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The target audience of the journal is all scientists working in the field of health, graduate students and researchers in this field.

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Middle Black Sea Journal of Health Science

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Examples: Hypotension is one of the most common and critical problems in hemodialysis patients (1,2).

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Chapter in Edited Book: Hornbeck P. Assay for antibody production. In: Colign JE. Kruisbeek AM, Marguiles DH, editors. Current Protocols in Immunology. New York: Greene Publishing Associates; 1991. p. 105-32.

Book with a Single Author: Fleiss JL. Statistical Methods for Rates and Proportions. Second Edition. New York: John Wiley and Sons; 1981. p. 105-32.

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Structure

Title

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Key words

Introduction

Methods

Results

Discussion

Conclusion

Acknowledgements

References (most 40)

Whole text should not exceed 4500 words except for resources and English summary.

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Structure

Title

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Key Words

Introduction

Methods

Results

Discussion

Conclusion

Acknowledgements

References (most 20)

Whole text should not exceed 2700 words except for resources and English summary.

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Title

Abstract (average 100-300 word)

Key words

Introduction

Case report

Discussion

Conclusion

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d) Review articles

Structure

Title

Abstract (average 200-400 word)

Key words

Introduction

The compilation text also including appropriate sub-headings,

Conclusion

Acknowledgements

References (most 50)

Whole text should not exceed 6550 words except for resources and English summary.

Middle Black Sea Journal of Health Science

FEBRUARY 2025 **VOLUME 11** **ISSUE 1**

CONTENTS

EDITORIAL

Our first issue of 2025

We are delighted to present original articles from various fields in this issue of our journal, aimed at offering new and valuable contributions to the world of science.
Enriched by the contributions of distinguished scientists, our content enhances the diversity of our journal.
We hope that the articles in this issue will make significant contributions to scientific knowledge, and we look forward to bringing you and again original works in future issues.

Prof. Dr. Ülkü KARAMAN

Editor

Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci **February 2025; 11(1): 1-9**

RESEARCH ARTICLE **DOI:** 10.19127/mbsjohs.1472536

Pregnant Women's Attitudes about the COVID-19 Vaccine

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Abstract

Objective: Detected in Wuhan, China in 2019, the coronavirus, which causes acute respiratory syndrome, is a global public health problem. Studies have also reported that COVID-19 infection poses a high risk for pregnant women. This study aimed to assess the attitudes of pregnant women toward the COVID-19 vaccine and the factors influencing these attitudes.

Methods: A descriptive and cross-sectional study was conducted with 280 pregnant women between April 7 and November 4, 2022. Data were collected using a Descriptive Information Form and the Attitudes Towards COVID-19 Vaccination Scale.

Results: The mean age of the participants was 27.04±5.53 years. The mean score on the positive attitude subscale of the Attitudes Towards COVID-19 Vaccination Scale was 3.46±0.91, while the mean score on the negative attitude subscale was 2.64±0.83. Pregnant women who were vaccinated or planned to be vaccinated had significantly more positive attitudes than those who were unvaccinated or did not plan to be vaccinated ($p<0.05$).

Conclusion: The study revealed that pregnant women who were vaccinated or intended to receive the vaccine exhibited more positive attitudes toward COVID-19 vaccination than those who refused the vaccine or were undecided. However, vaccine hesitancy persists, largely due to insufficient information regarding the efficacy and potential side effects of newly developed vaccines during pregnancy.

Keyword: Vaccine behavior, COVID-19, pregnancy, vaccination

Suggested Citation: Solt Kırca A, Karaman S, Hur S, Cambaz Z. Pregnant Women's Attitudes about the COVID-19 Vaccine. Mid Blac Sea Journal of Health Sci, 2025;11(1):1-9.

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INTRODUCTION

The coronavirus, first identified in Wuhan, China, in 2019, causing acute respiratory syndrome, has remained a significant public health concern globally (1,2). Studies have shown that COVID-19 infection poses a higher risk for pregnant women compared to the general population (2). Physiological changes and immune suppression during pregnancy increase susceptibility to infections, placing both the mother and fetus at risk (3). Recognizing pregnant women as a vulnerable population has led to their prioritization for COVID-19 vaccination (4).

Research indicates that pregnant women who receive the COVID-19 vaccine are at a reduced risk of preterm birth, neonatal intensive care unit admissions, stillbirth, and maternal mortality compared to unvaccinated pregnant women (5). However, the rapid development of COVID-19 vaccines, their inclusion of viral agents or components, and insufficient research on their effects in specific populations have raised concerns regarding their safety during pregnancy. Such uncertainties have contributed to vaccine hesitancy among certain groups, including pregnant women (3).

Although vaccination has been shown to mitigate perinatal complications associated with COVID-19, hesitancy during the perinatal period has resulted in low vaccination rates. Therefore, understanding pregnant women's vaccine intentions and identifying their perceptions and attitudes toward vaccination is critical (4,6).

Currently, there is limited research evaluating pregnant women's attitudes toward the COVID-19 vaccine. This study aims to explore the attitudes of pregnant women regarding COVID-19 vaccination and the factors influencing these attitudes.

METHODS

This study was conducted at Tekirdağ Çorlu State Hospital between April 7 and November 31, 2022. The total number of pregnant women who presented to the Gynecology Polyclinic at the hospital between January 1 and December 31, 2021, was 1,940. The sample size was calculated as 238 pregnant women using the known population sampling formula via Raosoft sample size calculation software (α=0.05, 1-β=0.90). To account for potential attrition, a total of 280 pregnant women were included in the study (http://www.raosoft.com/samplesize.html).

Data were collected using a structured questionnaire administered by the researcher through face-to-face interviews. Inclusion criteria for participation in the study were voluntary agreement to participate, age ≥18 years, being in the first, second, or third trimester of pregnancy, and having either a singleton or multiple pregnancy.

Measures and instruments

Descriptive Information Form: This form was developed by researchers based on a comprehensive review of the literature (6, 7, 8).

Attitudes Towards COVID-19 Vaccine Scale: This scale was originally developed by Genis et al. in 2020. It consists of nine items divided into two sub-dimensions. Items within the negative attitude subscale are reverse-scored. Cronbach's alpha coefficient for the overall scale is reported as 0.80 (6). In the current study, Cronbach's alpha coefficients were calculated as 0.92 for the positive sub-dimension and 0.85 for the negative sub-dimension, indicating high internal consistency.

Ethical consideration

Ethical approval was obtained from the Kırklareli University Clinical Research Ethics Committee (Reference Number: E-69456409-199-4253069, Date: 03.03.2022). Institutional permission was granted by the Tekirdağ Provincial Health Directorate on 07.04.2022. All procedures adhered to the ethical standards set forth by institutional and/or national research committees and were conducted in accordance with the principles of the 1964 Helsinki Declaration and its later amendments or comparable ethical guidelines.

Statistical analysis

The Kolmogorov-Smirnov test was applied to assess the normality of the data. Descriptive statistics and the Chi-square test were used for the comparison of categorical variables. The Mann-Whitney U test was employed to compare non-normally distributed data between two groups, while the Kruskal-Wallis test was used for comparisons among more than two groups. A p-value of <0.05 was considered statistically significant.

RESULTS

The mean age of the pregnant women included in the study was 27.04±5.53 years. Among the participants, 40.4% were primary school graduates, 85.4% had not contracted COVID-19 during pregnancy, 65.7% had received at least one dose of a COVID-19 vaccine, and 42.5% had obtained information about the vaccine from healthcare personnel (Table 1).

The analysis of the mean scores of pregnant women on the subscales of the Attitudes Towards COVID-19 Vaccine Scale (Table 2) revealed a mean score of 3.46±0.91 on the positive attitude subscale and 2.64±0.83 on the negative attitude subscale. A statistically significant difference was observed between the mean scores of pregnant women who had received the COVID-19 vaccine and those who had not, on both the positive and negative attitude subscales of the Attitudes Towards COVID-19 Vaccine Scale (Table 2).

In the study, a statistically significant difference was determined between the positive and negative attitude subscale scores of the Attitudes towards COVID-19 Vaccine Scale

obtained by pregnant women who responded using one of the "I have been vaccinated," "I will be vaccinated," "I am undecided," or "I do not think I will be vaccinated" statements (p=.000, p=.000). As a result of the further analysis conducted to determine which groups the difference originated from, it was determined that there was no statistically significant difference between the positive attitude subscale scores of the Attitudes towards the COVID-19 Vaccine Scale obtained by pregnant women who responded they did not want to be vaccinated and they were undecided about being vaccinated (p = .088), while there was a statistically significant difference between the positive attitude subscale scores of the Attitudes towards the COVID-19 Vaccine Scale obtained by pregnant women who responded they did not think of being vaccinated and they would be vaccinated, they did not think of being vaccinated and they had been vaccinated, they were undecided and they would be vaccinated, and they were undecided and they were vaccinated (p=.000, p=.000, p=.037, and p=.000). While it was determined that there was no statistically significant difference between the mean negative attitude subscale scores of the Attitudes towards COVID-19 Vaccine Scale In the study, a statistically significant difference was found between the positive and negative attitude subscale scores of the Attitudes Towards COVID-19 Vaccine Scale among pregnant women who responded with one of the following statements: "I have been vaccinated," "I will be vaccinated," "I am undecided," or "I do not think I will be vaccinated" (p=.000, p=.000). Further analysis to identify the sources of the differences revealed that there was no statistically significant difference between the positive attitude subscale scores of pregnant women who stated they did not want to be vaccinated and those who were undecided about vaccination (p = .088). However, a statistically significant difference was found between the positive attitude subscale scores of pregnant women who responded that they did not think they would be vaccinated and those who responded that they would be vaccinated, that they had been vaccinated, that they were undecided, or that they were vaccinated (p = .000, p = .000, p = .037, and p = .000, respectively).

Moreover, while no statistically significant difference was found between the mean negative attitude subscale scores of the Attitudes Towards COVID-19 Vaccine Scale among pregnant women who responded they would be vaccinated and those who were undecided (p = .585), a statistically significant difference was observed between the mean negative attitude subscale scores of pregnant women who responded that they had been vaccinated and those who were undecided, had been vaccinated and did not think they would get vaccinated, would be vaccinated and did not

think they would get vaccinated, and had been vaccinated and did not think they would get vaccinated ($p = .014$, $p = .000$, $p = .000$, and $p = .026$, respectively) (Table 3).

Table 1. Distribution of Sociodemographic and Descriptive Characteristics of Pregnant Women

Variables	**Mean±ss**	**Min-Max**
Age	27.04±5.53	(18-49)
Pregnancy weeks	29.09±10.70	(5-42)
	n	%
Education statues		
Illiterate	14	5.0
Primary education	113	40.4
High school	76	27.1
University	77	27.5
Economic statues		
Low	104	37.1
Middle	138	49.3
High	38	13.6
Use of cigaret		
Yes	42	15.0
No	238	85.0
Total	**280**	**100**

Table 2. Comparison of Characteristics of Pregnant Women Regarding Covid 19 Infection

Variables	**n (280)**	**%**
Has anyone in your family had covid19 infection?		
Yes	179	63.9
No	101	36.1
Did you have a covid19 infection during your pregnancy?		
Yes	41	14.6
1. Trimester (1 – 13 weeks)	10	3.6
2. Trimester (14 – 26 weeks)	28	9.9
3. Trimester (27 – 41 weeks)	3	1.1
No	239	85.4
Have you been vaccinated against Covid 19?		
Yes	184	65.7
Before pregnancy	152	54.3
During pregnancy	32	11.4
Not vaccinated	96	34.3
Are you planning to be vaccinated against Covid 19?		
Vaccination	184	65.7
I will be vaccinated	16	5.7
Undecided	23	8.2
I don't plan to get vaccinated	57	20.4
Do you think the Covid-19 vaccine is safe and protective for pregnant women?		
I think	93	33.2
Undecided	89	31.8
I don't think	98	35.0
Where/whom did you get information about the Covid-19 Vaccine?		
Institutions such as Ministry of Health / NGOs	65	23.2
Health personnel	119	42.5
From my friend	38	13.6
Television/radio	121	43.2
Book/magazine/newspaper	9	3.2
Conference/seminar	8	2.9
Social media	74	26.4
Total	**280**	**100**

Table 3. Comparison of Pregnant Women's Attitudes Towards COVID-19 Vaccination Scale Subscale Mean Scores

Variables	Positive attitude score (Min-Max:1-5)	Negative attitude score (Min-Max:1-5)
	3.46±0.91	2.64±0.83
Have you been vaccinated against COVID 19?		
Yes	3.81±.72	2.34±.71
No	2.82±.88	3.20±.74
*p	.000	.000
Are you considering getting vaccinated against COVID 19?		
Vaccination	3.81±.72	2.34±.71
I will be vaccinated	3.83±.66	2.51±.61
Undecided	3.19±.43	2.85±.53
I don't plan to get vaccinated	2.37±.74	3.53±66
**p	.000	.000

*Mann whitney u test, ** Kruskall Wallis test

DISCUSSION

In the study, it was determined that 54.3% of the pregnant women had received the COVID-19 vaccine prior to pregnancy, 11.4% during pregnancy, and 5.7% were planning to get vaccinated. Approximately 1 in 4 pregnant women were either undecided or reported that they would not be vaccinated. A review of the international literature revealed that 8.2% of pregnant women in a study conducted in Italy, 71.2% of 221,190 pregnant participants in a study conducted in Canada (as of December 2021), and 84.3% of 140 pregnant women in a study conducted in Saudi Arabia had been vaccinated either during or before pregnancy (4, 9, 10). Additionally, a 2021 study conducted in the United States assessed women aged 18-49 who had received at least one dose of the vaccine, revealing that pregnant women had the lowest vaccination rate (45.1%) (11). Local literature reported that 76.3% of 375 pregnant women had been vaccinated (12).

It was reported that 57.5% of 193 pregnant women in a study conducted in Canada and 43% of 387 pregnant women in a study conducted in California accepted the COVID-19 vaccine (13, 14). Similarly, a study by Sutton et al. (2021), involving 1,012 pregnant, non-pregnant, and breastfeeding women, found that pregnant women who agreed to be vaccinated or intended to be vaccinated had the lowest rate of acceptance (15). In a study involving 538 pregnant women who had not yet been vaccinated, it was reported that 82.7% agreed to receive the vaccine. Additionally, pregnant women who had been diagnosed with COVID-19 during pregnancy and were concerned about the fetus found vaccination during pregnancy to be more risky (4). A meta-analysis of 16,926 pregnant women indicated that 47% of them agreed to be vaccinated (16). A local study reported that only 2% of pregnant women had been vaccinated (17). In light of our study and the existing literature, it can be concluded that the vaccination rate is influenced by the possibility that the unborn or future babies may be affected. This is directly related to the perceived safety of receiving the vaccine during pregnancy, with many women

either already vaccinated or planning to be vaccinated based on these concerns.

In this study, it was determined that one-third of pregnant women considered receiving the COVID-19 vaccine during pregnancy to be safe and protective, one-third were undecided, and one-third did not find it safe or protective. A review of foreign literature revealed that 40% of pregnant women who had not been vaccinated expressed concerns about the vaccine's safety in a study conducted in Sub-Saharan Africa (18). Additionally, another study found that nearly all pregnant women who refused vaccination did so on the grounds that they did not find the vaccine safe (4, 13). In the local literature, 9.2% of pregnant women reported finding the vaccine safe (17). Both this study and existing literature indicate that pregnant women generally exhibited more positive attitudes toward the COVID-19 vaccine. Those who had been vaccinated or were considering vaccination showed significantly more favorable attitudes (17, 19).

CONCLUSION

It was concluded that hesitations regarding vaccines stemmed from their recent development, coupled with insufficient information about their effectiveness and potential side effects during pregnancy. This concern was not unique to pregnant women in our country but was also observed in special situations such as breastfeeding, pregnancy planning, and having chronic conditions.

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The Relationship Between Nurses' Mindfulness and Care-Focused Nurse-Patient Interaction

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Abstract

Objective: The aim of this research is to determine the relationship between nurses mindfulness levels and care-oriented patient-nurse interaction.

Methods: The study, which is descriptive and relationship-seeking study, was conducted with 330 nurses working in a university hospital. “Socio-Demographic Information Form”, “Care-Oriented Patient-Nurse Interaction Scale” and “Mindfulness Scale” were used as data collection tools. Skewness and kurtosis coefficients, percentage and frequency distribution, Pearson correlation analysis and simple linear regression analysis were used in the statistical evaluation of the data.

Results: It was determined that 78.5% of the participants were women, 57.3% were married, 77.3% had a bachelor’s degree, 67% were at the middle-income level, 79.1% had 10 years or less of professional experience, 55.5% chose the profession voluntarily, % It was determined that 83.9% did not have a chronic disease and 96.1% did not have a mental illness. It was etermined that there is a significant relationship between the Nurses’ Conscious Awareness Scale scores and the Care-Oriented Patient-Nurse Interaction Scale Materiality Dimension total and sub-dimension scores ($p<0.05$). It has been determined that mindful awareness explains 11.5% ofthe importance given to care-oriented nurse-patient interaction.

Conclusion: It has been concluded that nurses’ mindfulness levels affect the importancethey attach to care-oriented patient-nurse interaction; and, as the level of mindfulness increases, the importance given to care-oriented nurse-patient interaction also increases.

Keyword: Nursing, mindfulness, nurse-patient interaction, nursing care.

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INTRODUCTION

Nursing has a dynamic process that takes its source from human needs, is born to serve the society, defines helping healthy individuals not only in case of illness but also in healthy individuals as its basic function, treats the individual as a whole with his/her environment and provides care, plans to protect and improve the health of the society and implements and evaluates these plans (1, 2). In this respect, nurses constitute the group that interacts most with patients and healthy individuals in health services (3). While the nursing profession is based on the concepts of human and care, its main function is care. Care, which is of great importance in the healing process of patients, is among the important factors that affect the satisfaction of patients in health care and increase the quality of health-care. Being aware of the needs and expectations of patients increases the quality of nursing care (4). Peplau, one of the important nursing theorists who based nursing theory on the "patient-nurse" relationship, defines nursing as an interpersonal process consisting of communication between two or more individuals in line with common goals (2). When the literature is examined, it is seen that the mutual interaction of nurses with patients and healthy individuals plays an active role in the quality of care provided to the individual (5-7). The fact that nurses consider the patient as a whole and meet their needs while providing care helps the patient to receive better care and increase their satisfaction (8).

Watson, one of the nursing theorists, argues that the focus of the nursing profession is care in the 'Human Care Theory (HCT)' and that practices should be carried out by considering the individual as a whole in care (9). At the center of care-oriented patient-nurse interaction, the needs of the individual caregiver are included and met (10). In the literature, there are studies on the levels of care-oriented nurse-patient interaction of nurses and nursing students. These studies reveal that nurses have high attitudes and perceptions towards care-oriented nurse-patient interactions and that they attach importance to care-oriented patient-nurse interactions (5-7, 11). Nurses' attitudes towards care-oriented patient-nurse interaction are affected by factors such as their philosophies about health, human and nursing, their experiences, and their interpersonal relationship skills (2). On the other hand, in order for care-oriented patient-nurse interaction to be effective, nurses must first know themselves well, be aware of their impressions on the individuals around them and have high awareness of meeting the needs of the patients they care for (8, 12). It is important for nurses to pay attention with curiosity, kindness and compassion to what is happening in themselves, the environment and the individuals they care for during the care process. This situation points to the importance of the concept of

mindfulness, which has attracted the attention of researchers in recent years and has an ancient philosophy, in terms of nursing (13-15).

Mindfulness is defined as being in the present moment, being aware of our current experiences, and focusing on what is happening in the moment without judging what is happening in the internal and external world (15, 16). Mindfulness is the state of being aware of the experience in the present moment and accepting this experience in a friendly, compassionate, kind, non-judgmental way (17). Being aware of the people around us, their activities and our environment allows you to enjoy your life experience as a whole. One of the popular concepts of recent times, “Mindfulness”, or “Conscious Awareness” as it is translated into Turkish, is actually a kind of spiritual skill, although its origin is based on the concept of “Awareness” of Buddhism and Eastern Philosophy. Mindfulness is the last step of enlightenment and maturing the soul and people have been using this technique for thousands of years (18-21).

In the studies conducted, it was concluded that the high level of awareness of the individual reduces the stress, anxiety and depression experienced (14, 18, 22). There are various studies on mindfulness in literature. In a study conducted with nurses, it was found that the mindfulness levels of nurses were at a medium level (12). In another study conducted with nursing students, it was concluded that students' mindfulness levels were above average (18). In the literature, there are studies evaluating the effectiveness of interventions to increase the mindfulness levels of nurses (23, 24). In a study, it was concluded that burnout and stress levels of nurses decreased, and mindfulness levels increased after training (23). On the other hand, when the literature was examined, it was determined that there were limited studies on the subject and no study was found to examine the relationship between nurses' mindfulness level and care-oriented patient-nurse interaction. The results obtained from the studies show that the level of mindfulness is important for nurses. In line with this goal, it is thought that determining the relationship between these two concepts, which are important for nursing, will contribute to literature.

The aim of the study was to examine the relationship between nurses' level of mindfulness and care-oriented patient-nurse interaction.

Research Questions

What is the level of conscious awareness of nurses?

What is the level of caring patient-nurse interaction of nurses?

What is the effect of the level of conscious awareness of nurses on caring patient-nurse interaction?

METHODS

Type of Research

This research employs a descriptive and relationship-seeking study.

Time of Research

The study was conducted in a university hospital in Türkiye between February 2021 and June 2022.

Population and Sample of the Study

The population of the study consisted of 900 nurses working in a university hospital in Türkiye and the sample consisted of 330 nurses who met the research criteria. In this study, random sampling method was used. In the power analysis performed using the G*Power V 3.1.9.6 program, the minimum number of participants to be included in the research was determined as 100 participants in order to conduct the research with 95% confidence (1-α), 95% (1-β) and -0.35 correlation value.

Clinical nurses who voluntarily agreed to participate in the study, completed the questionnaires sent via social media accounts (Facebook, Instagram and Whatsapp) via smartphones, and worked in the hospital during the data collection process were included in the study. Nurses who did not meet these criteria were not included in the study. The study was completed with 330 nurses who met the study criteria between the dates of the study.

Data Collection

The data collection process of the study coincided with the Covid-19 pandemic period. The restrictive measures taken during this period were observed throughout the research, and the online questionnaire created with Google Form was used as the data collection method in the research. First of all, information about the research was announced to nurses via social media accounts, and nurses who met the research criteria were included in the study.

Data Collection Tools

The data were collected using the "Socio-Demographic Information Form" created by the researcher to collect information on the descriptive characteristics of the nurses, the "Care-Focused Patient-Nurse Interaction Scale (CFNPIS)" to determine their attitudes and behaviors regarding care, and the "Mindfulness Scale (MS)" to determine their level of mindfulness.

Socio-Demographic Information Form

This form, created to determine the descriptive characteristics of nurses, consists of 9 questions created in line with the literature (7, 8, 12).

Care-Focused Nurse-Patient Interaction Scale (CFNPIS)

It was developed by Cossette et al. based on Watson's Care Theory in 2005 to assess nurses' attitudes and behaviors regarding care. Turkish adaptation of the scale was conducted by Atar and Aştı in 2012. The scale consists of 3 sub-dimensions as "Materiality", "Competence",

"Applicability" and 10 guiding subscales as "Humanism", "Hope", "Sensitivity", "Helping relationship", "Expressing emotions", "Problem solving", "Teaching", "Environment", "Needs", "Spirituality". The scale has a total of 70 items. In the five-point Likert-type scale, the importance of the items is questioned and the participants are asked to choose one of the following options: "not at all" (1), "somewhat" (2), "moderately" (3), "very much" (4), "extremely" (5). The lowest score that can be obtained from the scale is 70 and the highest score is 350. As the individuals' scores on the scale increase, their attitudes and behaviors towards care-oriented nurse-patient interaction increase positively (Atar & Aştı, 2012). The Cronbach Alpha reliability coefficient for the importance dimension of this study was 0.91 in the importance dimension. In order to evaluate how important the conscious awareness of the care-oriented nurse-patient interaction, which is appropriate for the purpose of the study, the data were evaluated by considering the 'importance' dimension from the scale dimensions (25, 26).

Mindfulness Scale (MS)

The mindfulness scale was developed by Brown and Ryan in 2003 (27). It consists of 15 items and has a six-point Likert scale ranging from "almost always" to "almost never". The lowest score that can be obtained from the scale is 15 and the highest score is 90, and the increase in the total score indicates an increase in the level of mindfulness. Turkish adaptation was conducted by Özyeşil et al. (2011) (21). In this study, the Cronbach Alpha value of the scale was calculated as 0.89. In 2011, the total score obtained from the scale revised by Çatak is equal to the average of the sum of the items, and a high average score indicates that individuals have a high level of mindfulness (21, 27, 28).

Statistical analysis

The analysis of the data in the study was carried out in the SPSS 22.0 program, and the statistical significance level (p) was taken as 0.05. Skewness and kurtosis coefficients were used to determine the suitability of the data for normal distribution, percentage and frequency distribution were used to determine the descriptive characteristics of the nurses, Pearson correlation analysis and simple linear regression analysis were used to determine and explain the relationships between the scales.

Ethical Aspects of the Study

Before starting the research, permission was obtained from the Social and Human Sciences Ethics Committee of the university where the research was conducted (Date: 25.11.2020; Number: 2020/794) and the management of the hospital where the research was conducted (Number: E-15374210-100-11448).

Permission was obtained from the researchers for the scales used in the study. In addition, all nurses included in the study were informed

about the research and their a digital informed consent form consent was obtained.

RESULTS

It was determined that 78.5% of the nurses were female, 57.3% were married, 77.3% were undergraduate graduates, 67% were middle income level and the mean age was 28.54±6.54 years. In addition, 79.1% of the nurses had 10 years or less of professional experience, 55.5% chose the profession voluntarily, 83.9% had no chronic disease and 96.1% had no mental illness (Table 1).

The mean score of the nurses on the MS was 63.77±12.77, and the mean total score of the CFNPIS Materiality Dimension was 294.44±36.30. The mean scores of the sub-dimensions of the CFNPIS Materiality Dimension were 24.79±3.81 for Humanism, 29.87±4.01 for Hope, 23.99±3.96 for Sensitivity, 29.89±3.76 for Helping Relationship, 29.89±3.76 for Expressing Emotions, and 29.89±3.76 for Expressing Emotions. 76, 24.64±3.54 for Expressing Emotions, 24.39±3.98 for Problem Solving, 37.53±5.36 for Teaching, 30.06±3.97 for Environment, 44.08±5.50 for Needs and 25.19±3.84 for Spirituality.

It was determined that there was a positive and moderately significant relationship between the MS scores of the nurses and CFNPIS Materiality Dimension total and Humanism, Hope, Helping Relationship, and Environment sub-dimensions ($p<0.001$; Table 2). It was determined that there was a positive and low level significant relationship between the MS scores and the CFNPIS Materiality Dimension sub-dimensions of Sensitivity, Expression of Emotions, Problem Solving, Teaching, Needs and Spirituality ($p<0.001$; Table 2).

In order to determine the effect of nurses' mindfulness levels on the importance they attach to care-oriented nurse-patient interaction, a total of 11 different regression models were established between the MS and the total and sub-dimensions of the CFNPIS Materiality Dimension (Table 3). It was determined that there was a significant correlation between the BFQ scores of the nurses and the total and sub-dimension scores of the CFNPIS Materiality Dimension ($p<0.001$). It was determined that mindfulness explained 11.5% ($R2=0.115$) of the importance given to care-oriented nurse-patient interaction (Table 3). As the level of mindfulness of nurses increases, the importance they attach to care-oriented nurse-patient interaction also increases ($\beta=0.338$; Table 3). As a result of the regression analysis, it was determined that the level of mindfulness of the nurses explained 15.5% ($R2=0.155$) of the importance given to humanism; 14.6% ($R2=0.146$) of the importance given to hope; 6.9% ($R2=0.069$) of the importance given to sensitivity; 12.3% ($R2=0.123$) of the importance given to helping relationship; and 5.8% ($R2=0.058$) of the

importance given to expression of emotions (Table 3). As the level of mindfulness of the nurses increases, the importance they attach to humanism (β=0.394), hope (β=0.383), sensitivity (β=0.383), helping relationship (β=0.263), helping relationship (β=0.350), and expression of emotions (β=0.241) also increases (Table 3). It was found that the level of mindfulness of nurses explained 4.9% of the importance given to problem solving (R2=0.049); 4.5% of the importance given to teaching (R2=0.045); 10.1% of the importance given to the environment (R2=0.101); 8.7% of the importance given to needs (R2=0.087); and 8.8% of the importance given to spirituality (R2=0.088). As the level of mindfulness of nurses increases, the importance they attach to problem solving (β=0.221), teaching (β=0.212), environment (β=0.318), needs (β=0.295), and spirituality (β=0.296) also increases (Table 3).

Table-1. Distribution of descriptive characteristics of nurses (n=330)

Descriptive Characteristics		**Number (n)**	**Percentage (%)**
Gender	Woman	259	78.5
	Male	71	21.5
Marital Status	Married	189	57.3
	Single	141	42.7
Education Status	High Degree	37	11.2
	License	255	77.3
	Postgraduate	38	11.5
Income Level	Low	97	29.4
	Middle	221	67.0
	High	12	3.6
Professional Experience	10 years and below	261	79.1
	11-20 years	48	14.5
	21 years and above	21	6.4
Reason for Choosing Profession	Own will	183	55.5
	Family/environment request	93	28.2
	Ease of finding a job	54	16.4
Chronic Disease Status	Yes	53	16.1
	No	277	83.9
Mental Illness Status	Yes	13	3.9
	No	317	96.1
		Mean	**SD**
Age (Mean ± Standard Deviation)		28.54	6.54

Table-2. The relationship between total and subscale scores in the materiality dimension of the MS and the CFNPIS

		CFNPIS Materiality Dimension	**Humanism**	**Hope**	**Sensitivity**	**Helping Relationship**	**Expressing Emotions**	**Problem Solving**	**Teaching**	**Environment**	**Needs**	**Spirituality**
MS	r	0.338	0.394	0.383	0.263	0.350	0.241	0.221	0.212	0.318	0.295	0.296
	*p	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**

r: Correlation coefficient; * Pearson correlation analysis

Table-3. Regression analysis results between MS total and CFNPIS materiality dimension total and subscales

Dependent Variable	Independent Variable	β_1	β_2	t	p	% 95 Confidence Interval		Model Results		
								R^2	F	p
CFNPIS Materiality Dimension	Fixed	233.07		24.26	**0.000**	214.18	251.97	0.11	42.43	**0.000**
	MS	0.96	0.33	6.51	**0.000**	0.67	1.25			
Humanism Subdimension	Fixed	17.28		17.53	**0.000**	15.34	19.22	0.15	60.38	**0.000**
	MS	0.11	0.39	7.77	**0.000**	0.08	0.14			
Hope Subdimension	Fixed	22.21		21.34	**0.000**	20.16	24.26	0.14	56.21	**0.000**
	MS	0.12	0.38	7.49	**0.000**	0.09	0.15			
Sensitivity Sub Dimension	Fixed	18.78		17.76	**0.000**	16.66	20.89	0.06	24.43	**0.000**
	MS	0.08	0.26	4.94	**0.000**	0.04	0.11			
Helping Relationship Subdimension	Fixed	23.31		23.53	**0.000**	21.36	25.26	0.12	45.90	**0.000**
	MS	0.10	0.35	6.77	**0.000**	0.07	0.13			
Expression of Emotions Subdimension	Fixed	20.37		21.10	**0.000**	18.47	22.27	0.05	20.24	**0.000**
	MS	0.06	0.24	4.50	**0.000**	0.03	0.09			
Problem Solving Subdimension	Fixed	19.99		18.33	**0.000**	17.85	22.14	0.04	16.87	**0.000**
	MS	0.06	0.22	4.10	**0.000**	0.03	0.10			
Teaching Subdimension	Fixed	31.85		21.64	**0.000**	28.95	34.74	0.04	15.48	**0.000**
	MS	0.08	0.21	3.93	**0.000**	0.04	0.13			
Environment Subdimension	Fixed	23.76		22.45	**0.000**	21.68	25.84	0.10	36.78	**0.000**
	MS	0.09	0.31	6.50	**0.000**	0.06	0.13			
Needs Subdimension	Fixed	35.97		24.35	**0.000**	33.07	38.88	0.08	31.30	**0.000**
	MS	0.12	0.29	5.59	**0.000**	0.08	0.17			
Spirituality Subdimension	Fixed	19.52		18.94	**0.000**	17.49	21.54	0.08	31.53	**0.000**
	MS	0.08	0.29	5.61	**0.000**	0.05	0.12			

* Simple Linear Regression Analysis

DISCUSSION

The findings obtained from this study, which examined the relationship between nurses' level of mindfulness and care-oriented nurse-patient interaction, are discussed in this section in line with the relevant literature.

It was found that the nurses participating in the study had a moderate level of mindfulness. Similar results were found in another study conducted with nurses working in a university hospital and it was determined that the mindfulness levels of the nurses included in the study were at a medium level (12). In addition, it was determined in the study that nurses had a positive attitude towards the importance of care-oriented patient-nurse interaction. Similar results were obtained in studies conducted with nurses working in university hospitals (8), COVID-19 services and intensive care units (29) and it was determined that nurses had a positive perception of the importance of care-oriented patient-nurse interaction.

It was found that as the level of mindfulness of the nurses participating in the study increased, the importance they gave to care-oriented nurse-patient interaction also increased ($p<0.001$). In addition, it was determined that the level of mindfulness of the nurses affected the importance given to care-oriented nurse-patient interaction (Table 3). In the study, it was

found that the increase in the level of mindfulness of nurses positively affected the importance given to humanism, hope, sensitivity, helping relationship, expression of emotions, problem solving, teaching, environment, needs, and spirituality (Table 3). In the literature, there are separate studies on mindfulness and care-oriented nurse-patient interaction in nurses (7, 8, 11, 12, 23). However, no study was found in which the two topics were addressed together. Mindfulness skill has an important place in accepting oneself and other individuals without judgment, increasing empathy and compassion, increasing the sense of morality, encouraging the individual, leaving the autopilot, responding consciously to what is happening in the moment, and increasing the individual's self-discipline (30). Increasing mindfulness helps the individual to realize feelings of love, compassion and forgiveness and increases the level of self-understanding (21). In this respect, mindfulness is to produce results that overlap with the cognitive and affective skills inherent in nursing care. Watson argues in the Human Care Theory that nursing care should be humanistic, holistic and conscious in line with a certain goal (31). In the care-oriented nurse-patient interaction, the fact that nurses are aware of their own situation against the patient and engage in helping behaviors is effective in making the care honest, sincere and conscious (1). Because nurses with high awareness are aware of their own emotional states. It has been emphasized in many studies that when nurses are aware of their strengths and weaknesses, they act more consciously in meeting the needs of patients (32, 33). In this context, nurses with a high level of mindfulness approach wisely in interaction with both themselves and the individuals they care for.

CONCLUSION

In this study, it was concluded that the mindfulness levels of nurses affect the care-oriented patient-nurse interaction, and as the mindfulness levels increase, the importance given to care-oriented nurse-patient interaction increases. In addition, according to the results obtained from the study, nurses' high levels of mindfulness increase the importance given to the concepts of humanism, hope, sensitivity, helping relationship, expression of emotions, problem solving, teaching, environment, needs, and spirituality. Based on these results, it is recommended to start implementing strategies to increase the mindfulness levels of nurses from university education periods, to include practices to increase mindfulness levels in in-service trainings, and to increase the number of studies that address the mindfulness levels of nurses and care-oriented nurse-patient interaction.

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The Cost of The Use of Prophylactic Anticoagulant Drugs in the Covid-19 Pandemic on the Late Period of Neurosurgery Practice

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Abstract

Objective: After being reported for in Wuhan, China, -stranded RNA coronavirus, COVID-19 leading to the deaths of thousands of people. Patients hospitalized in intensive care units (ICUs) who develop acute respiratory distress syndrome (ARDS) due to COVID-19 typically exhibit respiratory and digestive system symptoms. However, coagulopathy, which indicates a poor prognosis, may also develop in some patients receiving care in ICUs.This article aims to examine the economic consequences of prophylactic anticoagulant and antiplatelet drug use on neurosurgery practice during the late period of the COVID-19 pandemic.

Methods: This study retrospectively examined patients hospitalized for surgical treatment in the Neurosurgery Clinic of Ordu University Training and Research Hospital between January 1 and December 31, 2022. A total of 38 out of 320 patients were diagnosed with COVID-19, and cost analysis was specifically performed on these patients. Data were obtained from the hospital's data system.

Results: An increase in costs was observed in both spine surgery and cranial surgery due to drug use. The Kruskal-Wallis Test showed a significant difference in bed costs between patients who received anticoagulant or antiplatelet-anticoaggregant medication and those who did not (P=.000).

Conclusion: The use of prophylactic anticoagulant and antiplatelet drugs significantly extended the length of hospital stay for patients in both pre-operative and post-operative periods, resulting in increased costs for the social security institution.

Keyword: COVID-19, anticoagulant drugs, antiplatelet drugs, treatment cost, spinal surgery, cranial surgery, healthcare economics

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INTRODUCTION

After being reported for the first time in Wuhan, China, the single-stranded RNA coronavirus, COVID-19, has spread rapidly around the world, leading to the deaths of thousands of people (1, 2). Patients hospitalized in intensive care units (ICUs) who develop acute respiratory distress syndrome (ARDS) due to COVID-19 typically exhibit respiratory and digestive system symptoms (3, 4). However, coagulopathy, which indicates a poor prognosis, may also develop in some patients receiving care in ICUs (5).

The devastating effects of pandemics throughout history have impacted not only human health but also various social, economic, and political spheres. Although these effects generally diminish after a pandemic end, they can persist for many years (6). The COVID-19 pandemic has had far-reaching and detrimental consequences, affected individuals and caused disruptions in the economic infrastructure of insurance companies, social security institutions, and entire nations. The social and economic impacts of COVID-19 are already worse than those of the Second World War (7).

The COVID-19 pandemic has profoundly impacted the field of neurosurgery and the dedicated professionals within it. The pandemic necessitated a significant overhaul of surgical and medical treatment protocols at neurosurgery clinics (8). New issues were encountered when returning to routine neurosurgery not only during the pandemic but also afterward. One of these issues was the complications caused by anticoagulant drugs administered to patients at risk of thrombosis during the COVID-19 pandemic. The association between COVID-19 infection and thrombosis has been demonstrated in many clinical studies (9). Consequently, COVID-19 treatment includes thrombosis therapy using anticoagulants and antiplatelet drugs (10).

Anticoagulant and antiplatelet medications, administered to protect COVID-19 patients from thrombotic complications, have been found to prolong the time it takes for blood to clot (11). This extended bleeding and clotting time can further elevate the risk of complications in cranial and spinal interventions during neurosurgical procedures. As a result, neurosurgical clinics experienced disruptions during the pandemic, including the postponement of elective surgeries and the suspension of outpatient services, except for emergencies. These challenges have had adverse economic effects on hospitals. One significant drawback was the extended hospital stays of patients who began anticoagulant treatment during the pandemic.

The aim of this study is to investigate the economic consequences of prolonged hospitalization for neurosurgery patients who do not require emergency surgical intervention

but need hospital monitoring and undergo elective surgeries.

METHODS

Patients who were hospitalized for surgical treatment in the Neurosurgery Clinic of Ordu University Training and Research Hospital between January 1 and December 31, 2022, and who had been started on prophylactic anticoagulant or antiplatelet therapy for COVID-19 by other departments were retrospectively examined. A total of 320 patients underwent surgery during this period. Cranial surgery was performed on 41 patients, while spinal surgery was performed on 279 patients. It was determined that 38 of the 320 operated patients had been prophylactically started on anticoagulant and antiplatelet drugs by other departments after being diagnosed with COVID-19. Among these 38 patients, 8 were cranial cases and 30 were spinal cases.

Table 1. Number of patients performed cranial and spinal surgery

Surgery Type	Patients Receiving Prophylactic Anticoagulant Drugs	Patients Not Receiving Prophylactic Anticoagulant Drugs
Cranial Surgery (N=41)	8	33
Spinal Surgery (N=279)	30	249

In the routine practice of our clinic, the preoperative hospitalization period for both spinal and cranial cases was typically 2 days. However, this period extended to 7 days for patients using prophylactic anticoagulants due to the increased risk of bleeding. Under normal circumstances, spinal cases are hospitalized for an average of 2 days postoperatively, while cranial cases are hospitalized for 5 days. However, the use of prophylactic anticoagulants increased the risk of bleeding, leading to longer postoperative hospitalization periods—4 days on average for spinal cases and 10 days for cranial cases.

The costs associated with the prolonged hospitalization periods were calculated based on the Health Practice Communiqué (SUT). All variables were analysed using the SPSS statistical analysis program.

Table 2. Duration of hospitalization (days) of patients who underwent cranial and spinal surgery

Surgery Type	Period	Patients Receiving Prophylactic Anticoagulant Drugs	Patients Not Receiving Prophylactic Anticoagulant Drugs
Cranial Surgery (N=41)	Pre-operative	7	2
	Post-operative	10	5
Spinal Surgery (N=279)	Pre-operative	7	2
	Post-operative	4	2

RESULTS

The economic impact of using anticoagulant or antiplatelet drugs and the subsequent prolongation of hospital stays on treatment costs were investigated (Table 3). According to the Health Implementation Communiqué (SUT), the Social Security Institution provides a daily payment of 53 Turkish Lira (₺) to healthcare institutions as a bed fee per patient in 2023.

As shown in Table 3, the total bed cost for a patient undergoing spinal surgery under normal conditions is 212 ₺. However, for a patient with spinal pathology whose surgery was delayed due to anticoagulants or antiplatelet drug use, the total bed cost increased to 583 ₺. For the 30 spinal cases included in this study, the total bed cost under normal conditions, covering both preoperative and postoperative periods, was 6,360 ₺. This cost rose to 17,490 ₺ due to the prolonged hospital stays associated with the use of these drugs.

Similarly, for cranial surgery cases, the total bed cost under normal conditions was 371 ₺ per patient. However, for patients with cranial pathology whose surgeries were delayed due to anticoagulants or antiplatelet drug use, the total bed cost increased to 901 ₺. A significant difference was observed between the patient groups receiving and not receiving anticoagulant or antiplatelet-antiaggregant drugs, as determined by the Kruskal-Wallis Test (P = .000) (Table 4).

Table 4. The Relationship Between Costs of Patients Using and Not Using Prophylactic Anticoagulants (Non-Parametric Kruskal Wallis Test)

	Chi-Square	df	P
Spinal Surgery	268,677	1	,000
Cranial Surgery	34,880	1	,000

Table 3. Cost of Patients Receiving and Not Receiving Prophylactic Anticoagulant Drug Treatment (₺)

Category	Spinal Surgery (N=30)	Cranial Surgery (N=8)	Total Cost
Patients not using anticoagulants			
Total	6,360 ₺	2,968 ₺	9,328 ₺
Cost per patient	212 ₺	371 ₺	583 ₺
Patients using anticoagulants			
Total	17,490 ₺	7,208 ₺	24,698 ₺
Cost per patient	583 ₺	901 ₺	1,484 ₺
Difference between the two groups			
Total difference	11,130 ₺	4,240 ₺	15,370 ₺
Difference per patient	371 ₺	530 ₺	901 ₺

LIMITATION

In both groups, direct or indirect medical and non-medical expenses, such as medication and meals during the hospital stay, were not included in the study. Only the bed fee paid per patient was considered as a cost. This limitation should be considered when interpreting the results of the study.

DISCUSSION

To our knowledge, this is the first study to investigate the economic impact of using prophylactic anticoagulant drugs in the later stages of neurosurgery practice during the COVID-19 pandemic. Our findings demonstrate that the prolonged hospitalization due to the use of these drugs has led to significant economic consequences, increasing treatment costs.

Globally, the COVID-19 pandemic has caused substantial cost escalations in healthcare, not only during its initial phases but also in its later stages. The administration of anticoagulant and

antiaggregant medications during the pandemic's late period significantly extended the length of hospital stays, both pre- and post-operatively, adding to the financial burden on social security institutions. Previous studies have similarly reported a considerable economic impact on hospitals due to increased admissions and extended hospitalization times caused by the pandemic (12, 13, 14).

Aghajani et al. (15) found that during the pandemic, the majority of costs associated with COVID-19 patients were attributed to hospitality services and medications. Furthermore, their study identified brain surgery as an independent factor increasing hospitalization costs. This is consistent with our findings, where the prolonged hospital stays caused by prophylactic anticoagulants in brain surgery patients significantly raised treatment expenses.

Another study revealed that the financial burden of COVID-19 hospitalizations on Spain's public health budget (12.3% of total public health expenditure) surpassed the costs of managing conditions such as multiple sclerosis, cancer, and diabetes (12). Prolonged hospital stays during the pandemic have strained healthcare budgets worldwide. Di Fusco et al. (13) specifically highlighted intensive care unit (ICU) admissions and invasive mechanical ventilation as major drivers of cost increases. Similarly, research conducted in the United States emphasized the rising costs associated with ICU utilization during the pandemic (14). Additionally, these studies observed that costs tend to decrease when patients are discharged or pass away, as hospital stays are shortened. Our study aligns with this observation, as the use of prophylactic anticoagulants also prolonged hospital stays and increased overall costs.

During the pandemic, hospitals in the United States faced significant financial challenges due to rising costs and the cancellation of elective surgeries (16). In China, gross domestic product (GDP) contracted by 6.8% in the first quarter of 2020 due to the pandemic's economic impact (17). In Brazil, the cost of elective neurosurgery operations increased by 65.06% during the pandemic (18). Globally, the pandemic has led to a significant reduction in surgical income levels (19).

The pandemic also prompted individualized assessments of risks associated with delaying surgeries for certain neurological conditions (20). Neurosurgery practices underwent substantial adjustments, including changes in surgical case planning and academic studies in the field (21). Furthermore, neurosurgery protocols were revised to adapt to the challenges posed by the pandemic (22).

CONCLUSION

The initiation of prophylactic medication to mitigate thromboembolic risks during the COVID-19 pandemic significantly prolonged

the pre- and post-operative hospitalization periods of patients admitted to our neurosurgery clinic for surgical treatment in the pandemic's late phase. This extended hospitalization resulted in substantial economic burdens on treatment costs. As demonstrated in this study, the increase in healthcare expenses caused by the COVID-19 pandemic reached critical levels globally, not only during the initial phases but also in its later stages.

The restrictions imposed during the pandemic disrupted healthcare systems and highlighted vulnerabilities, including the economic strain on hospitals. Given the challenges brought about by the pandemic, it is essential to explore and implement alternative strategies to address similar issues that may arise in future health crises. Additionally, a comprehensive reorganization of surgical training programs, particularly for neurosurgery trainees, is needed to adapt to potential disruptions and ensure continuity in medical education and care delivery. By addressing these challenges proactively, healthcare systems can be better prepared to manage the multifaceted impacts of future pandemics effectively.

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Investigation of the Antimicrobial Activities of Schiff Bases Containing Triazoles

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Abstract

Objective: Pathogen parasites and bacteria are microorganisms that have existed throughout human history and cause different diseases. Various antimicrobial agents have become one of the treatment options in the fight against these diseases. With the increase in the number of resistant microorganisms, existing agents became ineffective and there was a need to synthesize or produce new antibiotics, antiparasitic, antiviral and antifungal drugs. There are many studies showing that Schiff base derivatives have antimicrobial properties and proving the existence of their biological activities. In this study, it was aimed to determine the antimicrobial activity of two originally synthesized compounds, a triazole-containing Schiff base, against 16 different bacterial isolates and one different Leishmania species.

Methods: In our study, the biological activities of two different newly synthesized triazole-containing Schiff base derivatives against selected one Leishmania and 16 bacteria species were evaluated by the microdilution broth (alamar blue added) method. In the study, the in vitro antibacterial activities of the compounds were determined by measuring their Minimum Inhibitory Concentration (MIC) values.

Results: Leishmanicidal activity of *Leishmania infantum* parasite was determined by measuring its Leishmanicidal Concentration. The compounds were found to have antimicrobial activity against bacteria and parasite at different concentrations.

Conclusion: It was concluded that the in vitro antimicrobial activity results obtained in our study will be of significant benefit to future research due to the resistance detected against drugs used in the treatment of infectious diseases and health problems arising due to the side effects of the drugs. If in vivo animal experiments and toxicity studies are as expected; We believe that the in vitro antimicrobial activity results obtained in our study will make a significant contribution to future research due to the resistance detected against drugs used in the treatment of infectious diseases and the health problems caused by their side effects.

Keyword: Triazole-containing Schiff bases, antimicrobial activity, Leishmania infantum, MIC value

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INTRODUCTION

Infections have been seen since the beginning of humanity. Antibacterial agents have been used extensively for years, starting from the early 20th century. Bacteria have developed serious resistance over the years. Antibiotic resistance has also become a global problem today. Millions of people lose their lives due to different infections caused by bacteria. The loss of effectiveness of antimicrobial agents due to the rapid increase in the development of resistance of microorganisms to existing agents puts these drugs in danger (1). At the same time, the effects of these drugs lead to the failure of treatments associated with bacteria that are resistant to many drugs. With the emergence of antibiotic-resistant strains over the years, the production of different antimicrobial agents has increased (2). As a global consequence of this, alarming consequences arise for public health. Therefore, it is necessary to develop alternative antimicrobial drugs and to widely evaluate these drugs with antimicrobial susceptibility methods.

The Leishmania vector, a female phlebotomine sand fly, transmits parasites to humans during blood feeding (3). The disease affects both animals and humans (4). According to WHO, more than 98 countries and territories are endemic for leishmaniasis. Estimates suggest that 0.3 million new cases of visceral leishmaniasis (VL) and one million new cases of cutaneous leishmaniasis (CL) are diagnosed annually worldwide. The majority of cases are seen in countries such as Ethiopia, Syria, Bolivia, Brazil, Costa Rica, Iran, Peru, Sudan Nepal, Bangladesh, Colombia, India, and Algeria. Since our country is located in the Mediterranean basin, the disease is also seen in our country. Leishmaniasis is considered among the 6 most important infectious diseases worldwide (5). Visceral (VL, Kala-Azar) leishmaniasis is a highly fatal form that progresses in severe and untreated cases.

The disease has a geographical distribution in certain regions and is increasing due to climate change (6). There is no effective prophylactic vaccine against leishmaniasis yet. Due to the toxic side effects seen in the drugs used for treatment and the increased resistance seen in parasites, the discovery and development of new drugs is very important.

It has been reported that 1,2,4-triazole derivatives, among triazole-containing compounds, have significant antimicrobial, antituberculosis, anti-inflammatory, antihypertensive, antidepressant, enzyme inhibitor, antioxidant, and antitumor biological activities (7-9). Especially in the structure of drugs used as antifungal drugs today, there are structures containing imidazole, expressed as triazole and triazol-5-one nucleus or its bio isoester (10).

In this context, the study aimed to evaluate, for the first time, the antimicrobial activity of two originally synthesized compounds, triazole-containing Schiff bases, against 16 different bacterial isolates and one different Leishmania species.

METHODS

Supply of Triazole Schiff Some compounds

Compound I (5-methyl-4-((pyridin-4-ylmethylene)amino)-2,4-dihydro-3H-1,2,4-triazol-3-one) (Figure 1) and Compound II (5-benzyl-4- ((pyridine-4-ylmethylene)amino)-2,4-dihydro-3H-1,2,4-triazol-3-one) (figure 2) were previously synthesized and published in an article (11).

The antimicrobial activities of these compounds were evaluated in vitro against 16 standard ATCC bacterial isolates and 1 standard Leishmania isolate stored in the deep freezer. Bacterial isolates were obtained from the American Type Culture Collection (ATCC); ATCC 43300 Methicillin-resistant *Staphylococcus aureus* (MRSA), ATCC 29213 *Staphylococcus aureus*, ATCC 49619 *Streptecoccus pneumonia*, ATCC 13813 *Streptecoccus agalactiae*, ATCC 29212 *Enterococcus faecalis*, ATCC 700327 *Enterococcus casseliflavus*, ATCC 40247 *Haemophilus influenzae*, ATCC 700603 *Klebsiella pneumoniae*, ATCC 25933 *Proteus mirabilis*, ATCC 14028 *Salmonella typhimurium*, ATCC 13076 *Salmonella enterica*, ATCC 12022 *Shigella flexneri*, ATCC 9610 *Yersinia enterocolitica*, ATCC 8090 *Citorobacter freundii*, ATCC 13047 *Enterobacter cloacae*, ATCC 19606 *Acinetobacter baumannii*. The standard *Leishmania infantum* parasite isolate was included in the study.

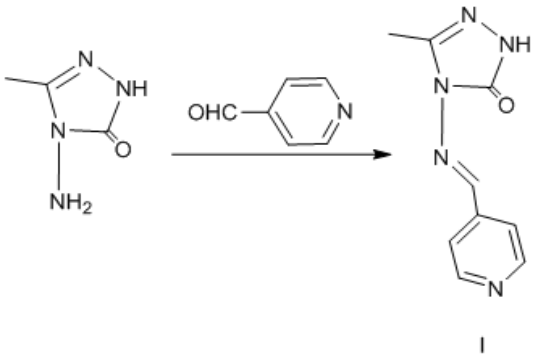

Figure 1. 5-methyl-4-((pyridin-4-ylmethylene)amino)-2,4-dihydro-3H-1,2,4-triazol-3-one

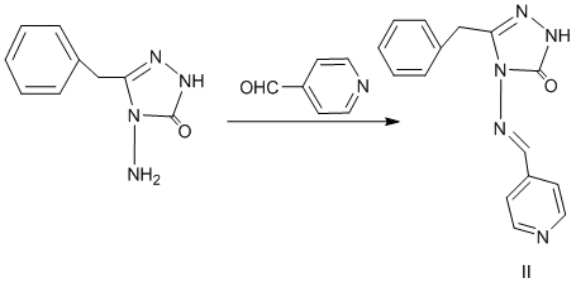

Figure 2. 5-benzyl-4-((pyridin-4-ylmethylene)amino)-2,4-dihydro-3H-1,2,4-triazol-3-one

Sixteen standard ATCC bacterial isolates stored in the deep freezer were removed from the freezer and thawed. After vortexing, the bacteria were passaged onto Blood Agar and Eosin Methilen Blue (EMB) Agar media using a sterile loop and cultured. The next day, the growths were checked, and their viability and purity were checked.

The synthesized compounds I and II, which were in powder form, were weighed and predissolved with dimethylsulfoxide. Then, distilled water was added, and the stock solution was diluted to 80 mg/ml. Compound solutions were sterilized by passing them through a membrane filter with a diameter of 0.45 micrometers.

In vitro Antibacterial Activity Test

The revived standard ATCC bacterial isolates were placed in a sterile tube containing 5 ml of physiological saline and mixed homogeneously. Bacterial density was adjusted in the McFarland device according to the McFarland 0.5 turbidity chart ($1.5x10^8$ CFU/ml).

Flat-bottomed 96-well sterile microplates were used to determine the minimum inhibitory concentration (MIC) of the compounds.

Briefly for antibacterial activity test; 100 µL of previously prepared and sterile MHB medium was added to all wells. 100 µL of the stock solution of the compound was added to the first well and mixed to ensure homogeneity. To dilute the compound concentration by 1/2, 100 µL was taken from the first well and transferred to the second well. This application was made in 10 wells. Thus, serial dilution of the compound was made in the microplates with a concentration range between 40 mg/ml and 78 µg/ml. Then, 100 µL of the previously prepared standard bacterial suspension was added to each diluted well and incubated. Wells 11 and 12 were used as negative and positive control wells, respectively. The microplate was incubated at 37°C in the incubator for 20 hours. When the incubation period was over, 20 µL of alamar blue was added to all wells and placed back in the incubator, and the color change was observed and waited for another 4 hours. During the evaluation of antibacterial activity, at the end of the incubation period, the indicator dye in the mixture in the wells turning pink was interpreted as positive bacterial growth, while the color of alamar blue remaining unchanged was interpreted as bacterial growth stopping. The last well in which the blue color did not change to the pink color was recorded as the MIC value. MIC values against all bacteria studied were determined by observation between approximately 21-24 hours. The antibacterial activity experiment of both compounds was repeated twice. In addition, Amikacin antibiotic was used as a standard drug for control purposes in the bacterial activity study.

In vitro Antiparasitic Activity Test

Whether compounds I and compound II had leishmanicidal activities on *L.infantum* promastigotes was evaluated by tests. In the study, for the culture of axenic standard *L.infantum* isolates 10% Fetal Bovine Serum, streptomycin, penicillin and fluconazole (100.000 units of penicillin, 10 mg streptomycin, fluconazole 2 mg/ml) were added to RPMI-1640 liquid medium to falcon tubes and kept at 26°C was also incubated. Reproducing parasites were washed three times in Phosphate Buffered Saline (PBS). Then, the final concentrations of promastigotes were adjusted by diluting them with RPMI-1640 medium using a thoma slide (hemocytometer) to $1x10^5$ cells.

Leishmanicidal activity in vitro

In the leishmanicidal activity (LA) study, stock solution concentrations of the compounds were prepared in the same way as for the antibacterial activity study. 100 µL of RPMI-1640 (FBS added) medium was added to all wells in the microplate. 100 µL of the stock solution of the sterile compound was added to the first well of the microplate and after mixing, 100 µL was taken from this well and transferred to the second well and diluted by 1/2. The application was made in this way, including the 10th well. The concentration range of the compounds was between 40 mg/ml and 78 µg/ml by serial dilution. 100 µl of *L. infantum* promastigotes was added to the wells. Negative control and positive control wells were added to the study. Microplates were incubated for 20 hours in the incubator at 26ºC. After 20 hours, 20 µl of sterile alamar blue (0.1 mg/ml) was added to all wells and incubated in the oven for another 4 hours at the same temperature. The results of the test were evaluated at the end of the 1st, 2nd, and 3rd day and the results were recorded. Amphotericin B was evaluated as the control drug in the study. The antiparasitic activity study was repeated twice. If the indicator dye turned pink at the end of the incubation period, it was interpreted as positive parasite growth, and if the dye remained unchanged, it meant that parasite growth had stopped. The last well in which the blue color did not change to pink color was recorded as the LA value. In addition, samples were taken from all wells, and the viability (motion) status of the promastigotes was evaluated under the microscope at forty-degree magnification between slides and coverslips and confirmed by comparing them with the alamar blue test results.

RESULTS

Antibacterial Activity Results

The 16 bacteria evaluated were studied in two different microplate groups. The 1st microplate *S. typhimurium, S. flexneri, E. faecalis, H. influenzae, S. enterica, K. pneumoniae*, MRSA and *S. aureus*, the 2nd microplate *Y. enterocolitica, C. freundii, E. clocae, A. baumannii, S. agalactiae, S. pneumoniae, E. caselliflavus*, and *P. mirabilis* were present.

Both compounds were found to be effective at different concentrations against 11 of the 16 bacterial isolates we studied. Since some bacteria have longer incubation periods, the positive controls were taken into consideration and incubated for another day and re-evaluated.

When the study results obtained after 48 hours were evaluated; Compound I exhibited antibacterial activity at different concentrations against MRSA, *S. aureus, S. pneumoniae, S. agalactiae, E. faecalis, E. casseliflavus, H. influenzae, S. flexneri, E. cloacae, C. freundii*, and *Y. enterocolitica* isolates. MIC values were found to be 625 µg/ml, 2500 µg/ml, <39 µg/ml, 312 µg/ml, 78 µg/ml, <39 µg/ml, <39 µg/ml, <39 µg/ml, 10.000 µg/ml , 312 µg/ml, and 312 µg/ml, respectively. It was determined that they had no antibacterial activity even at the highest compound concentrations studied against *S. typhimurium, S. enterica, K. pneumoniae, P.mirabilis,* and *A. baumannii* isolates. Compound II showed antibacterial activity at different concentrations against MRSA, *S. aureus, S. pneumoniae, S. agalactiae, E. casseliflavus, H.influenzae, S. typhimurium, S. flexneri, E. cloacae, C. freundii,* and *Y. enterocolitica* isolates. MIC values were found to be 625 µg/ml, 2500 µg/ml, <39 µg/ml, 312 µg/ml, <39 µg/ml, <39 µg/ml, 312 µg/ml, <39 µg/ml, 10000 µg/ml, 312 µg/ml, and 312 µg/ml, respectively. It was determined that they did not have antibacterial activities even at the highest compound concentrations studied against *E. faecalis, S. enterica, K. pneumoniae, P.mirabilis* and *A. baumannii* isolates. In Table 1, the determined MIC values of the compounds against all bacterial isolates studied are given (Table 1, Figure 3).

Leishmanicidal activity results

The antiparasitic activities of Compounds I and II against *L.infantum* promastigotes were determined in vitro by the alamar blue-supplemented broth microdilution method. In the evaluation of leishmanicidal activity, it was evaluated according to whether the indicator dye changed color or not. LA values obtained as a result of the test are given in Table 2. According to the data, Compound I was found to be effective against the studied leishmania specie at a concentration of 10000 µg/mL. It was observed that Compound II was effective against *L.infantum* promastigotes at the highest concentration studied (MIC: 20000). It was determined that amphotericin B, used as a control drug, was effective against leishmania specie, even at the lowest concentration studied (MIC: <39) (Table 2, Figure 4).

Table 1. The determined MIC values of the compounds against all bacterial isolates

Bacterial Isolates	MIC values (µg/ml)	
	Compound I	**Compound II**
Staphylococcus arueus (MRSA)	625	625
Staphylococcus aureus	2500	2500
Streptococcus pneumoniae	<39	<39
Streptococcus agalactiae	312	312
Enterococcus faecalis	78	>20000
Enterococcus casseliflavus	<39	<39
Haemophilus influenzae	<39	<39
Salmonella typhimurium	>20000	312
Salmonella enterica	>20000	>20000
Shigella flexneri	<39	<39
Enterobacter cloacae	10000	10000
Citrobacter freundii	312	312
Yersinia enterocolitica	312	312
Klebsiella pneumoniae	>20000	>20000
Proteus mirabilis	>20000	>20000
Acinetobacter baumannii	>20000	>20000

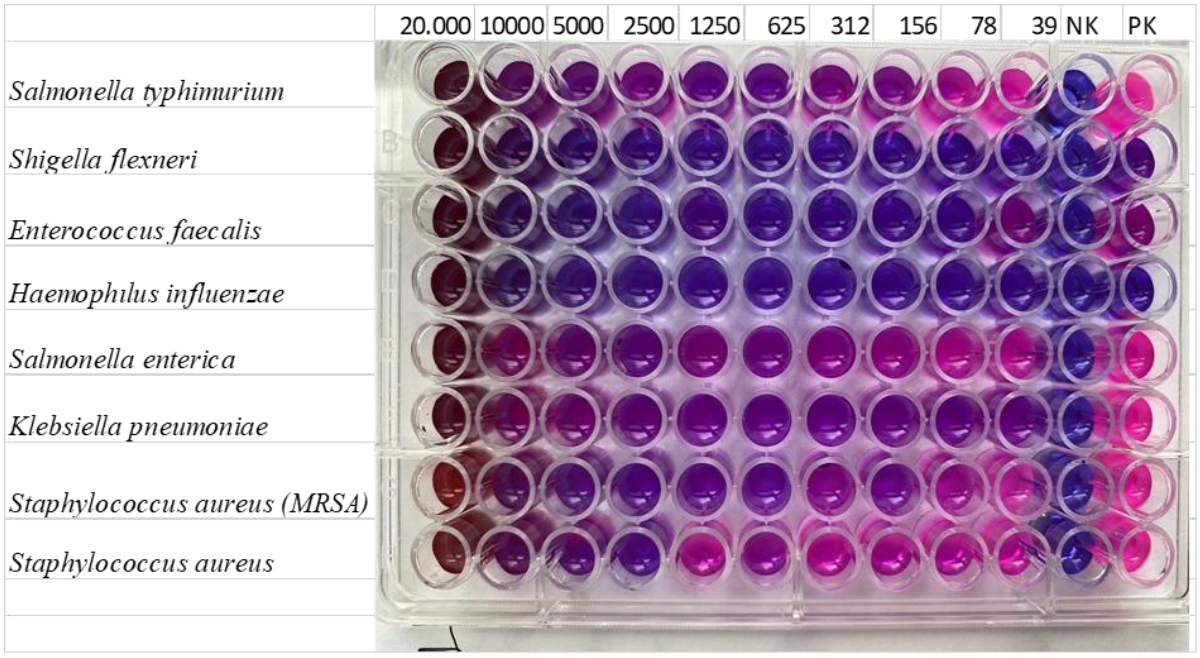

Figure 3. Antibacterial activities of Compound I against group 1 bacterial samples

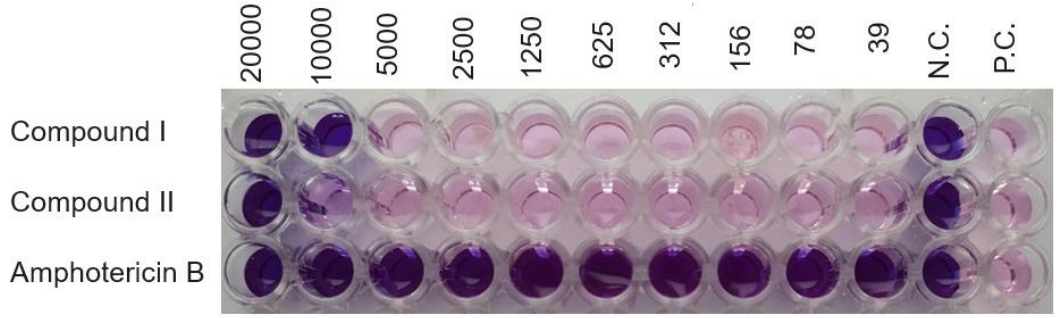

Figure 4. In vitro leishmaniacidal activities against *L.infantum* promastigotes

Table 2. Leishmaniacidal activity (LA) concentration values of the compounds against *Leishmania infantum*

promastigotes.

	LA (**µg/ml**)
Compound I	10000
Compound I	20000
Amphotericin B	<39

DISCUSSION

Despite advances in the field of treatments for microbial infections, resistance to antimicrobial drugs is occurring faster than the introduction of new chemical compounds into clinical practice, resulting in increased mortality rates due to various microbial infections. The rapid development of drug-resistant microorganisms, in addition to the biofilm formation of some microorganisms, has attracted the attention of pharmaceutical chemists and other scientists working in this field, leading them to design and develop chemical structures with increased efficacy along with various modes of action. Antimicrobial drugs currently used to treat different microbial infectious diseases have therapeutic limitations such as narrow spectrum, drug toxicity, and variable bioavailability, in addition to increased microbial resistance (12).

The number and structure of drugs used in the treatment of infectious diseases are constantly changing. This change is progresses in direct proportion to the resistance created by microorganisms. The need for drugs, disinfectants, and antimicrobial agents used today arises from the resistance of microorganisms to these substances (13).

Studies have reported that the *E. faecalis* strain has become resistant to many antibiotics (14, 15). In our study, compound I was observed to be effective even at a low concentration (MIC: 78), while compound II was found to be ineffective even at the highest concentration. Additionally, it was observed that both compounds were highly effective against the other Enterococcus specie, *E. casseliflavus*.

According to a study, it is stated that *A.baumannii* creates resistance against many agents (16). Likewise, similar studies report high resistance to *S.typhimurium, S.enterica, K.pneumonia*, and *P.mirabilis*. In our current study, *A. baumanni, K. pneumonia, S. enterica* and *P. mirabilis* were found to be highly resistant to both compounds.

Similar to our study, Benkli et al. (17.) reported in their study on fourteen different triazole derivatives, they reported that no major differences were observed between the compounds in terms of antibacterial and antifungal activity.

In another study, when the antimicrobial activity of 17 different triazole derivatives was tested, it was reported that MIC values could be determined only against *E. coli*, and no activity was observed against other bacterial and fungal species (18).

The effectiveness of the triazole derivative Schiff base in anticancer, antibacterial, and antiapoptotic studies was evaluated, and it was

reported that its activities against Gram positives were higher than those against Gram negatives (19).

In another study, when the antibacterial and antifungal properties of new thiazolyl-triazole Schiff bases were tested, Schiff bases showed good antibacterial activity against *L. monocytogenes* and *P. aeruginosa*; It has been stated that it is twice as active as ciprofloxacin, and its anti-Candida activity is twice as high compared to fluconazole (20).

Chohan and Hanif synthesized a new series consisting of four biologically active triazole derivative Schiff base ligands (l1–l4) and their cobalt (II), nickel (II), copper (II) and zinc (II) complexes (1–16). Antibacterial activity against four Gram-negative (*E. coli, S. sonnei, P. aeruginosa, S. typhi*) and two Gram-positive (*S. aureus, B. subtilis*) bacteria, and antifungal activity against to *T.longifusus, C.albicans, A.flavus, M.canis, F.solani* and *C.glabrata* were tested. They stated that metal (II) complexes showed stronger antibacterial and antifungal activity than the parent Schiff bases against one or more species of bacteria and fungi. Antibacterial activities of metal (II) complexes indicated that metal (II) complexes 1, 3–8, 10 and 12–14 showed significant activity (54–82%) against all observed bacterial strains (21).

In the study conducted by Strzelecka and Swiatek in Switzerland, it was shown that the compounds have strong antibacterial activity in the study conducted on 1,2,4-triazole and its quinolone agents and hybrids, as well as 4-amino-, 3-mercapto- and 1,2,4-triazole derivatives. They reported that these compounds inhibit the growth of both Gram-positive and Gram-negative bacteria, and that the most active compounds are equal to or more effective than antibacterial drugs commonly used on the market (22).

In a study by Holanda et al. (23), they evaluated the antileishmanial activities of 4-phenyl-1-[2-(phthalimido-2-yl)ethyl]-1H-1,2,3-triazole (PT4) derivatives against *Leishmania amazonensis* and *Leishmania braziliensis* amastigotes and promastigotes. They stated that PT4 and PI compounds had an effect on the parasite membranes of both parasite species. They emphasized that it has well-predicted pharmacokinetic properties that may be useful in the development of oral formulations, especially for the treatment of cutaneous leishmaniasis.

Meinel et al. (24) synthesized a series of 1,2,3-triazolium salts (TS) and corresponding 1,2,3-triazole (T) precursors containing novel epoxide derivatives and were tested against promastigote and intracellular amastigote forms of *Leishmania amazonensis*. Among these compounds, compound TS-6 exhibited promising activity on promastigotes (IC50 = 3.61 μM) and intracellular amastigotes (IC50 = 7.61 μM) of *L. amazonensis*, which was superior to miltefosine (IC50 > 10.0 μM) used

as the reference drug stated.

Almeida et al., (25) as in our study, synthesized seven new acetyl-functionalized 1,2,3-triazolium salts and four 1,2,3-triazole precursors, and investigated their effects against different *L. infantum* strains from dogs and humans. 1,2,3-triazolium salts have been reported to exhibit better activity than 1,2,3 triazole derivatives with an IC50 range of 0.12 to 8.66 µM. Among these compounds, compound 5 has been reported to show significant activity against promastigotes (IC50 between 4.55 and 5.28 µM) and is effective against intracellular amastigotes with the best selective index (SI~ 6-9) and reduced toxicity (5 IC50 from 0.36 to 7.92 µM)

Süleymanoğlu et al. (10) 1,2,4-triazole derivatives with morpholine; 4-((3-methylthiophene–2-yl)methyleneamino)-1-((4-(3-methylthiophene–2-yl)methyleneamino)-1-(morpholinomethyl)-5-thioxo-4,5-dihydro-1H -1,2,4-triazol-3-yl)methyl)-3-(thiophene-2-ylmethyl)-1H-1,2,4-triazol-5(4H)-one (compound I) and 1-((1-(morpholinomethyl)–4-(5-nitrothiophene–2-yl)methyleneamino)-5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)methyl)-4- In vitro antileishmanial activities of ((5-nitrothiophene–2-yl)methyleneamino)-3-(thiophene–2-ylmethyl)-1H-1,2,4-triazol-5(4H)-one (compound II) evaluated their antilesihmanial activity against *L. infantum* promastigotes by microdilution broth method with Alamar Blue dye. They stated that both compounds are antiparasitic and especially compound II has significant antileishmanial activity due to its MIC value of 312 µg/mL.

In a study in which thiol-thion tautomeric forms of 1,2,4-triazole derivatives were synthesized with the Schiff base, in vitro antileishmanial activity against *L. infantum* promastigotes was evaluated by microdilution method with Alamar Blue Dye. It has been emphasized that the 1,2,4-triazole derivative exhibits antiparasitic activity due to its MIC value of 1250 mg/mL (26).

Chen et al. (27) designed and synthesized a series of new myricetin derivatives containing the 1,2,4-triazole Schiff base. During antibacterial bioassays, 6f, 6i, and 6q showed a good inhibitory effect against *Xanthomonas axonopodis* pv at 10.0, 9.4 and 8.8 mg mL, respectively, and also in antiviral bioassays, most compounds showed excellent against tobacco mosaic virus (TMV) at a concentration of 500 mg mL-1. They revealed that it exhibited antiviral activity. It was determined that the triazole derivative Schiff bases we studied were highly effective against *S. flexneri, H. influenzae*, and *S. pneumoniae* (MIC <39).

CONCLUSION

With the ever-increasing antibiotic resistance and bacterial infections, the development of effective antibiotics to treat these infectious diseases has become a necessity. Schiff bases and their derived complexes are reported to be

important in medicinal chemistry. Triazole Schiff base ligands have applications as biological probes and potent drug agents.

In this study, it was observed that both of the newly produced triazole-containing Schiff bases were effective against *S.pneumonia*, *S.flexneri*, and *H.infulienzae*, which are known to be common infectious agents, at every concentration. The two Schiff base derivatives that we have studied can be investigated as a new drug derivative to be developed against these three types. It can also be considered among the new generation drugs to be produced against these microorganisms.

Neither compound was found to be effective against Gram-negative bacteria such as S. enteridis, *K.pneumoniae*, *A.baumannii*, and *P.mirabilis* at any concentration. Additionally, while compound 1 did not show activity against *S. typhimurium*, compound 2 was found to be ineffective against *E. faecalis*.

Both compounds whose antiparasitic activity was studied were determined to have leishmanicidal activity against *L. infantum*, albeit at high concentrations. In order for the synthesized compounds to be used in the treatment of leishmaniasis, *in vivo* control studies and toxicity tests in experimental animal models are required.

It is very important to discover new agents because the emergence of resistant isolates detected in microorganisms negatively affects human health. There are serious problems in the treatment of diseases caused by the spread of microorganisms showing multiple antibiotic resistance. This increases the need for the discovery of new antimicrobial agents. Therefore, we can positively evaluate the effectiveness of these two synthesized Schiff bases containing triazoles. We hope that this study will study the antimicrobial activities of these compounds for the first time and shed light on future studies.

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Protective Evidence of Clarithromycin after Ischemic Cerebral Injury; an Experimental Study

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Abstract

Objective: Acute ischemic stroke is caused by a reduction in cerebral blood flow, leading to brain ischemic and subsequent cell death. The therapeutic options available for this condition are limited. The inflammatory response associated with the ischemic injury may influence the outcomes of ischemic stroke. Clarithromycin is a widely used antibiotic in medical practice. This study aimed to investigate the effect of clarithromycin on brain ischemic injury.

Methods: In this study, 38 Sprague Dawley female rats were used and divided into four main groups: the pure control group, the ischemia group, the sham/control group, and the ischemic+claritromycin group. A temporary clip was placed in the bilateral carotid arteries of rats for 45 minutes. One group administered a dose of clarithromycin, and the tissue and blood samples of all four groups underwent biochemical evaluation. The results were subjected to statistical analysis.

Results: The administration of clarithromycin to animals resulted in a reduction in malondialdehyde levels in brain tissues within the study group. Furthermore, Bederson's motor scores were observed to be higher in the clarithromycin-treated group in comparison to the ischemia group (p=0.092).

Conclusion: A potential correlation exists between post-stroke infections and prognosis, suggesting that prophylactic antibiotic treatment may be beneficial. This study indicates that clarithromycin exerts a neuroprotective effect on cerebral ischemic injury following a stroke.

Keyword: Cerebral injury, clarithromycin, ischemic, neuroprotection

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INTRODUCTION

It has been extensively studied that hypoxia-ischemic can cause insufficient blood flow to the brain's tissues, which can cause severe organ damage and neuronal cell apoptosis. Ischemic stroke occurs due to the reduction of cerebral blood flow. Cerebral ischemic/hypoxic damage is a serious medical disorder that can arise from several different illnesses. It is one of the leading causes of worldwide disability and death. Ischemic cerebral injury results from a complicated web of molecular and metabolic processes, but its pathophysiology is still unclear. Knowing the mechanisms underlying white matter damage following a stroke is essential. Neuroprotection may stop the death of neurons. In the last decades, understanding of the pathophysiological events in cerebrovascular diseases has improved (1), but the fatality rate from ischemic stroke is still high. It is therefore imperative to develop novel therapy approaches that can improve functional recovery and lower morbidity (2). The goal of ischemic stroke therapy is to restore perfusion to the brain (3). Investigating appropriate therapeutic approaches for ischemic brain damage is an important issue. Researchers have been trying to find the best therapeutic agent for ischemic injury following stroke. Neuroinflammation is a key aspect of stroke. The inflammation in the ischemic injury may affect determining the outcomes of ischemic stroke, because it may cause a neurological deficit or there may be a link between the occurrence of post-stroke infections and outcomes. It is believed that neuroinflammation, which is a secondary neurological impairment, is the primary cause of cerebral ischemic injury. Increasing levels of cytokines in the central nervous system and systemic circulation mediate inflammatory responses to acute ischemic injury. Antibiotics may have a role in the management of stroke. They have been often used in medical practice. Macrolide antibiotics like clarithromycin have both antibacterial and anti-inflammatory properties, and this antibiotic may have a role in stroke-related ischemic/reperfusion injury. Using antibiotics as a preventative measure may be helpful. Antibiotic drugs may be a reasonable choice in this situation. Macrolides represent the preferred class of antibiotics, and as such, they are of significant clinical interest due to their applicability to human medicine. Currently, major changes in medical practice have been observed, however, despite the increased use of technology, our understanding of the histopathological mechanisms of the effect of clarithromycin on human stroke is still limited. When an ischemic stroke occurs, proinflammatory chemokines to activate leukocytes are released by brain tissues, and inflammation occurs. Antibiotics following a stroke may be a useful choice. Clarithromycin can reduce inflammatory processes in the brain and may have a neuroprotective effect (4).

Many treatments for ischemic cerebral strokes are vessel and blood-based, but brain-based therapies should be evolved. Many stroke studies have focused on antiplatelet drugs such as aspirin, clopidogrel, dipyridamole, ticlopidine as well as warfarin. There are a limited number of studies focused on the effect of clarithromycin. Brambrink et al. showed that group of macrolides (Erythromycin, clarithromycin, azithromycin, spiramycin etc) increases hypoxia tolerance (5). In this study, the neuroprotective effect of clarithromycin on focal brain ischemic and reperfusion injury was investigated.

METHODS

The study was conducted in the Experimental Research Center Laboratory of Karadeniz Technical University, Faculty of Medicine. All experimental protocols were approved by the Animal Experiments Local Ethics Committee of Karadeniz Technical University (with the decision of the Animal Experiments Local Ethics Committee of Karadeniz Technical University numbered 2016/55). The study was conducted under the ethical guidelines outlined in the 1964 Declaration of Helsinki and any subsequent changes, as well as any other relevant ethical guidelines. The biochemical analyses were carried out in the Research Laboratory of the Department of Biochemistry. In the study, 38 Sprague Dawley female rats, each weighing between 220 and 280 gr, were used. The general health of the rats was examined before the study and they were monitored under standard conditions and in individual cages without water and feed restrictions, and each rat was marked with the appropriate method according to the group in which it was included. The rats were divided into four groups.

Description of groups

Group 1 (Ischemic+Claritromycin)

Clarithromycin 100 mg/kg/day was intraperitoneally given to this group consisting of 12 rats every day after clipping of the bilateral carotid arteries for 30 min + hypotension induction (10 ml/kg). They underwent a neurological examination at the end of postoperative day 1, day 4, day 7, and day 10. At the end of day 10, they were sacrificed, and the brain tissue was removed.

Group 2 (Ischemic)

Clipping of the bilateral carotid arteries for 30 min + hypotension induction (10ml/kg) was performed in this group consisting of 12 rats. They underwent a neurological examination at the end of postoperative day 1, day 4, day 7, and day 10. At the end of day 10, they were sacrificed, and the brain tissue was removed.

Group 3 (Sham/Control)

The rats in this group were only anaesthetised, and neurological examinations were performed on day 1, day 4, day 7 and at the end of day 10.

At the conclusion of the 10th day, the rats were euthanised and the brain tissue was extracted.

Group 4 (Pure Control Group "Only Anesthesia and Drug")

Following the administration of anaesthesia, a single skin incision was made in this group of seven rats, and clarithromycin was administered intraperitoneally for a period of 10 days. They underwent a neurological examination at the end of day 1, day 4, day 7, and day 10. At the end of day 10, they were sacrificed, and the brain tissue was removed.

In this study, the experimental procedure of study Arslan et al (6), was used. The rats were individually numbered and placed in cages where they could easily access food and water. The anaesthetic agent was administered intraperitoneally at a dose of 10 mg/kg xylazine hydrochloride (Rompun®; Bayer Healthcare) and 30 mg/kg ketamine hydrochloride (Ketalar®; Pfizer). In the supine position, the surgical site of rats was shaved and stained with 10% povidone-iodine solution (Batticon®; Adeka). A midline skin incision was done, and a retractor was placed. After cervical midline blunt dissection, the common carotid arteries were found, and the arteriae carotid communis were dissected from the N. vagus. Then this artery was clipped by a Yasargil aneurysm clip and waited for 30 minutes. After 30 minutes, 3ccs intracardiac blood was taken and hypotension was induced. After removing the clip at the end of 30 minutes, the arterial flow was checked, the clamps were removed, and the layers were properly sutured. A neurological examination of the rats was performed at intervals (on days 1, 4, 7, and 10). The starting solution (Clarithromycin (Klacid® IV 500mg injectable vial) was prepared by adding 10ml sterile saline to a 500mg vial and administered intraperitoneally at the doses indicated. Clarithromycin 100 mg/kg/day was injected intraperitoneally for 10 days. Ten days later, 4 ccs of intracardiac blood were taken from the surviving rats and the rats were sacrificed and The hippocampus, c. striatum, corpus callosum and thalamus parts of the brain were dissected and stored in deep-freezer at -76^{o}C for histological and biochemical analysis. The rats in the SHAM group underwent a neurological examination at the end of day 1, day 4, day 7, and day 10. At the end of day 10, 4 ccs of intracardiac blood were taken into citrated tubes. Biochemical changes were evaluated by measuring the levels of malonaldehyde (MDA) in both blood and tissue.

Malondialdeyde Determination

In MDA measurement, the absorbance at 532 nm of the color of the component that the MDA produces with thiobarbituric acid (TBA) in an acidic state is measured. The preparation of solutions used in tissue and serum MDA measurements was made. Figure 1 shows the MDA standard chart. Using this chart, the tissue MDA level was calculated as nmol MDA/gram

wet tissue. The standard absorbance values are seen in Figure 2.

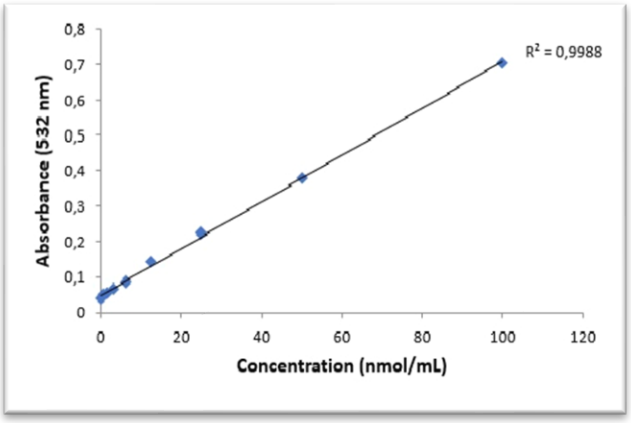

Figure 1: Shows the MDA standard chart.

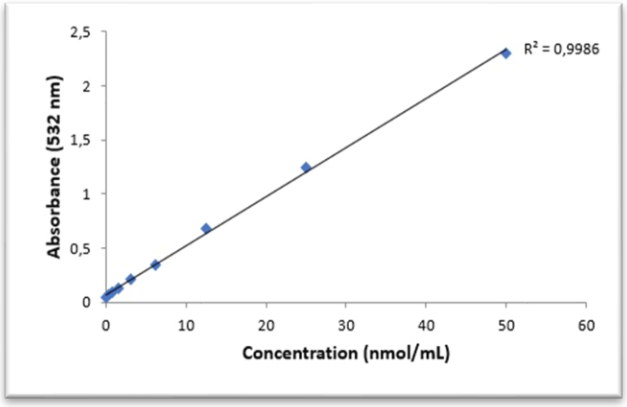

Figure 2: The standard absorbance values are seen.

Preparation of Solutions Used in Tissue MDA Measurement

1) Tissue homogenization buffer (0.01 M Phosphate Buffer Solution (PBS), pH: 7.4) Ten PBS tablets (Medicano, Uppsala, Sweden) were dissolved in a beaker containing approximately 900 mL of distilled water, then the pH of the solution was adjusted to 7.4 at a pH meter (Hanna Instrument, USA). The pH of the adjusted solution was brought to a final volume of 1 L.

2) 1% H_3POI_4 solution 2.94 mL of 85% H_3PO_4 (Sigma, St. Louis, MO, USA) was added to the distilled water and the volume was adjusted to 250 mL with the distilled water.

3) TBA solution: 0.67 g TBA (Sigma, St. was weighed, 50 mL of distilled water and 50 mL of acetic acid (Sigma, St. Louis, MO, USA) was added and dissolved by mixing with a magnetic bar.

4) Standard solutions: 82.5 µL of 1,1,3,3-tetrametoxypropan (Sigma, St. Louis, MO, USA) was added to 50 ml of 0.1 M HCL (Sigma, St. Louis, MO, USA) solution. The solution was incubated at 50°C for 1 hour. Thus, by diluting the main stock solution prepared at certain ratios, the standard solutions of 100, 50, 25, 12.5, 6.25, 3.13, 1.56, 0.78, 0.39 and 0.195 nmol/mL along with blind were prepared.

Preparation of Samples: Approximately 50 mg slices were cut from all of the tissues. These tissues were then homogenized in 2 mL of PBS at 9500 rpm (4x10s, 40 °C) with a homogenizer (Jane and Kunkel, Germany). The homogenates were centrifuged at 4000 rpm for 10 minutes. After the supernatants obtained after centrifugation were diluted at a ratio of 1:10 with PBS, MDA values were measured.

Measurement of Tissue MDA

1. 3 mL 1% H_3POI_4 was added to 500 µL of homogenate and a mixture was prepared.

2. 1 mL of 0.672% TBA was added to the mixture and mixed, then incubated in boiling water for 60 minutes.

3. At the end of the period, the tubes were placed at room temperature to cool down and centrifuged at 4000 rpm for 10 minutes at room temperature.

4. After the centrifugation, 200 µL was taken from the supernatant part and filled into 96-well plates, absorbances were read in a microplate reader spectrophotometer (Versamax, Molecular Devices, California, USA) at 532 nm wavelength. The standard absorbance results obtained were plotted against concentration and the MDA standard chart was created. (Figüre 4) Using this chart, tissue MDA level was calculated as nmol MDA/gram wet tissue.

Determination of malondialdehyde in plasma

The rat serum samples were kept at -80°C until biochemical measurements. The amount of malondialdehyde in the serum samples was calculated with the TBARS (Tiobarbituric Acid Reactive Substance) method developed by Yagi (90). The red color of the reaction between the lipid peroxidation product (MDA) and thiobarbituric acid (TBA) was measured spectrophotometrically. In order to separate the water-soluble components that react with thiobarbituric acid and give the same color, serum lipids were separated together with the protein in the phosphotungstic acid/sulfuric acid assembly.

Preparation of Solutions Used for Measurement of Tissue MDA

1) 0.084 N Sulfuric Acid (H_2SOA_4)

577 µL of 97% H_2SOA_4 (Sigma, St. Louis, MO, USA) was taken and the volume brought to 250 mL with deionized water.

2) 10% Phosphotungstic Acid ($H_3(W_3O_{10}).4H_2O$)

5.55 g of phosphotungstic acid (Sigma, St. (Louis, MO, USA) was dissolved in 50 mL of deionized water.

3)Thiobarbituric acid (TBA) solution

0.67 g of TBA (Sigma, St. was weighed, 50 mL of distilled water and 50 mL of acetic acid (Sigma, St. Louis, MO, USA) was added and dissolved by mixing with a magnetic bar.

4) Standard solutions

82.5 µL of 1,1,3,3-tetrametoxypropan (Sigma, St. Louis, MO, USA) was added to 50 ml of 0.1 M HCL (Sigma, St. Louis, MO, USA) solution. The solution was incubated at 50°C for 1 hour. By diluting the main stock solution prepared at certain ratios, the standard solutions of 100, 50, 25, 12.5, 6.25, 3.13, 1.56, 0.78, 0.39 and 0.195 nmol/mL and blind were prepared.

Measurement of Serum MDA

1. 150 µL of serum, 1200 µL of H_2SOA_4 and 150 µL of phosphotungstic acid were added to test tubes, and the tubes were kept at room temperature for 5 minutes after thoroughly mixed.

2. The mixtures were centrifuged at 1500 g for 10 minutes and the supernatants were discarded.

3. 2 mL of distilled water was added to the remaining precipitate and vortexed until redissolved.

4. 500 µL of TBA was added to the tubes and they were incubated at 100°C for 1 hour.

5. After the incubation, the tubes were centrifuged at 1000 g for 10 minutes.

6. Taking 200 µL from the transparent area above, it was filled in 96-well plates and absorbances were read in a microplate reader spectrophotometer (Versamax, Molecular Devices, California, USA) at 532 nm wavelength. The resulting standard absorbance values were plotted against concentration and the MDA standard chart was created (Figüre 5). Using this chart, serum MDA amount was calculated as nmol/mL.

Motor Examination

The motor scores of the rats in each group were recorded on the 1st, 4th, 7th, and 10th days according to the Bederson scale.

Bederson motor assessment

Grade 0: no neurological deficit 5 points,
Grade 1: Stretching the front legs 4 points,
Grade 2: Reduced resistance to lateral thrust without rolling movement 3 points,
Grade 3: addition of rotational movement in addition to grade 2, 2 points
Grade 4: Exitus receives 1 point.(7).

Statistical Analyses

Using the IBM SPSS software package, version 22, all statistical analyses were conducted. The Mann-Whitney U test was used to determine statistical differences and significance levels in all measurements, and results with a p-value of 0.05 or lower were regarded as significant. Multiple comparisons were made using Duncan's Multiple Range Test.

RESULTS

It was found that the brain tissue MDA level of the group 2 (ischemia) was significantly increased compared to the brain MDA levels of the group 3 (control) ($p<0.05$). The administration of clarithromycin significantly decreased the level of MDA when the group 2 (ischemia) and the group 1 (clarithromycin) were compared ($p<0.05$) (Figure 3). It was observed that the MDA level of the group 2 was significantly increased compared to the serum MDA level of the group 3 ($p<0.05$). Again, this result showed that significant ischemia was achieved. When the group 1 and group 2 values were compared, there was a significant decrease in the serum MDA level ($p <0.05$). (Figure 4)

No statistically significant difference in Bederson motor scores was found between the group 1 and groups 2 ($p>0.05$). (Table 1). A graphic abstract summarizes the result of the present study (Figure 5).

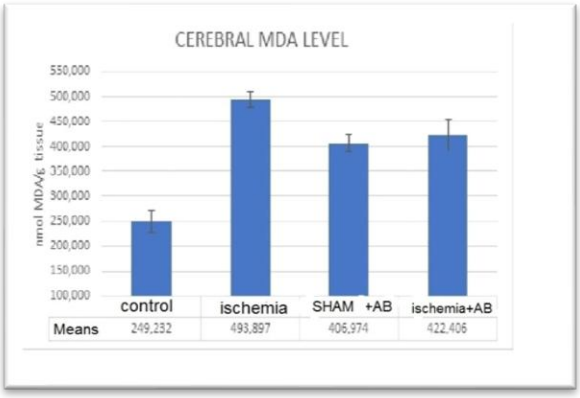

Figure 3. Group brain tissue MDA levels

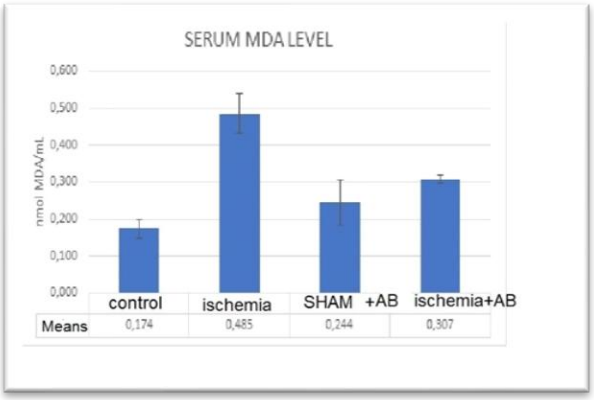

Figure 4. Serum MDA levels of the groups

Table 1: Means and minimum and maximum values of the Bederson scores of the groups on days 1, 4, 7 and 10.

Group	Day 1		Day 4		Day 7		Day 10	
	Mean	**Min-Max.**	**Mean.**	**Min-Max.**	**Mean**	**Min-Max.**	**Mean**	**Min-Max.**
Ischemia + Clarithromycin	2.25	1-5	2.75	1-5	2.83	1-5	3.25	1-5
Ischemia	2.16	2-5	2.25	2-5	2.33	1-5	2.41	1-5
Sham	4.85	4-5	5	5-5	5	5-5	5	5-5
Pure Control	4.14	3-5	4.71	4-5	4.85	4-5	5	5-5

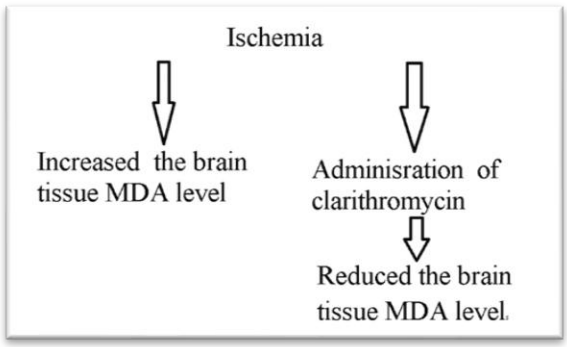

Figure 5: The results of the study are summarised below

DISCUSSION

This study indicates that clarithromycin has a neuroprotective effect on cerebral ischemic injury following a stroke.

Interpretation: In medical practice, having a thorough understanding of pathophysiology is crucial (8). An improved understanding of the pathophysiology of cerebrovascular disorders has been observed in the last decades (9). A continuous supply of oxygen is necessary for the proper functioning of brain cells (10). During a stroke, the blood flow decreases below the critical threshold in the cerebral tissue and

causes ischemic degenerative changes in the cerebral tissues. Ischemic neuronal damage after stroke remains a common cause of neurological disability and death. Reductions in infarct volumes can be associated with better neurological outcomes. Oxygen supplementation has been suggested to reduce secondary injury by minimizing damage to cerebral tissue in stroke because ischemic injury results in cell loss. There is a balance between cell death and cell proliferation in the nervous system. Restoring blood supply may lead to reperfusion injury, this reperfusion can paradoxically contribute to more brain damage. The intact blood-brain barrier (BBB) is required for maintaining the microenvironmental homeostasis of the CNS. BBB disruption following ischemia may lead to brain injury. Though contemporary healthcare has made significant advancements (11), post-stroke systemic inflammation can increase morbidity and mortality in stroke patients. Macrolide antibiotics have potent anti-inflammatory activities, likely by reducing pro-inflammatory cytokine production. During ischemia, structural and metabolic changes begin in the brain. Hypoxic-ischemic insult causes oxidative stress and the neuroinflammatory signaling cascade starts. Inflammation and oxidative stress have been linked to cerebral injury after stroke. This injury can be related to the activation of metalloproteases. Metalloprotease leads to the destruction of BBB. Systemic inflammation is known to change the permeability of the BBB (12), and BBB disruption following stroke promotes inflammation. Cerebral ischemia may lead to an inflammatory response that is believed to contribute to cell death. The fever sometimes increases following cerebral ischemia. The impairment and recovery of neurological functioning are impacted by post-stroke neuroinflammation. The occurrence of secondary neurologic deterioration in cerebral ischemia or cerebral tissue hypoxia may be linked to a pronounced increase in the inflammatory parameters inflammation, and apoptosis. Neutrophils have important functions in post-stroke pathogenesis. The anti-inflammatory actions of macrolide antibiotics are well-known. Inhibition of neuronal apoptosis by the inflammatory effect of clarithromycin may be a promising treatment strategy to improve neurological deficits following stroke. These changes can overly stimulate N-methyl-d-aspartate (NMDA) receptors, causing calcium overload and triggering apoptotic cell death in neurons. In our study, a significantly decreased level of MDA after the administration of clarithromycin may be explained by this mechanism. The blood-brain barrier is necessary for the normal function of the brain (10). Some antibiotics cannot pass between the blood-brain and blood-CSF barriers unless there is an infective process, such as meningitis (13).

Clarithromycin administration can prevent BBB disruption following ischemic stroke. In this study, the benefit of clarithromycin was shown in ischemic cerebral injury after stroke. Based on this property, we measured tissue and serum. In this study, the only outcome measures are malondialdehyde (MDA) levels in brain tissue and a crude assessment of behavioral outcome on the Bederson scale (7). MDA levels in this study found that the brain tissue MDA level of the ischemia group was significantly increased compared to the brain MDA levels of the control (sham) group ($p<0.05$), but the administration of clarithromycin significantly decreased the level of MDA in comparing the ischemia group and the clarithromycin group ($p<0.05$). It is an interesting part of this study, that functional recovery was not seen with no significant change in Bederson motor scores between groups ($p>0.05$). No statistically significant difference in Bederson motor scores was observed between the clarithromycin and ischemia groups ($p>0.05$).

The rationale for choosing MDA; why other markers were not selected:

Stroke is one of the leading causes of mortality and morbidity worldwide, for that reason, many studies have been conducted and many experimental models have been used for the pathology. In the early stages of an ischemic episode, oxidative stress and lipid peroxidation are significant factors. One form of secondary brain damage brought on by reperfusion following an ischemic stroke because of vascular obstruction is known as cerebral ischemia-reperfusion injury. Neuronal apoptosis, blood-brain barrier disruption, and malignant brain edema occur secondary to cerebral ischemia-reperfusion injury. There are reasons to concentrate only on experimental studies because the biomechanical, molecular, and cellular effects of diseases can only be investigated in experimental animal studies. The experimental studies may provide better evidence of the effect of clarithromycin in experimental brain ischemic injury than those of human subjects. malondialdehyde (MDA), is a biomarker of oxidative stress. The rationale behind the selection of MDA is attributable to its well-established role as a reliable indicator of oxidative stress (14). Rising MDA levels may be a sign of increased oxidative stress in patients with stroke. In this study, only the MDA level shows an effect of clarithromycin, while this agent does not show a significant improvement in stroke-induced behavioral deficits.

Limitation

Experimental studies have highlighted neuroprotective agents after ischemic strokes and neuroprotective drugs show efficacy in animal studies. Although the idea of neuroprotection has shown promise in experimental research, it cannot be successfully implemented in clinical settings. Although numerous neuroprotective substances have

demonstrated promise as potential therapies for ischemic stroke in both vitro and in vivo models of cerebral ischemia, patient outcomes have been inconsistent. Another limitation is the limited sample size of the study. The sample size may not be adequate. In studies, the calculation of sample size is an important issue (3). If a researcher selects a smaller number of animals, it may lead to missing significant differences even if they exist in the population. A good statistical analysis with more cases is required. If a greater number of animals are selected, then it may lead to unnecessary wastage of resources (3). Table 1 shows the mean values of all groups. Some changes in the SHAM group are also seen. The SHAM operation can sometimes lead to some changes in animals. In this study, the SHAM group also showed some improvement which may raise some concerns. We preferred to use malondialdehyde which may not be the best approach to measure "ischemia/reperfusion injury". Higher levels of MDA were associated with higher moralities; however, the infarct volume, edema volume, and cerebral blood flow (CBF) could have been measured and would be more clinically related. We are aware that mortality and other critical physiological parameters (cerebral blood flow, systemic blood pressure, and body temperature) are important factors in these kinds of studies but were not assessed in the present study.

CONCLUSION

Currently, there have been tremendous efforts made to manage patients with stroke. The disturbances in cerebral circulation are of particular importance after a stroke. This study provides novel insights into the effect of clarithromycin in reducing ischemic damage following a stroke. There may be a link between post-stroke infections and prognosis, making antibiotic treatment as a prophylactic measure advantageous, and this study indicates that clarithromycin has a neuroprotective effect on cerebral ischemic injury following a stroke. Restriction of oxidative stress in ischemic brain injury can be provided with substances such as clarithromycin that were found to be potentially beneficial in the present study. Clarithromycin may be adopted as a neuroprotective agent for the treatment of ischemic brain injury. More studies are needed.

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RESEARCH ARTICLE

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The Effect of *Pelargonium sidoides* Extract on Penicillin-Induced Epileptic Activity

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Abstract

Objective: The aim of this study is to investigate the effects of *Pelargonium sidoides* extract on penicillin-induced epileptic activity. Epilepsy is a neurological disorder characterized by seizures due to abnormal electrical activity in the brain. *P. sidoides* is a medicinal plant known for its anti-inflammatory and antioxidant properties, making it a candidate for research into natural therapeutic alternatives. This study seeks to evaluate the potential effects of this plant on epileptiform activity, contributing to the exploration of effective options for epilepsy treatment. This study represents the first investigation into the relationship between *P. sidoides* and epileptiform activity

Methods: A total of 18 female Wistar albino rats, aged 16-20 weeks and weighing 220-350 g, were randomly divided into three groups: Control group (n=6) received intracortical penicillin-G, Vehicle group (n=6) received intracortical penicillin with physiological saline, and Experimental group (n=6) received intracortical penicillin-G combined with *P. sidoides* extract. The rats were treated daily for 10 days with physiological saline and *P. sidoides* extract at a dosage of 60 mg/kg via gavage. Last day of the experiment neuromuscular blockade was induced with urethane, and electrophysiological recordings were obtained from the cortex.

Results: Statistical analysis was performed using SPSS 15.0, and normality of the datas was confirmed for all groups using the Kolmogorov-Smirnov test. No statistically significant differences were found in average peak frequency or amplitude between the penicillin group and the *P. sidoides* group ($p>0.05$). The average peak frequency for the penicillin group was 59±1.5 spikes/min, while for the *P. sidoides* group, it was 56.3±4.3 spikes/min.

Conclusion: Although *P. sidoides* may suggest a potential influence on epileptiform activity, the results indicate that it does not provide effective or significant protection under the tested conditions. Further research is necessary to explore its therapeutic potential in the treatment of epilepsy.

Keyword: Epilepsy, *Pelargonium sidoides*, antiepileptic, electrophysiology, neuroprotection

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INTRODUCTION

Epilepsy is a complex neurological disorder characterized by seizures caused by abnormal electrical activity in the brain, which can lead to alterations in an individual's consciousness, behavior, memory, and sensory perception (1). The incidence of epilepsy varies significantly across different populations worldwide. For instance, in Asian countries, the annual incidence rate is approximately 52.5 per 100,000 person-years. It has been observed that the burden of epilepsy in Asia may be more widespread in countries like Turkey compared to China. In Asia, Turkey is reported to have the highest prevalence of active epilepsy (6.7 per 1,000 people), while China has the lowest prevalence (4.1 per 1,000 people) (2). Among the various types of epilepsy, one of the most challenging is drug-resistant epilepsy (DRE), which, according to research, occurs in approximately 13.7% of community-based populations and 36.3% of clinic-based cohorts (3). A common challenge posed by DRE is the inadequacy of current treatment options and the presence of diverse pathologies in different individuals.

Traditionally, the definition of epilepsy is based on the occurrence of two unprovoked seizures. However, international epilepsy organizations have proposed recommendations to broaden this definition for more specific cases (4). In this context, understanding the underlying mechanisms of epileptic seizures is of critical importance for developing treatment approaches and strategies. Alongside advanced therapeutic options and medications, there is an increasing interest in natural products and traditional medicine practices. Promising findings regarding the antiepileptic effects of herbal treatments have emerged in the existing literature (5).

P. sidoides is a widely used medicinal plant in traditional medicine, utilized for treating various health issues. However, there is a limited number of studies specifically investigating the effects of this plant on epilepsy. Current knowledge highlights the anti-inflammatory and antioxidant properties of *P. sidoides*, suggesting notable potential for these characteristics to influence epileptic activity (5). Furthermore, the contributions of its components to neurological protection emphasize the need for research into new and effective methods for epilepsy treatment.

The aim of this study is to investigate the effects of *P. sidoides* extract on penicillin-induced epileptic activity. The research seeks to evaluate the potential effects of *P. sidoides* on epilepsy, contributing to the exploration of natural and effective alternatives in epilepsy treatment.

METHODS

Using 18 female Wistar albino rats (aged 16 to 20 weeks, weighing 220 to 350 g), three groups were formed: (1) control group, (2) vehicle group, and (3) experimental group (n=6, for each of the three groups). First group received intracortical (ic) penicillin-G (500 IU), the second group received penicillin (ic) + physiological saline, and the experimental group received treatment with penicillin-G (500 IU) + *P. sidoides* extract. Physiological saline and *P. sidoides* extract were administered daily for 10 days via gavage at a dose of 60 mg/kg in a volume of 1 ml per 100 g. Subsequently, neuromuscular blockade was applied to the rats with urethane, and access was obtained from the skull to the cortex by drill using a screw technique, allowing for electrophysiological recordings to be taken for 2-3 hours.

Statistical Analysis

All datas were statistically analyzed using SPSS 15.0. The normality of the dataset was assessed with the Kolmogorov-Smirnov test, and it was found that all groups exhibited a normal distribution. To evaluate differences in spike frequency and amplitude across each period among the groups, One-Way ANOVA followed by a post-hoc Tukey test was employed. Furthermore, all results are expressed as means ± standard error of the mean (SEM), with $p < 0.05$ considered to indicate statistical significance.

RESULTS

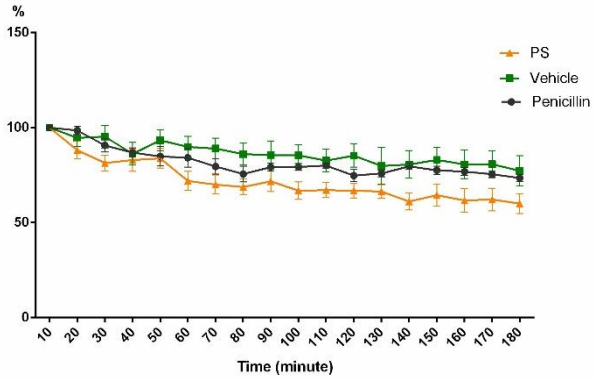

Figure 1. There was no significant difference in spike frequency between all groups. Frequency Value= 100 x The mean of spike frequency after substance administered/ The mean of spike frequency before substance administered

Our results indicate that there is no statistically significant difference in the average peak frequency between the penicillin group and the *P. sidoides* group ($p>0.05$). The average peak frequency in the penicillin group was found to be 59±1.5 spikes/min, while the average peak frequency in the *P. sidoides* group was determined to be 56.3±4.3 spikes/min (Figure 1). Another finding of our study is that there was also no significant difference in the average amplitude values among the penicillin, vehicle, and *P. sidoides* groups ($p>0.05$). These factors suggest that although *P. sidoides* may create an impression of a potential effect on epileptiform activity, it does not provide effective or significant protection under the current conditions. Figure 2 presents the representative ECoG recordings for all groups at the 90th minute: (A) Penicillin (500 IU, i.c.); (B) Vehicle group (Serum physiologic; 1 ml/100 g

p.o. for ten days); (C) *P. sidoides* (60 mg/kg p.o. for ten days).

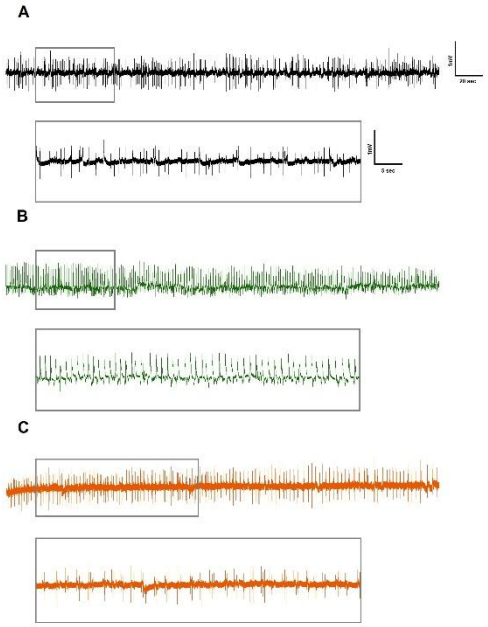

Figure 2. Representative ECoG recordings for all groups at 90th minute: (A) Penicillin (500 IU, i.c.); (B) Vehicle group (Serum physiologic; 1ml/100g p.o. for ten days); (C) Pelargonium sidoides (60mg/kg p.o. for ten days p.o.)

DISCUSSION

Epilepsy is a multifaceted neurological disorder demanding a comprehensive understanding of its etiology and effective treatment strategies. The symptomatic relief provided by antiseizure drugs (ASDs) is mediated through interactions with various cellular targets. The primary objectives of this research include the modulation of voltage-gated ion channels, the enhancement of GABA inhibition, the direct modulation of synaptic release, and the inhibition of synaptic excitation mediated by ionotropic glutamate receptors (6). The intricate mechanisms of these interactions aim to reduce the intrinsic excitability of neurons and hinder the synchronization of abnormal firing, ultimately mitigating seizure activity.

Antibiotics, specifically penicillin, have been documented to induce seizure activity due to neurotoxicity, representing one of the most thoroughly studied examples of antibiotic-induced seizures (7). GABA-evoked Cl^- currents in the context of penicillin show that penicillin blocks both postsynaptic and presynaptic inhibition mediated by GABAA receptors (8,9). This blockade may interfere with normal synaptic function, potentially exacerbating seizure susceptibility. Notably, the enhancement of GABAergic inhibition through ASDs can counteract these adverse effects, emphasizing the significance of targeting GABA receptors in seizure management.

P. sidoides, a medicinal plant known for its therapeutic properties, has garnered interest in the context of epilepsy treatment. The plant's extract exhibits anti-inflammatory and immunomodulatory effects and may influence neuronal excitability (10). Although research has shown that derivatives of *P. sidoides* can exhibit antiproliferative effects on cancer cells (11), its potential role in modulating GABAergic activity remains an area ripe for exploration. Given that penicillin-induced seizure models exhibit disruption in GABAergic transmission, it is plausible that *P. sidoides* may aid in restoring the balance of

inhibitory signaling, thereby contributing to seizure control.

Furthermore, current efforts in epilepsy research are directed toward understanding the pharmacological properties of natural products, particularly their mechanisms of action. *P. sidoides* has been observed to possess immunomodulatory activity (5), which may also play a role in managing inflammation-related seizure activity. Investigating the interaction of *P. sidoides* with GABA receptors could provide insights into its therapeutic potential for epilepsy.

In a recent study, we demonstrated that *P. sidoides* inhibits cell proliferation, induces apoptosis by increasing oxidative stress and genotoxicity, and thereby promotes cancer cell death in a neuroblastoma cancer cell line (12). This study may identify a pathway of *P. Sidoides* that could potentially be effective in epilepsy.

Despite being a traditional remedy, the scientific evaluation of *P. sidoides* has highlighted the need for well-designed clinical studies to confirm its efficacy and safety profile. The lack of comprehensive datas on its toxicological properties necessitates thorough investigation, especially given its increasing popularity in modern medical systems in Europe. The potential of *P. sidoides*-based products as alternative therapies could address the urgent need for safer and more effective treatment options, especially in the context of drug-resistant epilepsy or in individuals who are reluctant to use chemical medications as alternatives to antiseizure drugs.

This study has several limitations, including a small sample size of 18 rats, which may affect the generalizability of the findings. Additionally, the focus on a single dosage and treatment duration of *P. sidoides* may not adequately capture its therapeutic potential. Furthermore, the study did not investigate the underlying mechanisms of action, and additional research in diverse seizure models is needed to validate the results and assess safety and efficacy.

CONCLUSION

In conclusion, the exploration of *P. sidoides* as an adjunctive treatment for epilepsy, especially in penicillin-induced seizure models, warrants further research. Understanding its interactions with GABAergic systems could unveil new therapeutic pathways for managing epilepsy, providing hope for patients who are not well-controlled by conventional ASDs. However, the potential toxicological effects and optimal dosing of *P. sidoides* must also be thoroughly investigated to ensure safety and efficacy. Integrating traditional knowledge with modern pharmacological research may lead to innovative treatment strategies that enhance the quality of life for individuals living with epilepsy.

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Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci **February 2025; 11(1): 64-69**

CASE REPORT **DOI:** 10.19127/mbsjohs.1615286

Giant Radicular Cyst Involving the Maxillary Sinus

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Abstract

The most prevalent cystic lesions in the jaws are radicular cysts. They are made up of epithelial remains that multiply after pulp necrosis due to inflammation. Radicular cysts rarely grow to substantial sizes, while typically being tiny and asymptomatic. When localized, they are treated with root canal treatment; when large, they are treated with surgical procedures.

A 28-year-old systemically healthy male patient was admitted to our clinic due to extraoral swelling in the right maxillary posterior region. Radiographic examination revealed a well-defined lesion localized in the right maxillary region, extending into the nasal cavity and orbital floor, including the maxillary sinus. The lesion, in which cyst fluid was observed as a result of aspiration biopsy, was enucleated under general anesthesia and an excisional biopsy was performed. The biopsy confirmed the preliminary diagnosis of the radicular cyst.

Radicular cysts seen in the maxillary region may resorb adjacent anatomical structures and develop into the sinus. Such lesions should be diagnosed before they reach large sizes and the causative teeth should be treated.

Keyword: Radicular cyst, enucleation, maxillary sinüs

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Note: This study was poster presented at the 31th Turkish Association of Oral and Maxillofacial Surgery (TAOMS) congress.

INTRODUCTION

In the jaws, radicular cysts are the most prevalent cystic lesions. They constitute 52%-68% of all cysts seen in the jaws (1,2). They are thought to occur due to the inflammatory proliferation of Malessez epithelial cell residues in the apical region of a tooth with necrotic pulp (3,4). They can also be seen lateral to the roots in relation to accessory root canals. They are more common in the incisor-canine region of the maxilla. They are more likely to occur in the third decade and in males (5,6).

Radicular cysts usually cause no symptoms and are small in size. However, they can rarely reach large sizes. They can cause mobility, displacement, and root resorption in adjacent teeth (4,7). On radiographs, they are observed as a radiopaque, circumscribed round or oval radiolucency that is continuous with the lamina dura of the relevant tooth in the apical region of the necrotic tooth. When localized, root canal treatment; when they reach large sizes, they are treated with surgical techniques such as marsupialization, enucleation, or decompression (4,8). In this case report, surgical treatment of a large radicular cyst involving the maxillary sinus is presented.

CASE REPORT

A 28-year-old male patient applied to Oral and Maxillofacial Surgery Clinic due to extraoral swelling in the right maxillary posterior region. It was obtained that the patient had no systemic disease in his medical history; however, he had previously undergone an operation in the otorhinolaryngology department. Radiographic examination revealed a well-defined lesion in the right maxillary region, measuring approximately 44x34x40 mm in dimension, occupying most of the right maxillary sinus and extending into part of the nasal cavity. The lesion was associated with the expansion of both buccal and palatal cortical plates and resorption of the roots of adjacent teeth (Figure 1).

Figure 1. A. Panoramic radiograph; B. Axial, C. Coronal, and D. Sagittal CBCT views showing a large, well-defined expansile lesion in the right maxillary region.

Cyst fluid was observed in the aspiration biopsy performed for preliminary diagnosis. It was planned to enucleate the mass under general anesthesia. After providing general anesthesia with endotracheal intubation, local infiltrative anesthesia was applied to the right maxillary anterior and posterior regions. Following the sulcular incision extending from tooth 17 to

tooth 22, relaxing vertical incisions were made from the distal of tooth 17 and mesial of tooth 22, and a full-thickness mucoperiosteal flap was raised. The cyst wall perforating the buccal bone was dissected from the surrounding bone and the lesion was enucleated. (Figures 2,3). The sharp bone edges were smoothed and the flap was closed primarily. As a result of the biopsy, fibrotic-walled tissue, and benign osseous tissues were observed in the subepithelial area lined with nonkeratinized stratified squamous epithelium, hemorrhage, and lymphoplasmacytic infiltration (Figure 4). The preliminary diagnosis of a radicular cyst was confirmed. No complications were observed during the 10 months follow-up period.

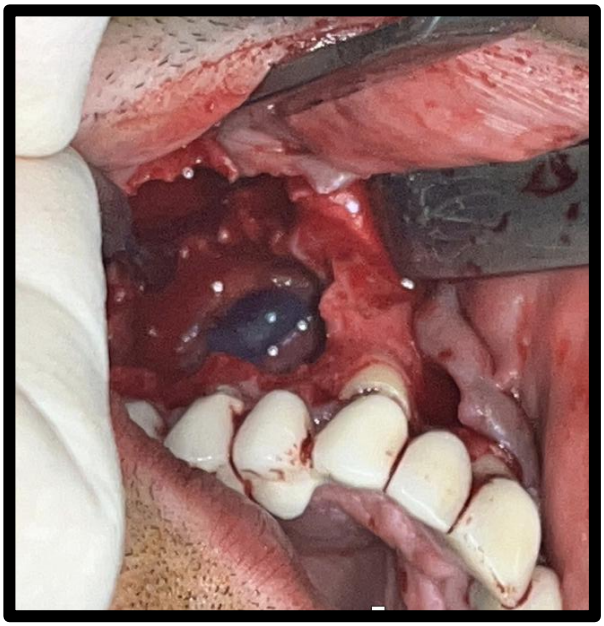

Figure 2. Image of the cyst cavity after enucleation

Figure 3. Specimen obtained after enucleation

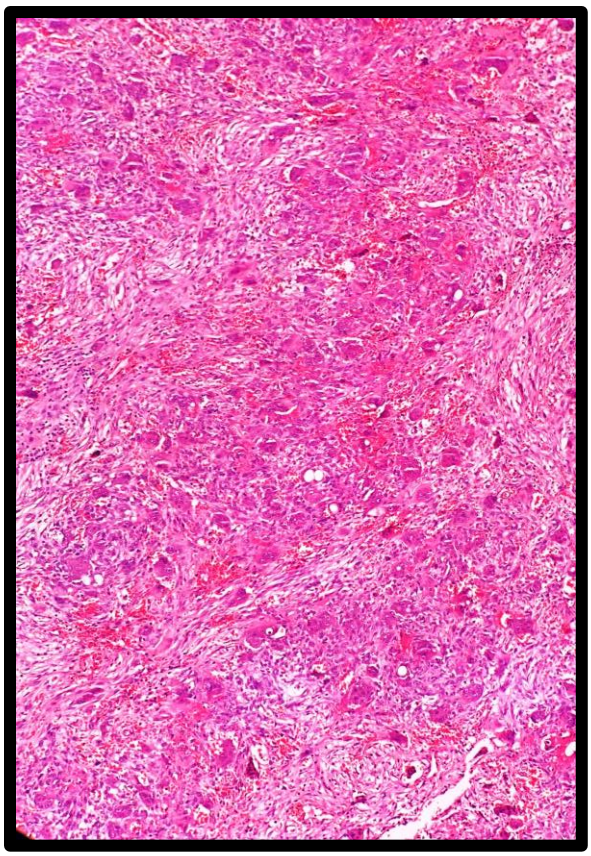

Figure 4. Histological image of the specimen obtained as a result of excisional biopsy at x200 magnification

DISCUSSION

In the oral and maxillofacial area, odontogenic cysts are common lesions. The cyst epithelium

originates from the tissues involved in tooth formation. They are examined in two main groups: inflammatory and developmental cysts. The most common inflammatory cysts are radicular cysts, which are formed as a result of the proliferation of epithelial remnants due to inflammation caused by pulp necrosis (9,10).

Radicular cysts are often discovered incidentally on radiographs without any obvious symptoms. They are usually painless unless infected. Although they tend to grow and expand slowly, they can reach significant sizes if not diagnosed and treated in time (1,11). Invasion of odontogenic cysts into the maxillary sinus depends on their proximity to the sinus and the type of lesion has no effect. Infected cysts spread to areas where the bone is weak, such as the sinus or nasal cavity. They do not cause any asymmetry unless the sinuses are filled. (4,7). In our case, the radicular cyst progressed asymptomatically and extended into the nasal cavity, involving the maxillary sinus.

Radicular cysts are radiographically present as unilocular radiolucent images with sclerotic borders related to the apex of the affected tooth. They are distinguished from follicular spaces by having a diameter of at least 1 cm. Lesions such as dentigerous cyst, odontogenic keratocyst, Pindborg's tumor, ameloblastoma, cementoma, and odontogenic fibroma can have similar radiographic characteristics to radicular cysts. Histopathological evaluation is usually required for the diagnosis of such lesions. While panoramic radiographs are inadequate, especially when cysts are large, computed tomography (CT) scans provide superior detail and allow visualization of the size and extension of the cyst. When radicular cysts extend to the maxillary sinus, mucoceles, pseudocysts, and retention cysts are also included in the differential diagnosis of the radicular cysts (5,12). In our case, radiographic evaluation was performed via cone beam computed tomography (CBCT), and the preliminary diagnosis was confirmed by histopathological examination.

In the treatment of radicular cysts, endodontic treatment or surgical treatments such as enucleation and marsupialization are applied. While endodontic treatment usually provides healing in cysts, when the lesion reaches large sizes, endodontic treatment is not sufficient, and surgical treatment is required (2,13). In our case, the cystic lesion, which reached large dimensions enucleation treatment was applied.

There are few cases of radicular cysts invading the maxillary sinus in the literature similar to our case Sagit et al. (7) reported a large radicular cyst located in the right maxillary sinus and caused destruction of the anterior wall of the maxilla in a patient presenting with extraoral swelling and nasal obstruction. The mass covered with calcified tissue was treated with an endoscopic approach. Pekiner et al. (12) reported a radicular cyst covering a large part of the right maxillary sinus in a patient who

applied bilateral swelling that does not cause pain in the anterior palatinal region and treated it with surgical enucleation under general anesthesia. Köse et al. (4) reported a giant radicular cyst extending into the bilateral maxillary sinus and nasal cavity. CBCT evaluation revealed that the lesion covered the entire left maxillary sinus and a large part of the inferior nasal cavity and extended into the right maxillary sinus. The cyst was enucleated under general anesthesia and apical resection of the relevant teeth was performed.

CONCLUSION

As a result, radicular cysts seen in the maxillary region may resorb adjacent anatomical structures and develop into the maxillary sinus. Such lesions should be diagnosed before they reach large sizes and the causative teeth should be treated.

Ethics Committee Approval: Ethics Committee Approval: The presented study is qualitative and consent was obtained by giving information about the study by one-toone interviews with the subjects who agreed to participate. The study was carried out by paying attention to the Declaration of Helsinki

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Monkeypox and Nursing: Prevention, Management, and Care Strategies

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Abstract

This study examines the clinical features of Monkeypox, its prevalence in outbreaks, and the critical roles of nurses in the prevention and management of this disease. Strategies for minimizing the effects of the disease on health systems and society are discussed by addressing the multifaceted tasks of nurses such as infection control, patient care, education and counseling.

This study is a comprehensive review. Current academic sources and reports were examined using the literature review method. In line with the data obtained from these sources, the symptoms, transmission routes, complications, and nursing practices of Monkeypox have been evaluated. The study aims to synthesize existing knowledge and analyze current approaches to nursing care and infection control measures.

Monkeypox is a zoonotic disease that can lead to serious complications, especially in individuals with weakened immune systems. In the management of the disease, nurses play a critical role in preventing the spread of the epidemic with tasks such as infection control, psychosocial support, and community information, as well as patient care. Nursing practices such as symptomatic treatment, use of appropriate personal protective equipment, isolation and education support the recovery process of patients and protect public health.

The role of nurses in the prevention and management of Monkeypox is vital for controlling the outbreak. Strategies for training and supporting nurses will make a major contribution to future epidemic preparedness and the development of existing measures. This study highlights the challenges nurses face in epidemic management and the support mechanisms needed to cope with these challenges

Keyword: Monkeypox, nursing care, prevention, management, infection control

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A. INTRODUCTION

1. What is Monkeypox?

Description and Origin

Monkeypox disease is a zoonotic infection caused by the Monkeypox virus in the genus Orthopoxvirus, which belongs to the Poxviridae family. This virus, which was first detected in monkeys in 1958, was first described in humans in 1970 in the Democratic Republic of the Congo (1). Although the virus has genetic similarities to the smallpox virus, it is usually milder and has a lower mortality rate. In recent years, monkeypox has been among the global health threats, with case reports also increasing, especially in regions outside of Africa (2).

Clinical Manifestations

The clinical manifestations of the disease are characterized by fever, headache, muscle aches, back pain, lymphadenopathy and rash on the body. The rash can spread to the whole body, usually starting on the face, hands and feet. The severity of symptoms can vary depending on the length of contact with the virus and the individual immune response (3).

2. Epidemiology of the Disease and Modes of Transmission

Epidemiology

: Monkeypox was first reported in Central and West Africa. However, in recent years, with the increase in global travel and trade, there has been a significant increase in the international spread of the disease. The worldwide pandemic in 2022 increased the pressure of the disease on international health systems and was among the global health threats (4).

Modes of Transmission

The Monkeypox virus can be passed to humans through direct contact with the bodily fluids, blood, or meat of infected animals. It can also be transmitted through respiratory secretions, skin rashes, or contaminated surfaces and items of infected people. These routes of transmission are important factors that facilitate the spread of the virus within the community (5).

3. Importance and Need of Nursing Care

Importance: Nurses

play a critical role in the management of Monkeypox. These roles cover areas such as controlling the spread of infection, symptom management, providing patient education, and coordinating care processes. Nurses increase the effectiveness of treatment processes by providing both physical and psychosocial support during the treatment process of patients (6).

Need

The importance of nursing care is increasing due to the contagiousness of the disease and the difficulties in the treatment process. Nurses need to have sufficient knowledge and skills in infection control, monitoring of patients and

implementation of treatment protocols. They also play a critical role in raising public awareness and educating (7).

4. Purpose and Importance of the Article

Objective

The aim of this article is to present a comprehensive analysis of Monkeypox from a nursing perspective. The main goal of this study is to evaluate the effects of nursing practices on infection prevention, management and patient care and to make suggestions on existing strategies.

Importance

The fact that Monkeypox is among the global health threats increases the importance of nursing care in terms of effective management of this disease. The article aims to provide a resource for developing nursing practices and strategies, overcoming challenges in disease management, and identifying best practices in patient care.

B. Monkeypox Disease: Clinical Symptoms and Diagnostic Process

1. Clinical Symptoms and Course of Disease

Monkeypox is clinically manifested by fever, headache, muscle aches, back pain, lymphadenopathy and rashes on the body. The course of the disease usually consists of the following stages:

Initial Stage: The disease usually begins with fever, headache, muscle aches and weakness. These early symptoms can create a flu-like picture and usually occur in the initial stage of the disease.

Rash Stage: Within a few days of the appearance of fever, rashes develop on the body. The rash first starts on the face, hands, and feet, and spreads to other parts of the body over time. The rashes develop from papules to vesicles and eventually to crusts.

Complications: Some patients may develop serious complications with rashes, including lumping, infected sores, and secondary bacterial infections. Usually, the disease resolves on its own, but individuals with weakened immune systems have a higher risk of complications (3).

2. Diagnostic Methods and Laboratory Tests

The diagnosis of Monkeypox is based on laboratory tests along with clinical manifestations:

Clinical Evaluation: The first step is usually an assessment of the patient's clinical symptoms and history. This means gathering information about the history of contact with the virus and the timing of symptoms.

Laboratory Tests: Various laboratory tests are used to confirm the diagnosis:

Polymerase Chain Reaction (PCR): It is used to detect virus DNA in samples taken from infected tissues or fluids and is the most reliable

method in making a definitive diagnosis of the disease.

Serological Tests: These are tests that detect antibodies against the virus in the blood of patients. These tests are used to assess the immune response to the virus in individuals who have had a past infection.

Viral Cultures: Amplification of the virus in vitro can be used to confirm the diagnosis, but this method is less common and can take time (5).

3. The Role of Nurses: Early Diagnosis and Follow-up

Nurses play a critical role in the management of Monkeypox, and this role is of great importance in early diagnosis and follow-up processes:

Early Diagnosis: Nurses carefully monitor patients' signs and evaluate clinical symptoms. Early diagnosis ensures that the disease is controlled and transmission is prevented. Nurses play an important role in reporting symptoms and ensuring that tests are carried out in a timely manner.

Track & Trace: Nurses regularly monitor patients' recovery progress and assess their response to treatment. It also follows the worsening of symptoms or the appearance of new signs. This process is critical to assessing the effectiveness of treatment protocols and making necessary changes.

Education and Support: Nurses provide training on infection management and care for patients and family members. It also provides patients with information and psychosocial support to prevent the spread of infection (6).

C. Prevention Strategies in Nursing

1. Infection Control Measures

Infection control measures are critical to limit the spread of Monkeypox and reduce the risk of infection in healthcare. These measures include the following elements:

- ***Patient Isolation:*** Infected patients should be isolated to prevent the spread of infection to other patients and healthcare workers. Isolation practices ensure that patient rooms are segregated and infected people are separated from other patients (8).
- ***Hand Hygiene:*** Hand hygiene is an essential way to prevent the spread of infection. Healthcare workers are required to wash their hands or use hand sanitizer before and after patient care (5).
- ***Cleaning and Disinfection:*** Regular cleaning and disinfection of patient rooms and healthcare equipment reduces the risk of infection. Surfaces and equipment should be

cleaned with appropriate disinfectants to eliminate infectious agents (7).

2. Use of Personal Protective Equipment

Personal protective equipment (PPE) ensures that nurses and healthcare workers are protected against Monkeypox. The use of PPE includes the following elements:

• ***Mask and Protective Glasses:*** Masks and protective glasses are used to prevent the spread of respiratory viruses. This equipment helps nurses protect themselves from respiratory infections (5).

• ***Gloves and Gowns:*** Sterile gloves and protective gowns are used during direct contact with infected patients. This reduces the risk of infection and ensures the safety of nurses (3).

• ***Proper Use and Disposal of PPE:*** Nurses should properly clean and dispose of equipment before and after use to minimize the risk of infection transmission (9,10). This includes thorough cleaning of reusable equipment, such as stethoscopes and thermometers, using appropriate disinfectants to prevent cross-contamination and adherence to institutional protocols for sterilization. For single-use items, including gloves, syringes, and disposable gowns, proper disposal involves placing them in designated biohazard bags or sharps containers as specified in infection control guidelines. These practices are essential for ensuring patient and staff safety within healthcare settings (9,10).

3. Education and Information: Patient, Family and Society

Education and information are an important part of preventing the spread of infection in nursing practice. These processes include:

• ***Patient Education:*** Infected individuals should be informed about the symptoms of the disease, treatment methods and personal hygiene. This education helps patients better manage the disease and prevent the spread of infection (8).

• ***Family Education:*** Family members should be informed about infection control measures and what to look for in patient care. This enables family members to contribute effectively to the nursing care process (6).

• ***Community Awareness:*** Awareness-raising campaigns should be organized for society, information should be given about the symptoms of the infection, transmission routes and prevention methods. Raising awareness throughout the community is an important step in reducing the spread of infection (7).

4. The Role of Vaccination and the Duties of Nurses in Vaccine Management

Vaccination plays an important role in controlling Monkeypox. Nurses' duties in vaccine management include:

• ***Vaccine Administering:*** Nurses ensure that vaccines are administered correctly. Vaccinations on schedule prevent the spread of infection and increase herd immunity (4).

• ***Vaccine Management and Monitoring:*** Nurses monitor the effectiveness and safety of vaccination. They are responsible for the evaluation of post-vaccination side effects and the implementation of vaccination protocols (5).

• ***Community Vaccination Programs:*** Nurses organize community vaccination programs and inform the community about the benefits of vaccination. They also play an important role in the planning and execution of vaccination campaigns (6).

D. Management of Monkeypox: Nursing Practices

1. Symptom Management and Medication

Symptom management is a cornerstone of Monkeypox treatment. Nurses employ specific, actionable approaches to enhance patient comfort and manage symptoms effectively:

• ***Fever and Pain Management:*** Nurses administer prescribed pain medications such as paracetamol or ibuprofen to manage pain and fever. Additionally, they may use cooling blankets or apply cold compresses to reduce body temperature. For hydration, nurses provide oral rehydration solutions or intravenous fluids for patients unable to drink adequately (8).

• ***Rash and Skin Problems:*** Nurses cleanse affected skin areas gently with saline solutions to reduce irritation. For moist lesions, they apply non-stick dressings to prevent further discomfort. Topical antihistamines or prescribed antiviral creams are used as per the treatment protocol (4).

• ***Medication Administration:*** Nurses ensure adherence to medication schedules by documenting each dose in patient charts and using reminders. They educate patients about the importance of completing prescribed medication regimens to avoid complications (6).

2. Patient Isolation and Infection Control

Preventing the spread of Monkeypox is essential, and nurses are instrumental in implementing isolation and infection control practices:

• ***Patient Isolation:*** Nurses supervise the setup of isolation rooms, ensuring features such as negative-pressure ventilation and minimal contact zones are in place. For example, they coordinate visitor restrictions and educate staff about isolation protocols (5).

• ***Infection Control:*** Proper donning and doffing of personal protective equipment (PPE) is demonstrated and monitored by nurses. They perform routine cleaning and disinfection of high-touch surfaces such as bed rails and

doorknobs, ensuring adherence to hospital protocols (7).

3. Pain and Discomfort Management

Managing pain and discomfort is a priority to improve the quality of life for Monkeypox patients:

• ***Pain Management:*** Nurses use validated pain assessment tools like the Numeric Rating Scale (NRS) to evaluate pain levels. For instance, if a patient reports pain exceeding a certain threshold, nurses promptly administer analgesics or suggest repositioning to alleviate discomfort (8).

• ***Discomfort Management:*** Nurses provide skin care by applying moisturizers or emollients to prevent dryness and cracking. Relaxation techniques, such as guided breathing exercises, may also be recommended to help patients cope with general discomfort (4).

4. Psychosocial Support and Nursing Approaches

Psychosocial well-being is a vital aspect of Monkeypox care, and nurses actively address patients' emotional and social needs:

• **Psychological Support:** Nurses perform initial screenings for anxiety or depression using standardized tools. Based on the results, they offer counseling sessions or facilitate access to professional mental health services. For instance, they might guide patients through relaxation techniques to manage stress (6).

• ***Family Support Programs:*** Educational workshops are organized by nurses for family members to understand the disease and care requirements. Practical demonstrations, such as proper hand hygiene and dressing changes, empower families to support the patient effectively (8).

5. Nutrition and Hydration Support

Optimal nutrition and hydration are essential for recovery, and nurses play a key role in this process:

• ***Nutritional Support:*** Nurses collaborate with dietitians to create meal plans that meet patients' specific needs, such as protein-rich diets for wound healing. They monitor food intake and encourage the consumption of easily digestible, nutrient-dense foods, particularly for patients with reduced appetites (7).

• ***Hydration Support:*** To prevent dehydration, nurses track fluid intake using a fluid balance chart. For patients with severe dehydration, they administer IV fluids and educate patients about the importance of electrolyte-rich beverages (4).

E. Care Strategies: Hospital and Home Care Processes

1. Nursing Care in a Hospital Setting

Nursing care in a hospital setting is essential for the effective treatment and recovery of

Monkeypox patients. Each aspect of nursing care is detailed with specific applications:

• ***Patient Monitoring and Care:*** Nurses monitor patients' vital signs at regular intervals, using tools such as blood pressure monitors, thermometers, and pulse oximeters. They document these observations in patient records and adjust interventions based on clinical changes. For example, if fever spikes, antipyretics are administered promptly, and hydration protocols are implemented (5).

• ***Infection Control:*** Infection control measures include sterilizing surfaces in patient rooms with hospital-grade disinfectants, enforcing strict hand hygiene practices through frequent washing or alcohol-based sanitizers, and ensuring the proper donning and doffing of personal protective equipment (7). Training on infection protocols is periodically provided to all healthcare staff.

• ***Pain and Symptom Management:*** Pain scales such as the Visual Analog Scale (VAS) or the Numeric Rating Scale (NRS) are used for assessing pain levels. Based on the findings, nurses administer analgesics or non-pharmacological interventions such as positioning or cold compresses to alleviate discomfort (8).

• ***Psychosocial Support:*** Nurses conduct daily check-ins to address patients' emotional well-being. They might use guided relaxation techniques or refer patients to counseling services if anxiety or depression is detected (6).

2. Home Care and Nursing Services

Home care ensures the continuity of treatment for patients transitioning from hospital to home settings. Specific nursing practices include:

• ***Organization of Home Care:*** Nurses provide detailed home care plans, including instructions for medication schedules, wound care procedures, and dietary recommendations. For instance, they may design a daily routine for applying topical treatments to Monkeypox lesions (3).

• ***Pain and Symptom Management:*** Nurses educate patients and caregivers on recognizing pain and symptom escalation. For example, they may instruct on using over-the-counter pain relief medications and maintaining a log of symptoms to report during follow-up visits (4).

• ***Family Education and Support:*** Training sessions include hands-on demonstrations, such as how to change bed linens while minimizing discomfort to the patient or how to properly use medical equipment like nebulizers. Emergency protocols, such as recognizing signs of secondary infections, are also covered (8). 5.3.

3. Creating a Care Plan and Patient Monitoring Effective patient care involves meticulous planning and regular monitoring, tailored to individual patient needs:

• ***Creating a Care Plan:*** Nurses conduct initial assessments, documenting patients' physical, emotional, and social needs. These assessments inform the creation of individualized care plans, including specific goals such as "reduce fever within 48 hours" or "achieve pain level below 3 on NRS within a week" (7).

• ***Patient Monitoring and Assessment:*** Nurses use mobile health technologies or telemedicine platforms to monitor patients remotely, ensuring adherence to treatment protocols. They provide feedback during routine home visits or teleconsultations, adjusting care plans based on progress (6).

4. Multidisciplinary Approach and the Role of Nurses in the Team

A multidisciplinary approach enhances the quality of care provided, and nurses play a pivotal role in this setup:

• ***Teamwork:*** Nurses actively participate in case discussions during multidisciplinary team meetings. For example, they share insights on a patient's response to pain management strategies, guiding decisions on modifying dosages or adding complementary therapies (4).

• ***Coordination and Communication:*** Nurses act as liaisons, scheduling consultations with dietitians for nutritional support or psychologists for mental health care. They also provide detailed patient reports to ensure seamless communication within the team (3).

• ***Patient-Centered Approach:*** By conducting surveys or interviews, nurses identify patients' specific concerns or goals, such as minimizing scarring or managing anxiety about recovery. They then work with the team to integrate these priorities into the treatment plan, fostering a personalized care experience (8).

F. Education and Patient Education: Awareness Raising and Behavior Change

1. Patient and Family Education

Patient and family education plays a critical role in managing Monkeypox and reducing the risk of transmission:

Disease Information and Symptoms: Nurses inform patients and their families about the definition, symptoms, and treatment processes of Monkeypox. Education ensures that patients are able to identify symptoms and seek medical attention at appropriate times (8).

Treatment and Care: Nurses provide detailed information about the treatment process and care requirements. This includes how to use medications, how to manage symptoms, and access to healthcare (6).

Infection Precautions: Patients and families are trained on the necessary precautions to prevent the spread of infection. These measures

include personal hygiene, isolation rules, and how to manage contact with the patient (7).

2. Trainings to Protect Public Health

Trainings to protect public health are important to reduce the spread of Monkeypox and to raise public awareness:

Awareness Campaigns: Nurses organize campaigns to raise awareness about Monkeypox disease in the community. These campaigns provide information on the symptoms of the disease, routes of transmission, and prevention methods (3).

Training Programs: Nurses provide training programs at school, workplace, and community centers, allowing the public to learn about infection risks and prevention strategies. These trainings can be in the form of health education materials, seminars, and workshops (4).

Crisis Response Training: Preparatory trainings are organized to inform and guide the society in crisis situations. These trainings include emergency management and response strategies to public health crises (5).

3. Educator Role of Nurses

Nurses occupy an important position in the role of educator and use a variety of strategies to fulfill this role effectively:

Knowledge and Skill Transfer: Nurses teach health knowledge and care skills to patients, families, and community members. As educators, nurses increase health literacy by presenting information in an understandable and applicable way (7).

Behavior Change: Nurses help individuals change their health behaviors. This includes motivational strategies for promoting health habits, reducing risky behaviors, and adopting healthy lifestyles (6).

Development of Educational Materials: Nurses develop effective educational materials and resources. These materials can be used to facilitate patients' and society's access to information (8).

G. Nursing Challenges and Ethical Issues

1. Challenges Faced by Nurses

Nurses face several challenges when dealing with epidemics such as Monkeypox:

• ***Workload and Stress:*** Nurses may experience excessive workload and stress due to the high number of patients and intense working conditions. This can negatively affect nurses' job performance and overall quality of life. High workload can threaten both the physical and psychological health of nurses (6).

• ***Psychological Effects:*** Epidemics can put psychological pressure on nurses. Long working hours, heavy patient load, and constant contact with infected patients can increase the risk of burnout and post-traumatic stress

disorder (PTSD). It is common for nurses to need emotional and psychological support (7).

• ***Risk of Infection:*** Nurses are at high risk of infection because they are in constant contact with infected patients. This situation necessitates taking additional precautions to protect their personal health and can lead to anxiety and anxiety among nurses (8).

2. Ethical Issues

Ethical issues in nursing practice can affect patients' rights and quality of care:

• ***Patient Privacy:*** Patient information related to infectious diseases such as Monkeypox is sensitive data that needs to be kept confidential. Nurses should be vigilant to ensure the confidentiality of patient information. Violations of confidentiality can jeopardize both patients' rights and the credibility of nursing practices (5).

• ***Isolation and Stigmatization:*** Isolation of infected patients is a sensitive issue from both a health and ethical point of view. Isolation of patients can increase the risk of stigmatization and social exclusion in society. Nurses should take an ethical approach, taking into account patients' emotional needs and social support needs (4).

• ***Distribution of Resources:*** It can be difficult to distribute limited resources (e.g., personal protective equipment, treatment methods) fairly and equitably during the pandemic. Nurses may have to make ethical decisions about the fair distribution of resources. This requires the equitable delivery of health services and ensuring social equality (3).

H. CONCLUSION

Main Findings and Recommendations for Nursing Practice

The main findings and recommendations regarding Monkeypox disease and nursing practices discussed in this article are as follows:

1. Disease Management: Comprehensive knowledge of the clinical manifestations of Monkeypox, treatment methods, and infection control measures enables nurses to play an effective role in caring for patients. It is critical for nurses to be knowledgeable about symptom management, patient isolation, pain management, and psychosocial support (8).

2. Education and Awareness-Raising: Nurses should provide effective training programs for patients and their families and organize awareness campaigns in the community. This requires nurses to take on the role of both educator and counselor. Education provides information about the symptoms of the disease, infection precautions, and the treatment process, while raising public awareness can also reduce the spread of infection (4).

3. Infection Control: Nurses should meticulously follow infection control measures such as the use of personal protective equipment, patient isolation and hygiene practices. These practices ensure the protection

of both patients and healthcare professionals (7).

4. Psychosocial Support and Coping with Challenges: Nurses should develop support systems and strategies to cope with the workload, stress and psychological effects they face in the epidemic situation. Psychosocial support can help nurses cope with burnout and stress (6).

5. Ethical Issues: To deal with ethical issues such as patient confidentiality, isolation, and stigmatization, nurses must act in accordance with ethical rules and professional standards. Ethical decisions contribute to protecting patients' rights and equitable healthcare delivery (5).

I. Recommendations for Future Research and Clinical Applications

1. Research Need: More research needs to be done on the long-term effects of Monkeypox, new treatment methods, and vaccine development. Future studies will help expand evidence-based knowledge for nursing practice and disease management (11).

2. Clinical Practices: Nursing practices need to be constantly updated and improved. Standards of nursing education and practice should be reviewed to increase effectiveness in disease management and improve the quality of health care (8).

3. Community and Health Education Programs: The scope of public health education programs should be expanded and nurses should be enabled to fulfill their educational roles more effectively. This can help prevent the spread of infections and protect community health (4).

4. Policies and Support Systems: It is important to develop policies and support systems to support nurses in coping with the challenges they face. More resources and support should be provided on psychosocial support and workload management (6).

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