intermittent	14	45.2	116	61.4	3	100.0	4.533	0.279
I sleep comfortably	11	35.5	41	21.7	0	0.0		
I suffer from insomnia	6	19.4	32	16.9	0	0.0		
Sleeping hours								
I sleep less than 6 hours a day	8	25.8	56	29.6	0	0.0	19.807	0.001**
I sleep 6-8 hours a day	18	58.1	96	50.8	0	0.0		
I sleep more than 8 hours a day	1	3.2	33	17.5	3	100.0		
I suffer from insomnia and the inability to sleep for days	4	12.9	4	2.1	0	0.0		
The condition of the colon during exposure to psychological stress								
Persistent diarrhea	6	19.4	24	12.7	0	0.0	15.091	0.009**
Constant constipation	3	9.7	28	14.8	3	100.0		
Abdominal pain and cramps	22	71.0	115	60.8	0	0.0		
Vomiting and nausea	0	0.0	22	11.6	0	0.0		
Do you suffer from irritable bowel disease?								
Yes	8	25.8	54	28.6	1	33.3	2.718	0.635
No	12	38.7	89	47.1	2	66.7		
Sometimes	11	35.5	46	24.3	0	0.0		
If the answer is yes, how long?								
I do not suffer	12	38.7	89	47.1	2	66.7	9.701	0.083
Less than one year	3	9.7	19	10.1	1	33.3		
1 –3 years	3	9.7	42	22.2	0	0.0		
More than 3 years	13	41.9	39	20.6	0	0.0		
Are you taking colon medications?								
Yes	0	0.0	7	3.7	1	33.3	5.339	0.248
No	27	87.1	155	82.0	2	66.7		
Sometimes	4	12.9	27	14.3	0	0.0		

χ^2: Chi-square test; MC: Monte Carlo; *:p<0.05; **:p<0.001

5. Discussion

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder associated with stress, which may emerge by an educational circumstance, given that students are exposed to requirements in the academic atmosphere during their education progression that may lead to extending diseases [22]. University students are subject to stress due to academic pressure, empowerment and changeover from adolescence to adulthood stage. This young population may have a higher risk of purposeful disorders such as eating disorders (ED) and irritable bowel syndrome (IBS) these disorders co-existing with ED and IBS are related to multiple mental health warning signs, which could lead to negative academic outcomes [23].

Additionally, [24] stressed that The COVID-19 pandemic negatively affected Irritable bowel syndrome (IBS) as the mainly significant self-determining factor correlated with worsening in gastrointestinal indicators which patients suffered from (IBS) require to take extra care in the post-COVID period.

Concerning students' sociodemographic characteristics, the present study exposed that more than half of the students were less than 22 years old followed by more than one-quarter of them in the fourth grade. Additionally, most of them are not smokers, more than half of the students have smoked in family and have enough income monthly while most of them are single, and half of participating students have natural sleep comfort. More than half of them suffered manifestations related to the colon during exposure to exams psychological stress as abdominal pain and cramps, in addition, more than half of students sleep 6-8 hours a day according to suffer from irritable bowel disease less than half not suffering. Finally, less than half of studied students no thought about leaving the nursing profession and college because of the pressure of studying and related to pressure in the nursing profession more than half having pressure in their job. These findings go in the same line with [25] who revealed that IBS is a widespread disorder among a university-based population aged 18-30 years and has a significant impact on their quality of life. In Taiwan, IBS is considered a chronic functional gastrointestinal disorder. The incidence of IBS among female university students was 10.1%, which is similar to that in Western countries [26]**.**

According to [27], the occurrence of (IBS) is varied based on geographical region, age, gender, occupation, and IBS diagnostic criteria and was higher among women than men. The frequency of sleep disorders was higher among students suffering (from IBS) compared to healthy students and may be linked with the pathogenesis of IBS. Also, recommended the needed to examine the possible causal relationship between sleep disorder and IBS. In addition, [28] concluded in their study that adjustment or adaptation to stressors among the U.S. population which Low adjustment negatively affects symptom severity of (IBS) and mental health.

As regards, the relation between Irritable Bowel Syndrome manifestations and student's Socio-demographic characteristics, the present study revealed that there are statistically significant relationships were found in the items related to the presence of a smoker in their family, marital status, the nature of sleep, sleeping hours, the condition of the colon during exposure to psychological stress, and taking colon medications. These findings go in the same line with [2] who highlighted that Irritable Bowel Syndrome (IBS) is considered one of the more highly widespread and costly gastrointestinal disorders. Despite its risk factors as stress and academic load, are well linked with the occurrence of Irritable Bowel Syndrome which medical students account for as a high rate of IBS resulting from stressful and challenging environments.

In contrast, Taiwan [29] mentioned that Irritable Bowel Syndrome (IBS) is prevalent among Young Taiwanese female nursing students which generally reveals both physical and psychological health problems resulting from academic stress with no effect on IBS symptoms.

In Lebanon, [30] concluded that IBS proportionately affected women more than men, as well as health behavioral factors, have significant influences on the presence and progression of IBS. Consequently, multifaceted interventions should be searched for strategies to reduce manifestations of IBS such as nutritional education and promoting proper ways to change lifestyles in order to control stress.

As regard distributions of the student level of psychological stiffen scale and irritable bowel syndrome manifestations, the present study revealed that most students have a moderate level of psychological stiffens scale with the presence of irritable bowel syndrome manifestations. Also, the total manifestations scores in irritable bowel syndrome are 17.20±4.57 and the psychological stiffness scale has 114.51±10.23. These findings were supported by Alaqeel et al.,2017 [31] In KSA who revealed that

the incidence of IBS was 21% and higher among females than males but was highest among fifth-year students for both genders. More than 50% of students had moderate or high levels of anxiety for both genders. The prevalence of IBS was highest among students in 5th fifth year. The study provides evidence that medical students in the higher year of their under graduation were having a higher level of anxiety which leads to IBS.

In China, [27] revealed results from logistic regression test that challenge to go down weight and anxiety were both combined with increasing odds of IBS, while exercise was not linked with IBS in either male or female students. In female students, snack consumption and depression were also both correlated with increased odds of IBS. Considering the high prevalence of IBS among students can get better for individual, students when there are sufficient education and counseling to progress their mental health and lifestyle, especially for female students in higher grades.

In Taiwan, [26] reported that there are some burden manifestations such as dysmenorrheal, food avoidance, class absenteeism, and the physical health domain of quality of life which are considered responsible factors for the occurrence of IBS among female university students and recommended construct more awareness and research for university students in northern Taiwan as well as male and female university students regarding understanding the position of gender in IBS.

In KSA, one of the most highly widespread and costly gastrointestinal disorders is IBS. It is an outcome of emotional arguments and stress. As a result, medical and intern students have a high percentage of IBS Moreover, female students have emotional tension in the past 6 months and family history of IBS which they considered the main prophet of IBS [32]**.**

Finally, there is an obvious need to implement educational programs aiming at self-care as well as gaining knowledge about academic stress-related study factors and the physical responses that may result in repercussions with stern outcomes for student life such as pain, illness, and dropping out of educating [22]**.** In this regard, [30,2] stressed the importance of engaging in healthy behaviors such as physical activity to minimize manifestations of Irritable Bowel Syndrome (IBS) and improve their quality of life. Additionally, determining the exact prevalence of stress among medical students which needed to investigate its impact on students' quality of life in order to diminish risk factors and implementing preventive strategies are essential to control the Irritable Bowel Syndrome (IBS) and reduce its adverse effects.

6. Conclusion and recommendations

Based on study findings we can conclude that there is a statistically significant correlation between students' psychological stiffness and manifestations of irritable bowel syndrome. Also, there is a statistically significant relationship was found between psychological stiffness levels and students' Socio-demographic characteristics in the items related to sleeping hours, and the condition of the colon or manifestations of Irritable Bowel Syndrome during exposure to psychological stress. From the foregoing conclusion, students need to receive regular; periodic in-service psychological adaptation program that contains methods of coping with study stress, especially during exams period which indirectly added stressor to students' psychological upset. There is evident necessitate for designed exams counseling preparation. Further studies are needed to study the factors that influence university students' psychological and physiological well-being during the study & exam period rather than stressors.

Ethical statement

The study was approved by the Applied Medical Sciences College administrative authority. Additionally, the participants were informed of the research purpose and their answers would be kept confidential and the answers do not affect or interfere with their evaluation. The study work does not involve chemicals, procedures, or equipment that have any unusual hazards.

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Conflict of interest:
There are no conflicts of interest

Authors' Contributions:
S.M: conceptualized; written introduction; methodology; organized reference and reviewed the manuscript. (%50)
Q. S, Designed tool; conduct analysis follow-up and interpretation; written discussion; conclusion; recommendations and reviewed the manuscript (%50)
All authors read and approved the final manuscript.

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Review Article

BASIC PARAMETERS OF LENS DESIGN

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Abstract: *The development of technology has increased computing power and the ability to make scientific calculations has also developed rapidly. One of the areas affected by the developing technology is optics. The lens design is a complex field of study that includes many infrastructures such as lens optimization, ray trace analysis, lens drawing, and modulation transfer function calculations. In this study, the basics of optical system design are presented. The calculation of complex optical systems is a demanding and extensive task. The reason for the complexity in lenses is due to the fact that all rays of wavelengths pass correctly through the image of a particular point of an object. The lens parameters include radii of curvature, thickness, air gaps, refractive indices, and dispersion forces of the glasses used for individual lens elements or the position of the aperture-limiting diaphragm or lens mount. It contains a series of formulations ordered by subject areas or topics representing typical lens design tasks and optical system design tasks. Different aspects are covered, such as the definition of starting systems and the creation, evaluation, and optimization of lenses and systems. The formulas of the most critical lens design equations are given in detail in the content of the study. It also provides an overview of basic mathematical models for calculating simple optical components such as single lenses, systems, and achromatic pairs. Such components represent the foundation of any optical system. The literature study on this study determined that studies on lens design in national publications are limited. The study differs in that it clearly articulates the fundamentals of lens design. It is thought that this study will contribute to the literature.*

Keywords*: Lens shapes, Lens planes, Optical imaging parameters, Acrotism parameters*

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1. Introduction

Optics, a branch of physics, includes developing tools, equipment, and optical systems to give direction and shape to light while examining light and vision events [1].

The calculation of complex optical systems is a demanding and extensive task. Before a lens is manufactured, it should be designed by determining the radii of curvature of its surfaces, their thickness, air gaps, diameters of various components, and the types of glass used [2]. Today, the calculation of an optical system is mainly carried out with the help of simulation tools, which significantly reduces the required work and time expenditure [3].

The reason for the complexity in lenses is due to the fact that all rays of wavelengths pass correctly through the image of a particular point of an object. That is, the lens should pass a flat object without any curvature or distortion [3]. According to the studies of scientists in the last few years, various so-called aberrations have been noticed in the wrong image formed by a lens, each of which can be created by changing the lens structure. Typical aberrations are spherical aberrations, chromatic aberrations

(inherent in specific optical designs, caused by a defect in a lens or other component and causing off-axis point sources), and astigmatic and chromatic (a lens's inability to focus all colors on the same point) aberrations. All aberrations appear mixed together in any lens, and correcting (or eliminating) an aberration only improves the resulting image by the specified amount of aberration. Some aberrations can be easily corrected by simply changing the shape of one or more lens elements, while others require a radical replacement of the entire system [4,5].

The lens parameters that the designer can change are called "degrees of freedom." These parameters include radii of curvature, thickness, air gaps, refractive indices, and dispersion forces of the glasses used for individual lens elements or the position of the aperture-limiting diaphragm or lens mount (Paul and Yoder, 2006). Besides, it is also necessary to always maintain the lens's focal length. Otherwise, the relative aperture and image height will change [6]. As a result, the designer might get a good lens, but not the lens he decided to design. So every structural change to keep the focal length constant must be accompanied by another change. Also, if the lens is to be used at a fixed magnification, this magnification must be maintained throughout the design. An overview of basic mathematical models for calculating simple optical components such as single lenses and systems is considered helpful.

2. Lens shapes and general information

2.1. Lens shapes

Single lenses can be categorized in quite different ways [7]:

- Based on lens function, i.e., convergence or divergence,
- According to the material used, i.e., glass lenses, crystal lenses, liquid lenses, etc.
- According to the shape of the optically active surface

According to the last category, cylindrical lenses, toric lenses, conical lenses, aspherical lenses, and spherical lenses can be identified. At least one surface of the lenses in this category is given a spherical shape and is named depending on the curvature direction of the spherical shape [8]. In Figure 1, lens naming according to the surface shape is given.

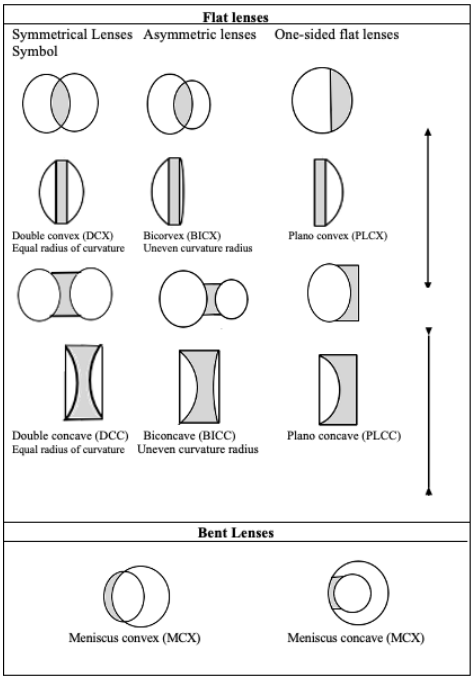

Figure 1. Different types of spherical lenses - convergent lenses and divergent lenses and their symbols

It can be seen in Figure 1 that the orientation of a given radius of curvature gives the overall shape and thus the lens type. Therefore, this orientation is of particular importance and interest for the design and manufacture of lenses. It is expressed by the algebraic sign of the radius of curvature as listed in Table 1.

Table 1. Different types of spherical lenses with marking definition of the specific radius of curvature (if arranged towards incident light as shown in figure 2) and related properties

Lens type	Sign Definition		Property
	First surface (left)	Second surface (right)	
Plano-convex	+	(∞)	$R_2=\infty$
Symmetrical biconvex	+	-	$R_1=R_2$
Asymmetrical biconvex (best lens form)	+	-	$R_1\neq R_2$
Positive meniscus (concave-convex)	+	+	R_1(convex)<R_2($concave$)
Plano - concave	+	(∞)	$R_2=\infty$
Symmetrical biconcave	+	-	$R_1=R_2$
Asymmetrical biconcave	+	-	$R_1\neq R_2$
Negative meniscus (convex-concave)	+	+	R_1(convex)>R_2(concave)

Apart from radii of curvature, other parameters are needed for a complete definition of an optical lens as visualized in figure 2: center thickness (tc), lens diameter (D) and lens material (e.g., glass or optical medium as appropriate), refractive index (n), absorption coefficient (α) and *V*-number (V).

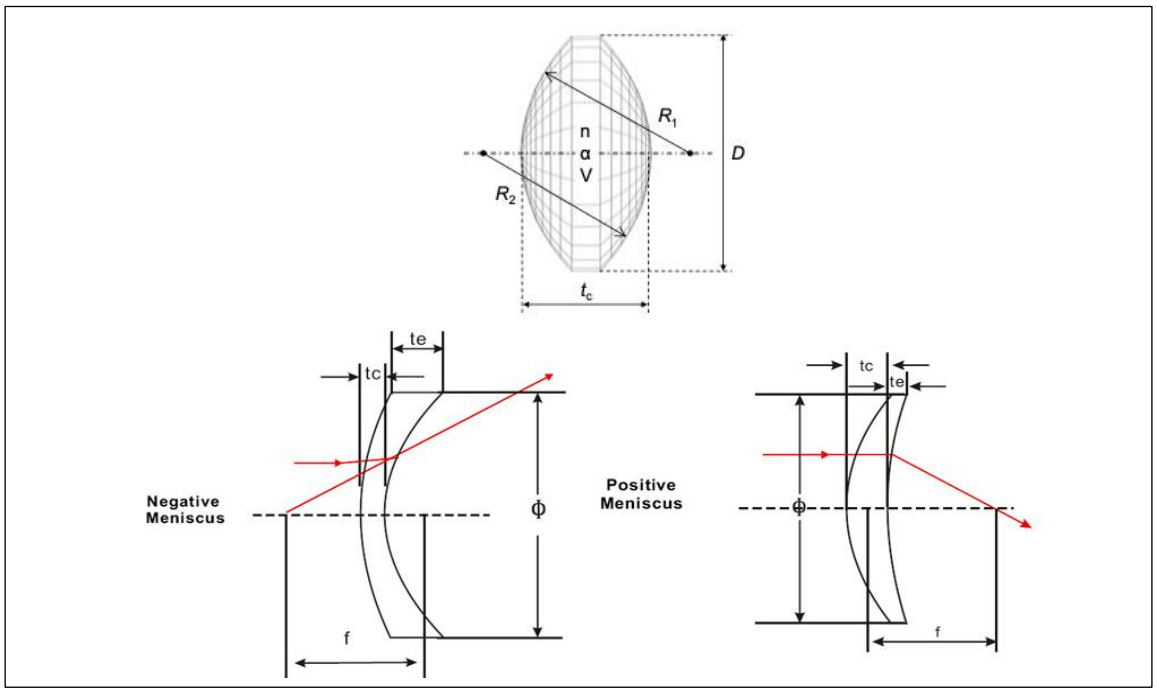

Figure 2. Lens parameters necessary for the definition of a lens: radius of curvature *R*, focal length *f*, center thickness *tc*, edge thickness *te*, diameter *D* and the lens material, refractive index *n*, absorption coefficient *α*, and V-number *V* [2].

For fundamental considerations in optical system design, the actual shape of a lens may not matter. Such simple calculations are sufficient to determine the primary function of the lens [9]. In addition to optical power, the focal length, including its algebraic sign, must be known to describe the behavior or function of a lens. Convergent lenses have a positive algebraic sign, whereas divergent

lenses have a negative focal length. The basic behavior of the lenses is visualized by the symbols shown in table 1.

2.2. Basic planes

Any imaging optical component or system can be described by two virtual planes, called principal planes, where refraction theoretically occurs. The location of such principal planes can be established graphically based on a simple rule, which is explained as follows: after passing through a physical lens, the light beam, initially emitted parallel to the optical axis, passes the focal point and vice versa. This transformation is due to the refraction of the lens surfaces [10]. Virtual intersections should be considered when estimating the paths of all rays in front of and behind a lens or optical system, as shown in figure 3.

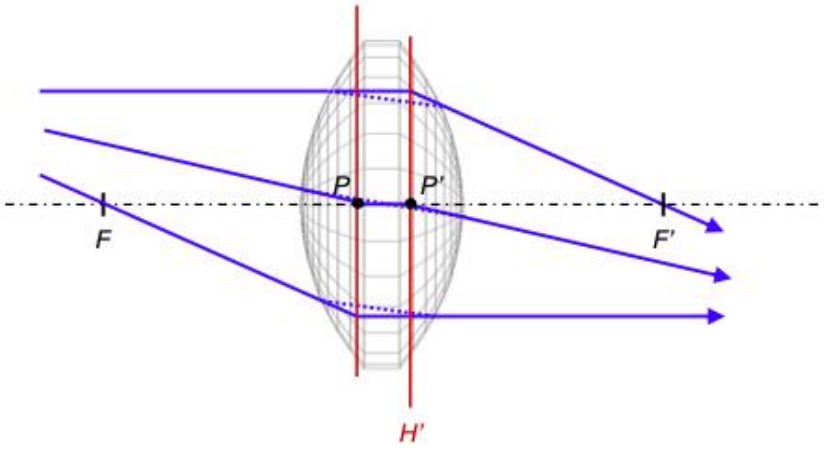

Figure 3. Graphical structure of a biconvex lens's principal plane H and H'.

Planes that join these points are called principal planes orientated perpendicular to the optical axis. Two principal planes can be defined, one on the object side (H) and the other on the image side (H'). Depending on the shape of a physical lens or system, the principal planes may even be located outside the lens material, as shown in some examples in figure 4.

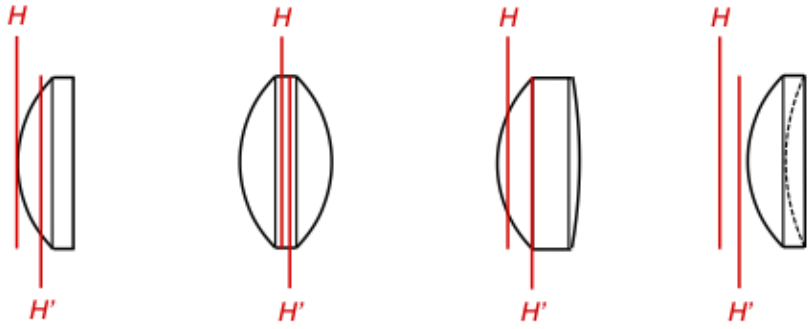

Figure 4. Qualitative visualization of the location of the principal planes for different types of converging lenses

The surface of the lens is not essential since the principal planes are effective when determining the focal length. For an idealized and simplified description of any imaging system, even just one principal plane is sufficient for estimating the relationships between the object area and the image area of an optical system.

Table 2. Overview of the main elements

Elements	Abbreviation	Description
Main point	P, P'	The intersection points of the principal plane and the optical axis (in case of axial-parallel incident light)
Corners	V, V'	Points of intersection of lens surfaces and the optical axis
Focal point	F,F'	front and rear focal point
Effective focal length	EFL	The focal length above the base plane (commonly called the focal length f)
Rear focal length	BFL	Focal length at the vertex in the image field
Front focal length	FFL	Focal length at the vertex in the object area
Node points	N, N'	Point equivalent to the main point in case of diagonal interference (incidence) of light

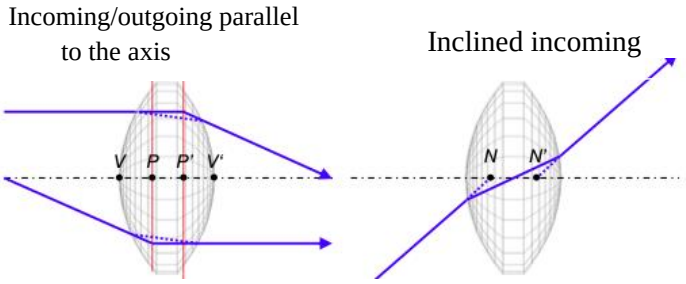

Figure 5. Main elements of the biconvex lens are listed in table 2 for axial-parallel light and inclined light

2.3. Main elements

Other than the aforementioned principal planes, more characteristic locations or points can be detected on lens surfaces or inside the lens material and at distances. These points and distances are the main elements listed in table 2 and partially illustrated in figure 5.

The main elements are of paramount importance, as any imaging system's computational and layout design is based on these parameters. For example, the radius of curvature of a physical lens comes from its focal length [7,11].

Here, it is necessary to explain the radius of curvature. The radius of curvature has a special meaning and sign rule in optical design. A spherical lens surface has a center of curvature along its optical axis away from the center. The apex of the lens surface is located on the local optical axis. The distance from the lens vertex to the center of curvature is the radius of curvature of the surface.

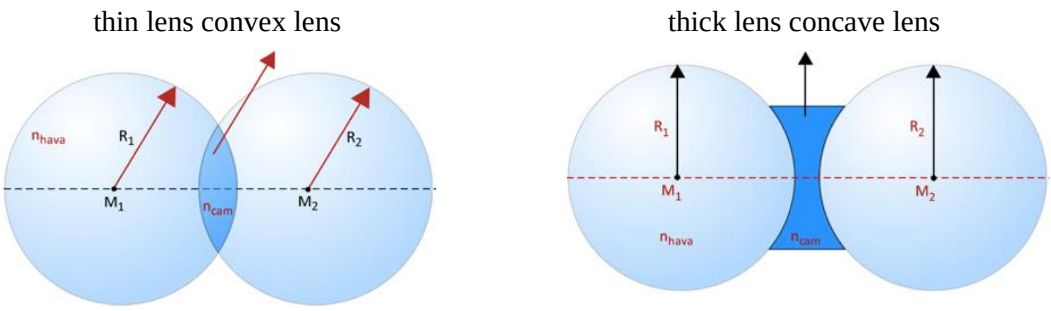

Figure 6. Determination of radii of curvature of convex and concave lenses

The sign rule for the optical radius of curvature is as follows:

• The radius of curvature is positive if the apex of the lens is to the left of the center of curvature.

• The radius of curvature is negative if the apex of the lens is to the right of the center of curvature.

3. Basic lens parameters

3.1. Lens manufacturer's equations

The lens manufacturer's equations allow specifying the necessary parameters for realizing a physical lens with a given focal length (and vice versa). As summarized in Figure 2, the basic parameters of a lens are the refractive index of the lens material (α[1] and V number[2]), the radius of curvature, and center thickness. It may turn out that the calculation of these parameters is based on a few assumptions due to the relatively high number of variables. Professional experience and intuition gain importance here. Sometimes simple economic considerations may suffice to define some of the desired parameters [11].

3.1.1 The convex lenses

In most cases, it's enough to start with a very simple approach to optical design: the convex lens. Although such a lens does not really exist in practice, it is a useful model for initial predictions and calculations of the optical system [12, 13]. By definition, the medium thickness of a convex lens is much smaller than the radius of curvature, $tc < R_1, R_2$. Consequently, the lens can be described as a single principal plane, as the principal planes of both surfaces are congruent due to the marginal center thickness. The effective focal length of such a thin lens usually comes from the following for plano-convex or plano-concave thin lenses.

for BICX lenses

$$\frac{1}{\mathrm{EFL}} = (n_l - 1) \cdot \left(\frac{1}{R_1} - \frac{1}{R_2}\right). \tag{1}$$

Here, n_1 is the refractive index of the lens material. For convex symmetrical biconvex or biconcave lenses, this equation can be simplified as follows:

for DCX lenses

$$\frac{1}{\mathrm{EFL}} = \frac{2 \cdot (n_l - 1)}{R} \tag{2}$$

for PLCX lenses

$$\frac{1}{\mathrm{EFL}} = \frac{(n_l - 1)}{R} \tag{3}$$

3.1.2 Concave lenses

In real life, the thickness of a lens cannot be neglected. This is especially true for lenses where the center thickness is in the order of magnitude of the radius of curvature, as, for example, with hemispherical lenses [12, 13]. Such lenses are called concave lenses. As a matter of fact, the principal planes of both optical interfaces are separated. The center thickness tc should be taken into account during the calculation. Equation (3.1) is then rewritten as follows:

[1] Absorption coefficient

[2] In optics and lens design, the Abbe number, also known as the V number or density of a transparent material, is an approximate measure of the material's dispersion (the variation of refractive index with wavelength). High V values indicate low dispersion.

$$\frac{1}{\mathrm{EFL}} = (n_l - 1) \cdot \left(\frac{1}{R_1} - \frac{1}{R_2} + \frac{(n_l - 1) \cdot t_c}{n_l \cdot R_1 \cdot R_2} \right). \tag{4}$$

3.2. Parameters of optical imaging

3.2.1 Conjugate parameters of optical imaging

There are two different areas of interest in optical imaging. These areas are called the object area in front of the lens or system and the image area behind it. The basic parameters in the object area and the corresponding parameters in the image area are called reciprocal parameters, interconnected through the focal length or magnification of the imaging optics, respectively [14]. Thus, it means transferring an object with a specific height y and a certain distance in the optical system to an image with a distance a' following the characteristics of the appropriate image height y' and the features used (Fig. 7).

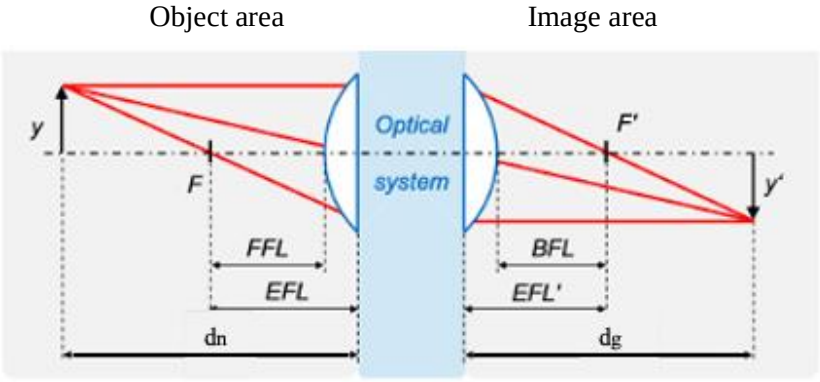

Figure 7. Scheme of optical imaging by an optical system or component with reciprocal (conjugated) parameters [2].

Table 3. Overview of key parameters for optical imaging. Specific heights and distances are conjugated parameters.

Object Area		Image Area	
Abbreviation	**Parameter**	**Abbreviation**	**Parameter**
y (or u)	Object height	y' (or u')	Image height
d_n	Object distance	d_g	Image distance
EFL	Effective front focal length	EFL'	Effective back focal length
FFL	Front focal length	BFL	Back focal length
F	Focal point	F'	Focal point
H	Principal plane	H'	Principal plane

According to these reciprocal parameters of imaging and other fundamental factors listed in Table 3, the imaging means the transfer of an object with a certain height y and a distance α from the optical system to an image with image height y' and distance α' appropriate to the characteristics of the optics used. Of the effective focal lengths on the principal plane, it should be noted that the back focal length is at the back of the lens and the front focal length is in front of the lens.

3.2.2 Structure of beams

At least two rays are required for the graphical structure of optical imaging through a lens or system with a given focal length [15]. There are three different rays that come parallel to the optical axis in the object area, pass through the focus in the object area, and pass through the optical center. The parallel incident beam passes through the focal point in the image area after passing through the lens

(→ 'parallel beam becomes the focus beam'). The incident beam, passing through the focal point in the object area, propagates parallel to the optical axis after passing through the lens (→ 'focus beam becomes parallel beam'). The ray that passes through the optical center passes without changing its direction [8, 12].

3.2.3 Imaging equation and magnification

In the general imaging equation, the interrelation between effective focal length (EFL) and object distance dn, and image distance dg can be described by the following equation:

$$\frac{1}{EFL} = \frac{1}{dn} - \frac{1}{dg} \tag{5}$$

Object and image distance are evaluated in relation to focal length. That is, for specific heights and distances in the object area, a certain image height and distance in the image area are obtained (It also means vice versa).

The associated parameters can also be expressed by Newton's equation:

$$EFL \cdot EFL' = (d_n - EFL) \cdot (d_g - EFL') \tag{6}$$

Another essential parameter that connects not only the object distance (d_n) and the image distance (d_g) but also the object height (y) and the image height (y') is the magnification of the optical system and is denoted by "m."

$$m = \frac{d_g}{d_n} = \frac{y'}{y} \tag{7}$$

In practice, this parameter (m) is usually given and is very helpful for determining object distance, for example, if the image distance is unknown:

$$d_n = EFL \cdot (1 - \frac{1}{m}) \tag{8}$$

Or vice versa,

$$d_g = -EFL \cdot (1 - m) \tag{9}$$

Optical systems consist of at least two or even more lenses. A classic and simple optical element is a compound lens consisting of two single lenses. Such an installation can be accomplished with air-gapped lenses or cemented lenses, called doubles. Cementitious lenses have no air gap between both lenses. The total effective focal length (EFL_{tot}) of a lens pair is as follows, respectively.

$$\frac{1}{\mathrm{EFL_{tot}}} = \frac{1}{\mathrm{EFL_1}} + \frac{1}{\mathrm{EFL_2}} - \frac{d}{\mathrm{EFL_1} \cdot \mathrm{EFL_2}} \tag{10}$$

or

$$\mathrm{EFL_{tot}} = \frac{\mathrm{EFL_1} \cdot \mathrm{EFL_2}}{\mathrm{EFL} + \mathrm{EFL_2} - d}, \tag{11}$$

Here, EFL1 is the effective focal length of the first lens, EFL2 is the effective focal length of the second, and d is the distance between both lenses. The total magnification of such pairs of lenses is the product of the magnifications of the respective lenses alone and is therefore evaluated by the following equation.

$$m_{tot} = m_1 \cdot m_2 \tag{12}$$

It can also be expressed by object and image distances.

$$m_{tot} = \frac{d_{g_1}}{d_{n_1}} \cdot \frac{d_{g_2}}{d_{n_2}} = \frac{d_{g_1} \cdot d_{g_2}}{d_{n_1} \cdot (d - d_{g_1})} \tag{13}$$

3.2.4 Parameters of compound lenses for achromatism

Achromatic binary or achromatic lenses are a special type of lens. In a colorless lens, two wavelengths, red and blue, are brought into the same focal point. An achromatic lens is a lens designed to limit the effects of chromatic and spherical aberration. Achromatic lenses are corrected to focus two wavelengths (typically red and blue) in the same plane [6, 13]. The most common type of achromatic lens is the achromatic duo, which consists of two separate lenses made of glasses with different amounts of dispersion.

This simple optical system is used to avoid chromatic aberrations caused by scattering white light passing through a single lens into its spectral fractions. For the two selected wavelengths, the dispersion can be compensated quite easily by combining two lenses with different V numbers and, therefore, different dispersion properties. The focal length of such an achromatic binary comes from the focal lengths of the respective single lenses (convergent or divergent). Compensation for chromatic aberration at two wavelengths is determined by equating the absolute value of the product of the effective focal length (EFL) and the V number (V) of the first lens to the development of the effective focal length (V) of the second lens:

$$\mathrm{EFL_1} \cdot V_1 = -\mathrm{EFL_2} \cdot V_2 \tag{14}$$

Algebraic indications of this general condition indicate that an achromatic lens consists of a convergent lens or a divergent lens. Both lenses are usually glued, so the distance is d = 0. The total effective focal length of the Colorseme (achromatic) binary EFLal, therefore, calculates as follows:

$$\frac{1}{\mathrm{EFL_{al}}} = \frac{1}{\mathrm{EFL_1}} + \frac{1}{\mathrm{EFL_2}}. \tag{15}$$

For the assumed or predetermined effective focal length of an achromatic binary, certain parameters of the respective single lenses can be determined quite easily: Solving the general condition for achromatism given by equation 3.14 for the effective focal length of the second lens,

$$\mathrm{EFL'2} = \frac{\mathrm{EFL'1} \cdot V_1}{V_2} \tag{16}$$

By adding the equation in 2.16 to the equation in 2.15, the following equation is obtained;

$$\frac{1}{\mathrm{EFL_{al}}} = \frac{1}{\mathrm{EFL_1}} \cdot \frac{V_1 - V_2}{V_1} \tag{17}$$

This expression can then be solved to determine the effective focal length of the first lens:

$$\mathrm{EFL_1} = \mathrm{EFL_{al}} \cdot \frac{V_1 - V_2}{V_1} \tag{18}$$

or for the second lens,

$$\mathrm{EFL_2} = -\mathrm{EFL_{al}} \cdot \frac{V_1 - V_2}{V_2} \tag{19}$$

Once the focal lengths of both lenses have been determined, the geometric lens parameters can be calculated based on the lens manufacturer's equations. The refractive indices required here are implicitly defined by the V-numbers and the type of glass used for both lenses. Choosing eyeglasses is an interesting and challenging task where some experience in optical design is beneficial. Normally, a standard crown glass with a high V-number and low dispersion, respectively, is used as an approximation for the convergent lens of an achromatic binary [2, 3, 4]. For the divergent lens, a flint or strong flint glass with a low V-number and high dispersion is chosen, respectively. The achromatic binary of these glasses is given in figure 8:

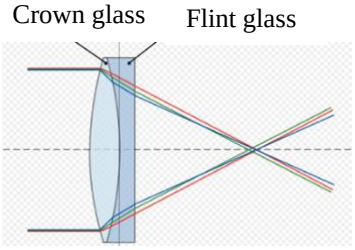

Figure 8. An achromatic duo combining Crown glass and Flint glass

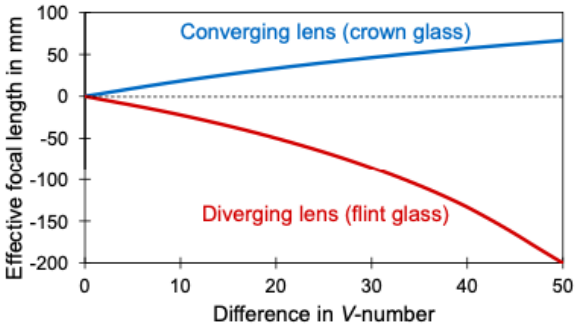

Figure 9. Correlation of increase in V number with the increase in effective focal length for an achromatic binary with a total focal length of 100 mm

As a simple rule, the difference in the V number of both glasses should be as large as possible (Fig. 9). The effective focal lengths of the respective single lenses increase as the difference in V number increases [16]. As a result of the lens manufacturer's equations, the radius of curvature increases with increasing effective focal length. As a result, an image defect can be reduced due to a certain reduction in the angle of incidence and a certain degree of refraction on the lens surface. Therefore, the use of a colorless binary provides not only the correction of chromatic aberration but also some degree of spherical aberration correction [17].

4. Conclusion

The first step in optical system design is the analysis of a particular imaging task and the definition of given/desired parameters. Simple calculations and considerations allow for determining the focal length of a required optical system. The start-up system is an optical setup that acts to provide the best imaging performance for a given imaging task. The start-up systems can be defined on the basis of the area of view and the f-number of an imaging system. Based on an appropriate start-up system, the optical setup is evaluated and optimized during an iterative process where manufacturing tolerances can also be taken into account. An optical system can be optimized directly or indirectly. Direct optimization can be defined as the modification of physical parameters such as radii of curvature or materials. Direct optimization is based on the definition and application of the utility function, taking into account variables (parameters to change) and imperfections (eg deviations).

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Review Article

AN OVERVIEW OF PERIOD POVERTY AND THE PUBLIC HEALTH IMPACT OF PROVIDING FREE FEMININE HYGIENE PRODUCTS

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Abstract: *Feminine hygiene products such as tampons, pads, and sanitary tissues are crucial to a menstruating person's health. This review outlines obstacles to accessing female hygiene products and the consequent downstream impacts on societal health, by compiling relevant articles. To perform this review, we performed a search for 'menstruation', 'challenges', 'costs', and 'obstacles' in PubMed, Google Scholar, EMBASE, and Cochrane. Feminine hygiene products are a multi-billion-dollar industry, and over the course of a menstruator's life, they spend between roughly $3000-$5000 on over 16,000 feminine hygiene products. Many financial barriers exist that prevent menstruators, most of whom self-identify as women, from accessing safe and healthy menstrual hygiene products. A disproportionately high number of women, especially women of color, live in poverty. As a result, purchasing feminine hygiene products often poses a substantial financial burden, sometimes preventing women from being able to buy feminine hygiene products at all or forcing them to choose between purchasing food or feminine hygiene products. This phenomenon is referred to as "period poverty." In conclusion, due to a lack of access to appropriate menstrual products, many women report substituting debris items, which leads to severe health complications such as toxic shock syndrome and cervical cancer. In addition to potential health risks, there are often negative social consequences associated with menstruation as many women report having to leave their workplace or school due to experiencing an emergency menstruation event and not finding feminine hygiene products publicly available. A plethora of slang words and negative cultural connotations are frequently associated with menstruation, and many women report feelings of stress and anxiety due to the many facets of menstruation symptom management and resource allocation. New York City made feminine hygiene products free in public schools, prisons, and homeless shelters, providing 323,000 menstruators with free products at a cost of roughly $5.88 per person per year, which is cost-effective. Nations such as Kenya, Australia, New Zealand, and Scotland have also led initiatives highlighting the cost-effective public health benefit of improving access to menstrual hygiene products.*

Keywords: *Period poverty, Feminine Hygiene Products, Public Health, New York City, Cost-Effectiveness*

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1. Introduction

Feminine hygiene products, such as tampons and pads, are a staple personal item for individuals who menstruate. Feminine hygiene products account for a multi-billion-dollar industry [1]. Since the average menstruator experiences one week of menstruation per month on average over the course of roughly forty years, the average menstruator experiences 480 periods in their lifetime [1]. Therefore, the

average menstruator is estimated to purchase upwards of 16,000 feminine hygiene products in their lifetime [2]. This amounts to burdensome lifetime costs that could range from roughly $3000 to over $5000, depending on an individual's preferences for tampons, pads, or other feminine hygiene products [1]. In addition, individuals who menstruate, a majority of whom identify as women, face further financial strains through state sales taxes on feminine hygiene products. Many of these taxes are imposed in states that do not levy taxes on products that are geared toward consumption by men, such as condoms with spermicide and medication for erectile dysfunction [3]. The purpose of this review is to highlight structural barriers experienced by women in accessing feminine hygiene products and to identify efficacious methods to improve healthcare outcomes for women through the subsidization of feminine hygiene products. Increasing access to feminine hygiene products will decrease healthcare expenditures from preventable conditions and manage them in less acute settings, both increasing the health of communities. This problem is faced by women across the globe, with disproportionately large impacts on minority populations, so providing free feminine hygiene products would be a step toward rectifying these inequities.

2. Materials and Methods

This paper was completed after searches were queried for 'menstruation' and variants of the words 'obstacles,' 'challenges,' and 'costs.' A preliminary search, performed on May 1st, 2021, yielded 32 articles, of which 9 were ultimately considered relevant for this review. Inclusion criteria consisted of English language articles, topic relevance, and verification of MEDLINE indexed journals. These searches were performed in PubMed, Google Scholar, EMBASE, and Cochrane. Summary findings of these searches are compiled in this review.

3. Results

3.1. Barriers to Feminine Hygiene Product Access

A total of nine articles were reached for inclusion in this study. A lack of access to feminine hygiene products exacerbates period poverty, which is a major public health issue that disproportionately affects women, particularly those with low socioeconomic status. Women with low socioeconomic statuses have the greatest structural and societal barriers to accessing adequate healthcare, which prompted our focus on this cohort as a first step in shedding light on this issue. Recent U.S. Census Bureau data suggests that compared to men, women are 35% more likely to be living in poverty [4]. Furthermore, 1 in 16 American women lives in extreme poverty, earning less than half of the income constituting the federal poverty line [4]. Poverty disproportionately affects women of color, as 23.1% of African American women, 22.7 of Native American women, 20.9% of Hispanic women, and 11.7% of Asian women live in poverty compared to 7.1% of white women [4]. In addition, approximately 29% of transgender and non-gender-conforming individuals are estimated to be living in poverty [5]. The stark poverty rate, especially among minority communities in the United States, translates to period inequality as 64% of low-income women were unable to afford feminine hygiene products at some point in 2018 [6]. Furthermore, 21% of low-income women have trouble affording feminine hygiene products on a monthly basis [6]. Nearly 50% of low-income women report having to choose between purchasing food and purchasing feminine hygiene products in 2018 [6]. Period inequality is especially experienced by poor mothers, who tend to focus their attention on their children rather than opting to fulfill their own basic needs first [6]. These barriers compositely increase obstacles to care disproportionately for women of lower socioeconomic classes, and addressing them would lessen health disparities experienced by communities.

3.2. Social Costs of Menstruating

Significant social costs exist in addition to the economic costs associated with access to feminine hygiene products. In situations in which a person menstruates unexpectedly without having feminine hygiene products, 79% of menstruators report using items such as napkins, paper towels, toilet paper, and even socks to address their necessity [1]. The use of such makeshift feminine hygiene products can be unsafe and possibly lead to complications such as infections, fertility issues, toxic shock syndrome, and cervical cancer [1]. However, using alternative products or items in times of extreme need is deemed acceptable by a majority of women given that most public bathrooms do not readily offer free feminine hygiene products [7-11]. Easy access to feminine hygiene products is crucial in order to prevent menstruations from having further detrimental impacts on an individual's productivity as well as their mental and emotional health, especially in emergency situations. During 72% of emergent menstruation situations, women have reported having to leave school or their workplace due to the unavailability of feminine hygiene products, citing feelings of panic, stress, and humiliation [1]. The social stigmatization of menstruation further highlights the need to ensure adequate access to proper feminine hygiene products. A study conducted by the International Women's Health Coalition revealed that worldwide, over 5,000 slang terms are used to refer to menstruation, many of which are profane or disparaging [12-13]. In addition, 5% of women report that they avoid bringing their purses to public restrooms to dodge potential stigma from others thinking they may be menstruating [1]. The social costs of menstruating are also disproportionately undertaken by minority populations.

3.3. Analyzing Access to Female Hygiene Products in New York

3.3.1 Improving Access to Feminine Hygiene Products

Access to feminine hygiene products is of paramount importance to women's mental, emotional, and physical health. The public benefit of providing free feminine hygiene products to a large group was recognized by New York City legislators, who in 2016 unanimously voted to provide free access to feminine hygiene products in homeless shelters, prisons, and New York City public schools [14]. This legislation was groundbreaking as it made New York City, the most populated city in the United States, the first American city to proactively provide assurance of access to feminine hygiene products. Mayor Bill de Blasio supported the legislation, stating that the goal for young women in school is to be focused on learning, the goal for women in a homeless shelter is to be focused on restoring their lives, and the goal for women in prison is to focus on their rehabilitation [15]. Providing free feminine hygiene products in these public settings allows women to pursue what is important to them without having to worry about the potential embarrassment or adverse health effects of menstruating and not having the proper products to use. In addition to the direct benefits of providing feminine hygiene products free of charge in public restrooms, news about legislation aiming to rectify period poverty brings menstruation into the limelight as something society acknowledges and is compassionate about rather than something that is stigmatized and hidden as it has historically been.

3.3.2 Costs Associated with Providing Free Feminine Hygiene Products

The aforementioned legislation in New York City had a first-year implementation cost of $4.2 million and an annual maintenance cost of $1.9 million in each subsequent year [14]. This program covers feminine hygiene products for approximately 323,000 menstruators each year, which averages out to about $5.88 per person per year [1]. These costs are minimal when compared to other public bathroom supplies. For example, the Pentagon spent $2 million annually on providing toilet paper in its bathrooms each year from 2010 to 2012 [1]. Since the Pentagon employed roughly 23,000 individuals in each of these years, the cost for providing toilet paper averaged to $86.96 per person, which is nearly 15 times greater than the estimated cost of providing feminine hygiene products in public facilities [1].

Furthermore, substituting debris for feminine hygiene products or keeping feminine hygiene products in place for an extended period of time can lead to significant illnesses that require medical care and occasionally hospitalization [7-8, 16-18]. Given the high costs associated with hospitalization, especially for individuals without comprehensive health insurance, providing free feminine hygiene products can be considered a preventative public health measure. Implementing free feminine hygiene products in highly visited venues and areas of interest will destigmatize and reduce the adverse events experienced by women who lack access to hygiene products.

4. Discussion

A handful of American states in addition to New York have made strides towards eliminating period poverty, but as 1.9 billion individuals menstruate around the world, access to feminine hygiene products is of obvious global concern [19]. Several countries have made headlines in recent years for their menstrual equity efforts. The first country in the world to abolish taxes on period products entirely was Kenya in 2004 [20]. Furthermore, since 2011, the Kenyan government has budgeted approximately $3 million annually to distribute free feminine hygiene products to schools and low-income communities [20]. Also of note, in 2018, Australia axed its controversial tampon tax that was in place for 20 years [21]. With this decision, pads and tampons were no longer classified as non-essential, a label that previously tagged feminine hygiene products with a whopping 10% goods and services tax [21]. In 2020, Scotland became the first country to make all period products free. The Scottish bill passed unanimously, making tampons and sanitary pads available free of charge at designated pharmacies, community centers, and youth clubs at an estimated cost to taxpayers of $32 million annually [22]. Additionally, in 2020, the New Zealand government announced that it would be backing a program investing $2.6 million to provide period products to high school students [23]. It is evident that eliminating period poverty and promoting menstruation equity is feasible and on the minds of global citizens and leaders abound, and other countries should take similar stances to improve their citizens' access to feminine hygiene products. More countries should strive to provide free feminine hygiene products to especially at-risk populations as the interventions of the aforementioned regions of the world have yielded benefits to women's health at a cost-effective, scalable rate.

5. Conclusion

When women do not have access to proper feminine hygiene products, it detrimentally affects their self-esteem, reducing their participation in the spheres of employment and education [24-25]. Our review highlights the structural inequities and barriers that women using feminine hygiene products face, and the granular analysis of New York suggests that a multi-pronged approach of disseminating feminine hygiene products may be the most effective and viable option. By ensuring women have free access to safe feminine hygiene products, governments can strive to reduce gender inequalities while also improving the health of women and other menstruators. An increased government focus on providing free menstrual hygiene products would proactively empower millions of women to take more control over their health.

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Ethical Statement

This paper is exempt from the Institutional Ethics Committee review since it does not involve human subjects.

Conflicts of Interest

All authors have no conflicts of interest to report.

Authors' Contribution

U.D., A.P., E.G.L., and B.D.G. all designed the article. U.D., A.P., E.G.L. wrote drafts. U.D., A.P., E.G.L., and B.D.G. critically reviewed the articles. U.D., A.P., E.G.L., and B.D.G. approved the article for submission.

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