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## INTERESTS AND OPINIONS OF THE SOCIETY ON HEALTH NEWS AND PROGRAMS: A SAMPLE STUDY IN TRABZON

*Assoc. Prof. Sedat Bostan<sup>\*1</sup>, Dr. Beyler Yetkiner<sup>2</sup>, Tuğba Çolak<sup>3</sup>*

<sup>1</sup>Gumushane University, Health Sciences Faculty, Healthcare Management Department

<sup>2</sup>İnönü University Fac. Of Communication

<sup>3</sup>Trabzon Kanuni Research and Education Hospital

\*Corresponding author; [sbostan29@gmail.com](mailto:sbostan29@gmail.com)

**Abstract;** *Health journalism can be defined as the sharing of all kinds of health-related information, practice and development both in printed and visual media to raise public awareness. However, this sharing in health publications or news has the potential to affect the followers either positively or negatively. This study was conducted to measure the perception and effectiveness of health news and radio and TV programs on society. The study was carried out on the selected samples in Trabzon universe. The scale developed by Bostan was used and its validity was verified by exploratory factor analysis and its reliability was determined. The data was analyzed using frequency and significance tests in the SPSS program.*

*In print and visual media, it has been understood that audiences or readers are more likely to follow news about cancer and seasonal illnesses, as well as healthy lifestyles and innovations in healthcare. People found the health news and publications reasonably clear and effective, but not reliable enough. It was found that the confidence index of high school educated people was higher than those of other groups who had higher education levels. In other words, as the level of education increased, the confidence index decreased. Accordingly, it was suggested that the Ministry of Health should conduct a study to follow such publications and programs and make explanations when necessary.*

*Keywords: News, Journalism, Health, Patient*

### 1.Introduction

The development of communication technologies facilitated access to information in the field of health. The sharing of health information has been encountered at any moment by means of communication tools such as TV, Radio and Newspaper. On the other hand, the information sharing related to health with these tools remains out of control. For this reason, the accuracy and scientific knowledge of the information is discussed. It has become important to investigate how citizens are affected by health news and programs and how they are reflected in their behavior. This study was carried out to contribute to meet this need.

### **1.1. News and News Values**

“News” as a term can be described as conveying the latest, most recent and remarkable information to the people about real life in an objective way [1]. News, in general, is facts and events that enable people to be informed, educated and entertained [2]. News is one of the things that human beings need and enjoy in life. This factor plays a crucial role in the sense of the future of society and individuals, in its development, in choosing the truths, in recognizing wrong and right, in the sense of itself and its environment, and finally in the integration of individuals with each other [3].

Events, phenomena, ideas or a problems are required to carry some news values so that they can be read and followed by the masses. These values constitute the basic principles of journalism [4]. The most important of the values mentioned are "Currentness, Reality, Significance and Intelligibility of Contents". These qualities arouse curiosity in the masses who are reading / watching or hearing and it is important to perceive the news in this respect. It can be said that such news generates interest and this interest is brought to our attention by experts. Expert journalism, in parallel to this, is on the agenda in recent times to increase the relevance of the masses to the news.

### **1.2. Developing Expert Journalism and Health News Reporting**

With the development of today's economy, science, sociology, psychology and technology, new concepts have empathized with our world of emotion. These developments also do affect the sense of journalism, the media and publishing sectors. Especially in recent years, the concept of expert journalism is being discussed with journalists who are specialized in certain areas. Gamze Erdogan [5] states that today's journalists should always be ready to deal with any issue or inquiry, interviews and news on current issues, whether or not they are experts in their own fields, indicating that today's journalism has changed inevitably. Kucukyilmaz and Çopur [6] say that the basic knowledge of expert journalism must be known; hence, it is necessary to follow the process closely. One of the areas that needs to be closely monitored is news on the health that deals with public health.

A health news reporter working in the media sector is the person who is in charge of the related-subject of his/her own and who is interested in informing people about developments and innovations in the field of health [7-5] defines a health journalist as the person who communicates the print and visual media to the readers and audiences in order to enlighten them about any kind of health-related field. As for health journalism, almost every publication has its own specialist. With the emergence of health journalism, ethical violations and unsubstantiated news began to appear in news bulletins and newspaper pages. It can be said that health news reporting has substantially increased since the 90's and that there is a visible increase in the number of health-related news of many printed-visual-digital media today [8]. People and patients learn about health-related developments and information in a big way from the media, and the media responds to the interest of those people [9]. The media is producing by developing different strategies and alternatives to improve this interest.

Nowadays, the popular newspapers are exploring the star doctors and the health news is specifically published by doctors and specialists. [10]. Patients who are aware of this have started to use media to attain their own health [11]. According to İrfan Erdoğan, in this sense of journalism, there is a need to

be read much as a newspaper, apart from the rating ratios [12]. With respect to this, people who follow the media in Turkey in recent years are now able to discuss new things such as: which type of leukaemia bone marrow transplant can be performed, vitro fertilization practices or how to treat with acupuncture without surgery... and so on [13]. Usually, every year those, in their own way, talking about cancer has a new so-called remedy and ironically, different secrets of the brain are solved by them. Every disease is diagnosed broadly and an ordinary plant is becoming drug. However, this is not absolutely the case and this should be particularly noted. The readers are often faced with expressions such as "miracle discovery" [14]. Tunçel and his colleagues [8] have pointed out that these reports mostly refer to the daily lives of individuals, not the social and public aspects of the subject, adding the cosmetic health issues that are mostly shown in the news. It can be said that this causes some problems. Especially wrong information brings inevitable problems. Sezgin states that the situation that may be caused by this false information is as follows: It may lead to new diseases, unwanted situations including death, increase treatment costs as a result of misunderstanding about health and health culture [15]. "From this point of view, it is considered very important for the media to act in accordance with ethical values in terms of health communication." [11]. As for the media and human health, we see that there are different studies about this phenomenon.

When looked at the studies related to the subject, it is found that the media-health relationship is frequently discussed. In her study "The role of health communication in the medicalization of health", İnce Çınarlı " has reached the conclusion that the human health is commoditized by the news' contents and this can have negative consequences [16]. Birsen and Şentürk [10] say that the news made is evaluated in the context of "consumer culture" in their work titled "Health News from the perspective of Consumer Culture". Yıldız and Tanyıldızı [17] in their study titled "The health news in 2012 in Turkey and the way they were handled in national print media, as well as their informative levels in national daily newspapers- Habertürk, Hürriyet, Posta, Sabah and Sözcü" emphasized that in a six-month period, a total of 480 health-related news articles were appeared in the newspapers. However, from their point of view, this number was inadequate compared to the other news reports although 96 percent of them were convincing. On the other hand, in her study "Health Communication, Media and Ethics: Analysis of An Health News" Hülür states the fact that people benefit from the media; yet, she adds that irresponsible misinformation, sometimes, is offered to people that could lead to ethical violations [11].

In another study from Öztürk ve Birsen (2013) titled " Health News from the perspective of Consumption Culture ", It was found that 56 news items published in the Hürriyet Daily which were examined at certain intervals during two days of the week and one for the weekend day came true. These included diet and nutrition, chronic diseases, aesthetics and beauty, gynaecological diseases, healthy lifestyle advice and sexuality." Similarly, Demir [13] conducted a content analysis of a total of 194 articles in his study and stated that people are very interested in health issues and are closely following at least a few of the publications in this field. Sezgin insisted in his study of "understanding health literacy", which examines health and health news, that the mass media has an important role to play in the rapid flow of information about health [15].



## 2. Method

### 2.1. Sample

Within the scope of the research purpose and constraints, a research with easy sampling method was carried out in Ortahisar with a population of 327 thousand, which is the central district of Trabzon universe. Only 286 surveys were available due to limitations such as the return of distributed surveys, incomplete questionnaires, and so on. By using the formula  $n = N t_2 pq / (d_2(N-1) + t_2 pq)$  [19], the sample size to represent the parent mass (Trabzon universe) reached 271 personality samples, with an acceptable 0,05 error level and  $\alpha = 0,10$  confidence level. The demographic characteristics of the people included in the sampling are given in table 1. The number of men and women samples is very close to each other. In the age distribution, there are a majority of people aged 26-35 and over 46 years old. About two-thirds of the people are married. High school and college graduates were in the forefront due to numerical superiority. They were mostly housewives, civil servants and workers. In addition, a local media group of 69 employees were involved in the survey to understand how far the media workers' opinions differed from the others.

**Table 1.** Demographic Characteristics

<u>Occupations</u>	<u>n</u>	<u>(%)</u>	<u>Education</u>	<u>n</u>	<u>(%)</u>
1. Worker	44	15,5	1. Primary school	38	13,4
2. Unemployed	14	4,9	2. High school	96	33,8
3. Civil Servant	51	18,0	3. Vocational High School	43	15,1
4. Tradesman	6	2,1	4. Graduate	94	33,1
5. Housewife	63	22,2	6. Postgraduate	13	4,6
6. Retired	37	13,0			
7. Media Worker	69	24,3			
<u>Age</u>			<u>Gender</u>		
1. <25	50	17,6	1. Male	140	49,3
2. 26-35	89	31,3	2. Female	144	50,7
3. 36-45	51	18,0			
4. 46+	94	33,1	<u>Marital Status</u>		
			1. Single	92	32,4
			2. Married	192	67,6

### 2.2. Scale, Validity and Reliability Analysis

The questionnaire that constituted the research scale was developed by Bostan after making a literature survey and by taking the opinions of the media and health experts. The questionnaire contained items questioning 9 demographic characteristics and five Likert-type scale items about the perception of 20 health reports and television programs. Five-point Likert scale items are as follows; I do not agree at all, I fully agree with a level of participation score between 1-5. Negative items were converted into

positive during the analysis phase, and the point values were changed in the same direction. Three (3) mean score was taken as basis in interpreting the arithmetic means in the frequency analysis. It is suggested that the structural validity of the scale also encompasses other types of validity (surface, content, criterion, merger and separation) [20]. In parallel with this approach, Exploratory Factor analysis was used to test the structural validity of the scale.

According to the result of exploratory factor analysis; out of a total of 20 items on the health news and radio/television programs evaluation scale, **6<sup>th</sup>, 7<sup>th</sup>, 16<sup>th</sup>, 19<sup>th</sup>, and 20<sup>th</sup>** items were removed and the remaining 15 items were combined under 3 factors.

In terms of being the conceptual aspects, **clarity, reliability** and **efficacy** were the factors taken into consideration while classifying the health news and media programmes. While the obtained factor structure explained 48,556% of the total variance, the **clarity** (21,766%), the **reliability** (13,762%) and the **efficacy** (13,018%) became the factors with the greatest explanatory power, respectively. When the factor loadings of the items were examined, it was seen that these loads varied between 0,361 and 0,806. The Barlett sphericity test- Approx. Chi-Square: 853,499 ve df: 105 (P: 0,000)- for assessing the suitability of the data for factor analysis was seen to meet the assumption that data should not come from unit matrices [21]. KMO sampling adequacy criterion (0,795) also indicated the suitability of the data. The Cronbach's Alpha statistic was calculated to be 0.757 for the whole scale.

**Table 2.** Factor Analysis

	Factors		
	Health news and the media programmes		
	Reliability	Clarity	Efficacy
s1		,745	
s2		,806	
s3			,361
s4		,539	
s5		,396	
s8	,670		
s9	,654		
s10	,697		
s11	,724		
s12	,698		
s13	,732		
s14			-,501
s15			,578
s17			,717
s18			,696

As for the analysis of the findings, frequency and significance analyses were performed using the SPSS program. Significant differences between independent variables and dependent variables were analyzed with T-test and ANOVA tests and in post hoc analysis Tukey test was used.

### 3. Findings

The subjects issued in the survey are categorised as below:

- 1- The healthcare issues
- 2- Media devices and how often people follow the news on healthcare
- 3- The frequency of receiving health care services

**Table 3.** Status of people following health news and programs

<u>Top five topics</u>	<u>n</u>	<u>(%)</u>	<u>The first three media devices</u>	<u>n</u>	<u>(%)</u>
1. Cancer	285	21	1. TV	481	44
2. Healthy life	429	32	2. Internet	331	30
3. Reproduction	50	4	3. Newspapers	168	15
4. Seasonal diseases	235	17			
5. Innovations	322	24			
6. Other	30	2			
<u>Level of follow-up</u>			<u>Number of people receiving health care services in the last year</u>		
1. Everyday	83	13,4	1. 1-3	218	35,2
2. A couple of times a week	160	25,8	2. 4-6	207	33,4
3. When there is something worth watching	290	46,8	3. 7-9	126	20,3
4. When I have a health problem	77	12,4	4. 10-12	49	7,9
5. Never	8	1,3	5. 13 +	18	2,9

As shown in table 3, we see that news of healthy life and health innovations are watched the most at the rate of 32% and 24%, followed by cancer and seasonal diseases, respectively. 46.8% of the people stated that they only watched health news and programs when the issue was sufficiently noticeable, while 25,8% of them informed that they watched health news and programs regularly once or twice a week. It has been understood that the rate of those visiting a health clinic 1-3 times in order to get health service within the last year is 35,2% and that of 4-6 times is 33,4%.

**Table 4.** People's views on health news and programs

<b>Factors and Items</b>	$\bar{x}$	<b>SD</b>
<b>Clarity of health news and programs</b>	<b>3,36</b>	<b>0,6</b>
I understand the language used.	3,66	1,0
The subject is processed in detail.	3,35	0,9
I do not think there is an effort to exaggerate and just to draw attention to the given information.	3,14	1,0
Medical ethics and moral responsibility principles are paid attention.	3,29	1,0
<b>Reliability of health news and programs</b>	<b>2,58</b>	<b>0,6</b>
I think that alternative treatment practices are sufficiently reliable and are not intended only to make money.	2,77	1,1
I do think the news presented as ‘miracle therapy’ is not deceptive.	2,40	1,0
I think that they are accurate and sufficient informants, and I do not think people will suffer from them.	2,65	1,1
I think that it is not wrong to do medical treatment with the medical information given by the specialists, it is not absolutely necessary to go to a doctor.	2,20	1,1
Debators are trying to help audience solve their health problems, they do not make an effort to advertise.	2,78	1,0
I think that the news in the media about the subject is followed by the Ministry of Health and that public statements are made when necessary.	1,99	1,0
<b>Impact of health news and programs</b>	<b>3,11</b>	<b>0,5</b>
People are able to choose which of the media reports are correct and which are wrong.	2,84	1,2
Enough attention given to the patient confidentiality.	3,02	1,0
Health-related disclosures do not fuel violence against healthcare professionals.	3,28	1,0
Reports of violence against health workers do not increase the violence against health workers.	2,97	1,1
The information provided is useful.	3,45	0,9

According to Table 4; The health news and programs were found to have a clarity and efficacy over the average with 3,36 and 3,11 points, with a reliability below average of 2,58. The view that the language of the programs is understandable and that the issues are handled with careful attention to detail and ethical rules is shared above the average score.

It is noteworthy that the health news of the public media is followed by the Ministry of Health and necessary explanations are made when a misunderstanding situation arises has the lowest (1,99) perception rate.

People did not participate in large scale (2,20) that it would be right to undergo any treatment without going to a doctor, based solely on the current knowledge even if they are made by experts. Again, it is understood that people are not very confident that the methods presented as ‘miracle treatment’ are not deceptive (2,40). People are not very credible in that these informants are entirely correct and sufficient, and they are not sure whether or not they will be the victims of them. (2,65).

People are significantly involved in the opinion that health news and programs are useful for them despite all (3,45). The view that health-related programs do not cause violence against healthcare professionals is also at the forefront and the opinion that patient confidentiality is paid attention above the average has also been determined. People, however, participated below the average on the fact that violence reports on health do not increase the violence in health (2,97) and that people can correctly and accurately distinguish between right and wrong (2,84).

That all of the issues in which the opinions of the people are differed in terms of the confidentiality of news sources and their being confusing somehow is also remarkable. It is understood that age, education level and professional differences can be regarded as the factors that affect the confidence in health news and publications.

**Table 5.** Significant Differences showing Confidence Factors According to Independent Variables

Independent Variables	Factors	N	$\bar{x}$	SD	F	P
Age	25 and under	50	2,7433	,79910	2,923	,034*
	26-35	89	2,3408	,76083		
	36-45	51	2,4510	,62919		
	46 and over	94	2,4610	,83902		
Educational Status	Primary school graduate	38	2,4912	,79502	2,548	,028*
	High school graduate	96	2,6475	,86998		

	Associate degree	43	2,3566	,75731		
	Bachelor's degree	94	2,3936	,69983		
	Master's degree	13	2,0513	,77096		
Occupation	Worker	44	2,7045	,61827	3,722	,001*
	Unemployed	14	2,7738	,57217		
	Civil servant	51	2,1176	,64143		
	Tradesman	6	1,9722	,85256		
	Housewife	63	2,5979	,93739		
	Retired	37	2,5315	,86499		
	Media worker	69	2,4179	,70225		

As is shown in Table 5, the confidence index of young people aged between 26-35 on health news and programs differs from the other groups, especially from those of 25 and younger, with the lowest average confidence level of 2,34 points. When considered from the educational point of view, the highest level of confidence in the health news is that of high-school graduates with an average of 2,64, while the confidence level, which is down to 2,05 in average, is gradually decreasing in those with higher education. The confidence in the health news is understood to have the lowest level of confidence in the civil servants (2,11) and the tradesmen (1,97) when examined from the point of occupation. In particular, civil servants are significantly less confident about the information given in the health news compared to housewives. There was no significant difference in terms of gender and marital status.

#### 4. Discussion

This study was conducted in the Trabzon universe to enable people to evaluate the health news and programs and tried to measure the intelligibility, reliability and efficacy of the programs in its content. The results apply to their own sample and universe. Comparisons with similar investigations on this subject have been given below:

As Hülür emphasized in his study "Health Communication, Media and Ethics: Analysis of a Health News", the fact that people benefit from health news on the media, except for the ethical violation, was supported by our work [11].

In their study titled "Health News in the Context of Consumer Culture", Öztürk ve Birsen (2013) stated that the distribution of the news was in the form of dietary and nutrition, chronic diseases, aesthetics and healthy lifestyle. In our study, people also expressed greater interest in publications related to healthy life, health innovations, seasonal diseases and cancer.

Tunçel and his colleagues [8] pointed out that health reporting, especially misinformation, might be a problem; in parallel, the fact that the low reliability of health journalism according to our study supports similar possibilities. Kaya and his colleagues [9] stated that people and patients' health-related knowledge are largely being learned from the media and the media also responds to this interest. Our survey supports this claim as well.

## 5. Conclusions and Recommendations

It has been understood that people are most likely to follow the news on healthy lifestyle and health innovations, along with cancer and seasonal diseases on visual and print media. The people have been found to be following health news and programs both in printed or visual media several times a week or just when media devices get their attention.

People find health news and programs to be reliable under average while they find them clear and effective above average. Especially, the language that is used, for them, is understandable and avoiding the healthcare terminology dominated by Latin in these programs is also important. Because, one of the important reasons of medical information asymmetry is that it has its own Latin jargon. Health news programs seem to have solved this problem. A detailed examination of the issues has also been found to be positive for the people to have in-depth knowledge in healthcare. The positive perception that citizens are avoiding from exaggerations and that they are paying attention to ethical rules can be seen as another success of health news.

Nonetheless, people have cause for cautious optimism due to monetization and advertising efforts and so-called miracle treatment approaches being effective in making health news; accordingly, they think the information provided may not be valid and accurate for everyone. This attitude can, in fact, be evaluated positively for the health of the people and healthcare system. It has been found that the confidence of the young people aged between 26-35 in health news and programs is lower than other age groups. The high school graduates have higher confidence indices than the other groups and it has been seen that the key element of confidence has fallen in those of higher education graduates. It was understood that especially civil servants find the content of their health news to be less reliable, compared to workers and housewives.

People find the information provided in health news and TV or radio programs primarily useful. In general, according to the findings of health news and programs, it can be said that the news on media does not lead to any kind of violence. However, it can be interpreted as a sign that the news of violence may have negative adverse effects on health. The people are cautiously optimistic about how much attention has been paid to patient privacy in printed or visual media and hope to be informed more about right and wrong. As a result, it is recommended that the Ministry of Health should conduct a study to follow such news publications and programs closer and make necessary explanations when needed.

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**ULTRASTRUCTURAL EXAMINATIONS ON DIABETIC RAT SKIN TISSUE WITH  
TOPICAL APPLICATION OF  
*Salvia euphratica* ETHANOL EXTRACT**

*Ebru GOKALP-OZKORKMAZ*\*<sup>1</sup>, *Nursel GUL*<sup>2</sup>, *Yusuf OZAY*<sup>3</sup>, *Sevda GUZEL*<sup>4</sup>,

*Ahmet KAHRAMAN*<sup>5</sup>, *Hakan ESKIZENGIN*<sup>2</sup>

<sup>1</sup>Ankara Yildirim Beyazit University Faculty of Health Sciences & Dicle University Faculty of  
Medicine Department of Histology&Embriyology

<sup>2</sup>Ankara University Faculty of Science Department of Biology

<sup>3</sup>Adiyaman University Faculty of Medicine Department of Medical Biology

<sup>4</sup>Mersin University Faculty of Pharmacy, Department of Pharmacognosy

<sup>5</sup>Usak University Faculty of Science, Department of Biology

\* Corresponding author; [egozkorkmaz@ybu.edu.tr](mailto:egozkorkmaz@ybu.edu.tr)

**Abstract:** *Several medicinal plants to treat diabetic wound healing were researched and are still under investigation. A variety of processes contributed to diabetics such as; inhibition of inflammatory response, generation of reactive oxygen species, differentiation of the extracellular matrix and reduced collagen production. The purpose of this study was to examine the ultrastructural alterations in diabetic rat skin tissue treated with the ointment prepared with *Salvia euphratica*. Male Wistar albino rats were used in this study (n: 24), divided into 4 groups. Non-treated, diabetic, diabetic and cicatrizant treated, ointment prepared with ethanol extract of 1% *Salvia euphratica* topically applied for 14 days. A single dose of 45 mg/dL streptozotocin (i.p.) was given to rats to induce diabetes. Excisional wound model was created under anesthesia. A cicatrizant, fitocream, was used as positive control. Normal skin tissue was observed in non-treated group. Diabetic skin tissue revealed hyalinization of the cytoplasm and loss of cytoplasm. Ointment treated diabetic group revealed altered cellular elements suggests healing. At the wound area, number of fibroblast cells synthesizing connective tissue were increased and the collagen fibers were regularly oriented. Neutrophil and monocyte cells besides mast and macrophage cells were found in the capillaries of dermis in *S. euphratica* ointment treated group. Wound healing in diabetic tissues is known to be slow. Using phytocream therapy to expedite the healing process is a long time known phenomenon. Our observations demonstrated that *Salvia euphratica* promoted changes in skin tissue that may contribute to wound healing at the cellular level.*

**Key words:** *Diabetes, *Salvia euphratica*, Wound Healing, Ultrastructure, Phytotherapy*

## 1. Introduction

One of alternative method used for the treatment of wounds is phytotherapy [1]. Herbal medicinal products are being used as a primary source of healthcare and traditional medical practice in several communities [2]. The plant, its parts and their extracts are potentially used for wound treatment [3]. The use of herbal medicine demonstrated several healing properties on wounds such as improved tissue regeneration and anti-inflammatory response, increased wound contraction and higher collagen content according to the previous studies [4]. Medicinal herbs, which are subjected to multidisciplinary researches and are widely used in public, induce wound healing and regeneration in tissue [5]. The wound healing activities of several herbal remedies were investigated using different pharmacological models. However, many are still undiscovered [6].

As well-known, wound healing is slow and difficult in diabetic patients and wound remains open for prolonged periods and affects quality of life [7]. Tissue repair occurs in order beginning with a 3 days lasting inflammatory response, followed by the formation of granulation tissue and finally remodeling phase that may take several months [8].

*Salvia* species have active secondary metabolites acting as free radical scavengers such as flavonoids, phenolic acid & terpenoids. *Salvia* species are applied for their anti-inflammatory, antidiabetic, anti-oxidative, anti-proliferative, antibacterial, antifungal, antiviral and cytotoxic effects [9]. Different *Salvia* species have been used in wound treatment studies. Narayan *et al.* (2011) in their study with extract of *Salvia splendens* reported improvement of dead tissue as a result of the application [10]. In a study with *Salvia hypoeuca*, it was observed that this plant extract provides new epithelial formation of wounds created in Albino Wistar rats [11]. Another study by Suntar *et al.* (2011), *Salvia cryptantha* plant ethanol extract treated group was determined to be a significant increase in wound contraction [12].

The present study was performed to examine the alterations arising from the application of endemic medicinal plant *Salvia euphratica* on experimental diabetic rat skin wound in the ultrastructural level.

## 2. Material and Methods

### 2.1. Experimental Animals

This study was done with the permission of ethical commission of Mersin University, Turkey. Male Wistar rats weighting 180–240 g were used (n:24). Their care were maintained in Mersin University Research Laboratory of Experimental Animals. Rats were kept in separate cages at room

temperature, humidity of % 65 and 12:12h light:dark photoperiod. They were fed with standard laboratory chow and had free access to water. Experimental groups were shown in Table 1.

**Table 1.** Groups of experimental animals

Groups	Number of experimental animals
1. Non –treated group	6
2. Diabetic control group-negative control	6
3. Diabetic and cicatrizant healing cream treated group-positive control	6
4. 1% (w/w) <i>S. euphratica</i> ointment treated diabetic group for 14 days	6

## 2. 2. Plant material and ointment processing

*S. euphratica* plant samples were collected from Van, Turkey by A. Kahraman. Air dried aerial parts of each plant material were powdered mechanically and macerated three times with ethanol. After filtration, solvents were evaporated under reduced pressure using vacuum evaporator at 35-40 °C and extracts were stored in the dark at 4 °C until use. Ointment base was prepared with glycol stearate: propylene glycol:liquid paraffin in the ratio of 3:6:1 [12] . Ointment prepared with 1% (w/w) *S. euphratica* extract was topically applied on the wound area for 14 days. Cicatrizant healing cream-fitocream including aqueous solution of *Triticum vulgare* was applied topically as a reference cream and positive control.

## 2.3. Induction of diabetes

A single dose of 45 mg/dL streptozotocin (Sigma Chemical Co.,USA) dissolved in citrate buffer (0.1 M, pH 4.5) was given to rats (i.p.) to induce diabetes. Blood glucose levels were measured using a rapid glucometer (Bayer, Germany). After STZ injection, animals with blood glucose levels above 300 mg/dL were used in the study.

## 2. 4. Anesthesia and Wound creation

Excisional wound model was created under intraperitoneal injection of xylazine hydrochloride (10 mg/kg) and ketamine hydrochloride (30 mg/kg) anesthesia. In order to create excisional wound, skin

tissue of 1.5 cm diameters in a circular manner was removed by punch biopsy on the dorsal interscapular region of rats and left open [12].

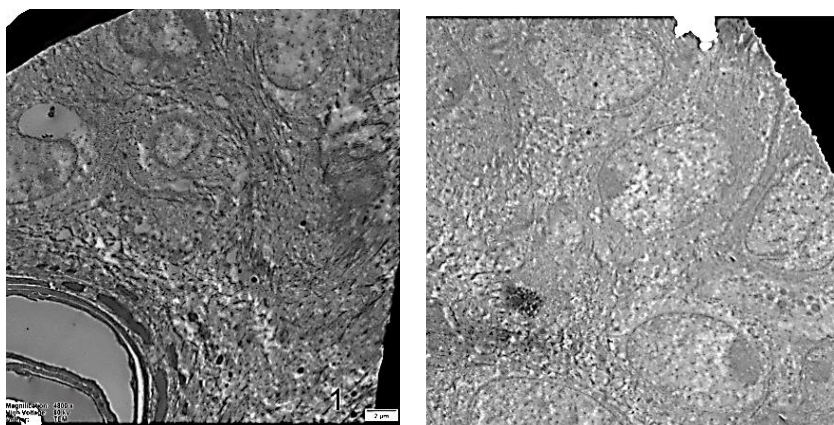
### 2.5. Preparation for Electron Microscopy

Rats were killed on the 14th day by excess sodium pentobarbitale anaesthesia. Skin samples were resected and rinsed in sodium phosphate buffer (0, 1 M, pH 7,4). Tissues were sliced into pieces of 1-2 mm<sup>3</sup> and immersed in 2.5% glutaraldehyde for the first fixation. Following post fixation in 1% osmium tetroxide solution for 2h they were dehydrated by graded ethanol series of 70-100 %, placed into propylene oxide and embedded in araldite 502 [13]. Sections were cut with an ultramicrotome (Leica) stained with uranyl acetate-lead citrate and examined with transmission electron microscope (JEOL JEM 100 CXII) at 80-100 kV in Electron Microscope Laboratory of Ankara University, Faculty of Science, Department of Biology.

### 3. Results

Normal appearance of keratinocytes and other epithelioid cells were observed in non-treated group (Figs. 1, 2). Diabetic skin tissue sections revealed hyalinization (Fig. 3) and loss of cytoplasm (Figs.4, 5). and also nucleus of epithelioid cell was seen in heterochromatic appearance. After *S. euphratica* ointment application to diabetic rats it was found to have altered cellular elements suggesting wound healing at the cellular level. At the wound area it was seen that number of fibroblast cells synthesizing connective tissue were increased and active to synthesize collagen fibers. Distribution of collagen fibers were regular (Figs.6, 7). In the ointment group, Langerhans cells and keratinocytes were in normal appearance in Stratum spinosum. Intercellular connections were almost normal, Nucleus of cells were oval shaped with homogen euchromatic appearance (Fig 8). Electron lucent regions were observed next to the cell nuclei and ER cisternae were regular (Fig 9). Macrophages and fibroblasts were observed in dermis and monocyte was seen in capillaries (Fig. 10) may be differentiate into macrophage.

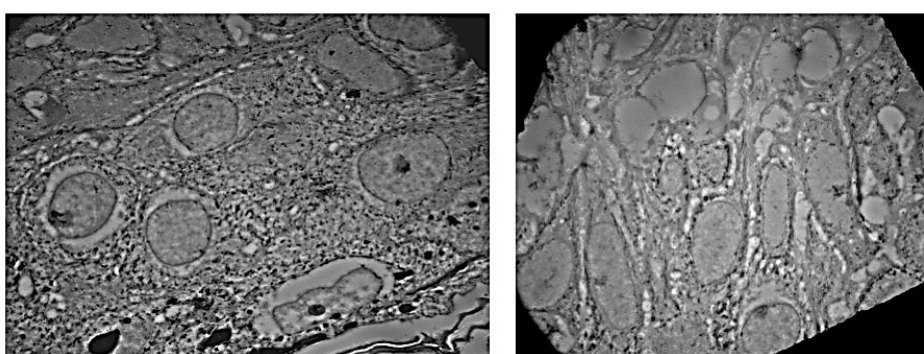
In the ointment treated sections; fibroblasts, macrophages and neutrophil cells were seen frequently (Figs.11-13). In the same sections mast cells (Fig.14). Diabetic and cicatrizant healing cream treated group demonstrated regular orientation of epithelial cells in epidermis layer, Langerhans cells and melanocytes between the epithelial cells of epidermis. In the same section, cisternae of ERs were dilated in fibroblast cells of dermis layer to synthesize collagen for healing (Figs.15-16).



**Figures 1-2.** Non-treated control group, normal appearance of keratinocytes and other epithelioid cells. Borders of cells were regular, arrangement of cytoplasmic organelles were apparent.

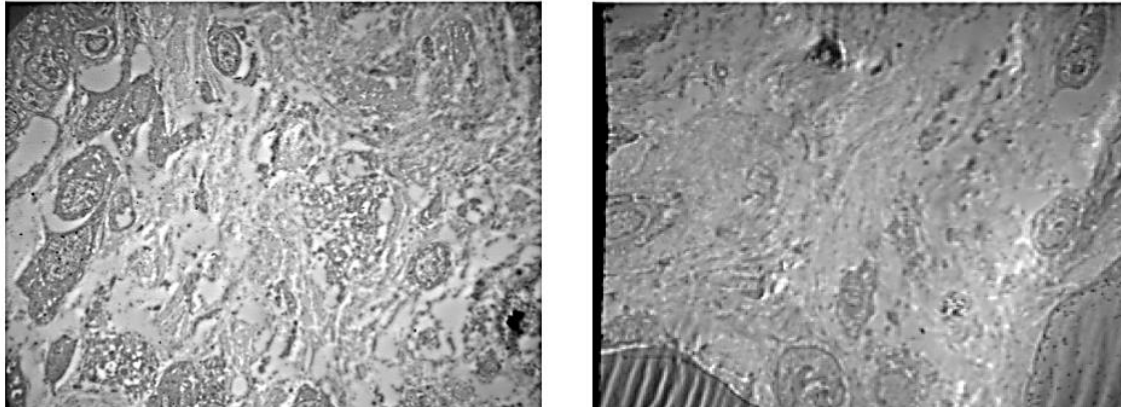


**Figure 3.** Diabetic group, nucleus of epithelioid cell was in heterochromatic appearance. Neighboring cell seem to be undergone pycnosis. Hyalinization was observed between epithelioid cells.

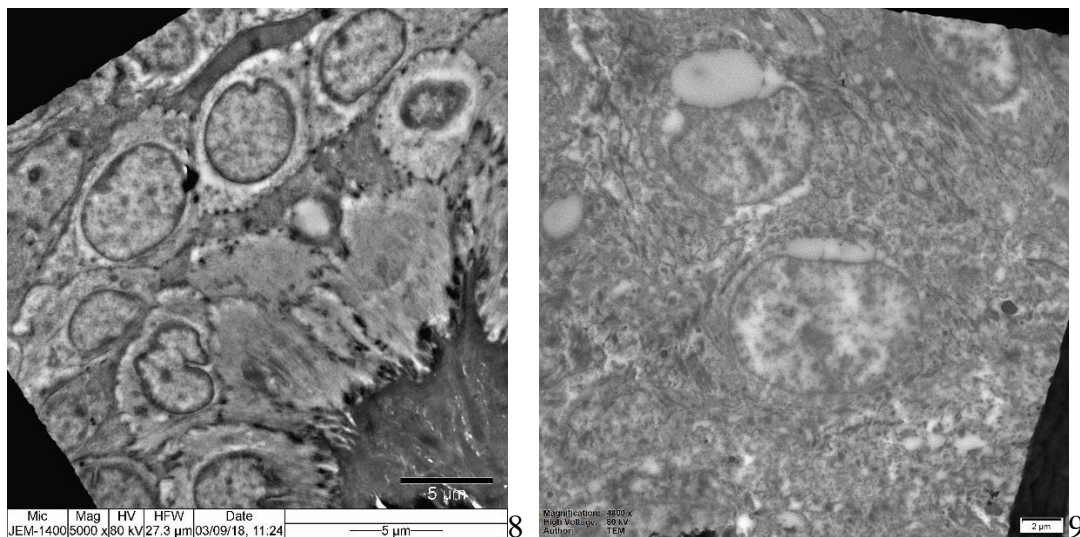


**Figures 4, 5.** Diabetic group, in the Stratum lucidum and Stratum granulosum layer, around the nucleus of epithelial cells, cytoplasmic material was hyalinized and an electron lucent region became evident. Apoptotic appearance in a few cells (Fig.4). Loss of cytoplasmic material and nucleus, loosening of intercellular connections and vacuole formation were observed in cells (Fig.5).

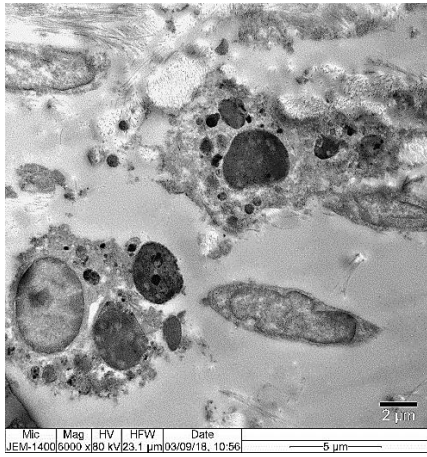




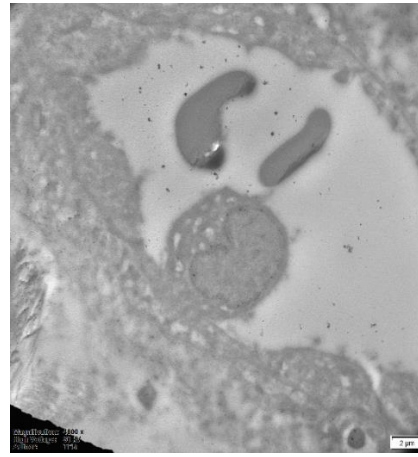
**Figures 6, 7.** *S. euphratica* extract applied for 14 days, distribution of collagen fibers were regular. Macrophage and other connective tissue cells were observed. Fibroblast cells were seem to be active (Fig.6). Collagen fibers were aligned parallel but distributed irregularly (Fig.7).



**Figures 8, 9.** *S. euphratica* applied group, Langerhans cells and keratinocytes were in normal appearance in Stratum spinosum. Intercellular connections were almost normal, Nucleus of cells were oval shaped with homogen euchromatic appearance (Fig 8). Electron lucent regions were observed next to the cell nuclei. ER cisternae were regular (Fig 9).

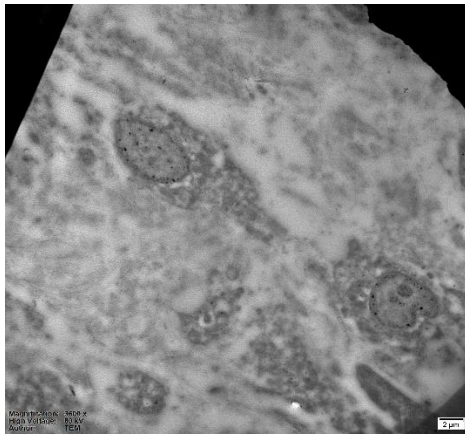


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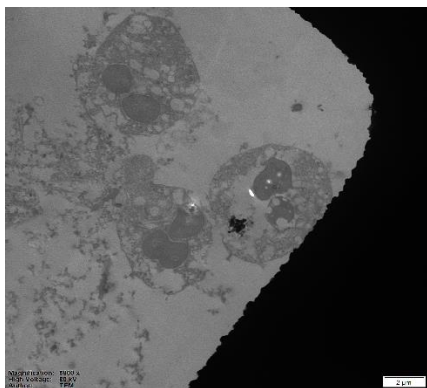


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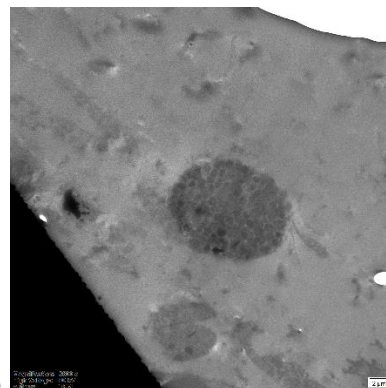
**Figures 10, 11.** *S. euphratica* applied group, macrophages and fibroblasts were observed in dermis (Fig. 10). Monocyte cell was seen in capillaries of dermis that may be differentiate into a macrophage as a tissue response (Fig. 11).



**Figures 12.** *S. euphratica* applied group, fibroblast cell synthesizing protein and active macrophage cells with phagosomes.



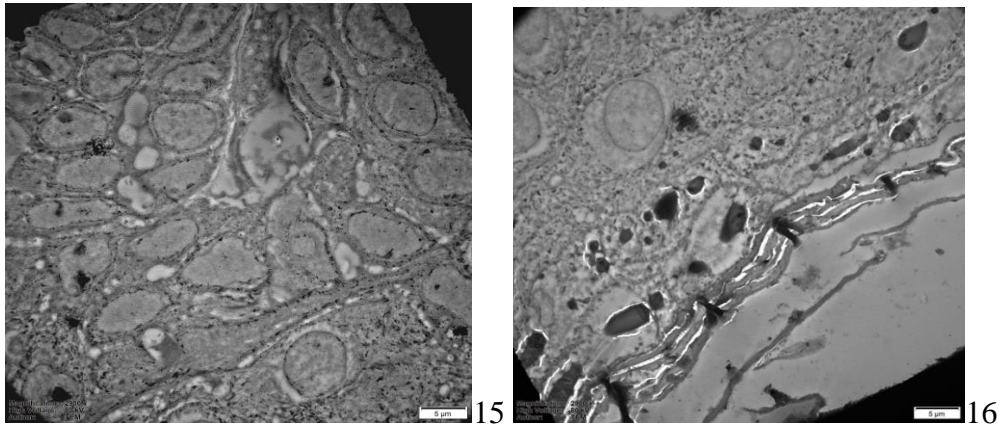
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**Figures 13-14.** *S. euphratica* applied group, neutrophil cells (Fig. 13). In the same section mast cells (Fig.14)





**Figures 15-16.** Diabetic and cicatrizant healing cream treated group, regular orientation of epitheloid cells in epidermis layer, hyalinization of cytoplasm in a few cells was observed (Fig. 15). Cornified cells with the influence of fito-cream and keratinocytes and keratin layer was observed in Stratum corneum (Fig. 16).

#### 4. Conclusion

Diabetes mellitus is one of the major factors leading to chronic wound healing problems. There is a complex relationship between diabetes and impaired wound healing. A series of processes take role in impaired wound healing in diabetics such as; dysfunction of immune system, neuropathy and vascular problems [7, 14]. According to a review by Dorai (2012), in the treatment of wounds, using herbal medicine is easily accessible, functional and moreover, an ongoing culture [4]. Another study of Medagama and Bandarar (2014) discussed in their study if the use of alternative medicines in the treatment of diabetes is effective [15]. Many experimental wound models were created by the researchers. A study of Narayan et al. demonstrated that herbal ointment formulated with *Salvia splendens* had a wound healing effect on experimentally induced excisional skin wounds [10]. *Salvia* species were reported for their anti-inflammatory, antidiabetic, anti-oxidative, anti-proliferative, antibacterial, antifungal, antiviral effects [9]. Our study was constructed on this idea and a *Salvia* species; *Salvia euphratica* was used as a medicinal plant for observing wound healing activity in experimental diabetes.

Wound healing is a complex process involving multiple cellular and extracellular components, which are present in a normal healing process. It is known that inflammatory cells, fibroblasts and keratinocytes are important cell types during the healing process, modulating the reconstruction of the injured area. A study on effects of acute diabetes on rat cutaneous wound healing by Komesu et al. indicated that in diabetics wound healing phases; inflammation initial healing phase was slow and lasted longer [16]. They also found lower density of neutrophils in healing areas up to 3 days after surgery in diabetic animals and in addition, after day 3, when the neutrophils should leave the healing area, and be replaced by macrophages, compared to controls, diabetic animals showed higher numbers of neutrophils

[16]. Neutrophils are first defense cells of skin so, alterations in the number and function can be sign of a pathology [17]. We observed neutrophil and monocyte cells besides mast and macrophage cells in the capillaries of dermis layer of skin in ointment prepared with *Salvia* extract treated group. The presence of these cells indicates the process of wound healing. At the wound area treated with the herbal extract, it was examined that the number of fibroblast cells synthesizing connective tissue was increased and the collagen fibers were in a regularly oriented. In addition, the cytoplasm of some epithelial cells was seem to undergone melting and hyalinization, perhaps where the wound healing at the cellular level was not fully completed. As a result, we predict that topical application of herbal ointment prepared with *Salvia euphratica* ethanol extract depicted alterations on diabetic wound tissue at the cellular level.

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## EVALUATION OF DIASTOLIC DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS

Özge TURGAY YILDIRIM\*<sup>1</sup>; Emel GÖNÜLLÜ<sup>2</sup>, Fatih AYDIN<sup>1</sup>, Ercan AKŞİT<sup>3</sup>,

Ayşe HÜSEYİNOĞLU AYDIN<sup>1</sup>, Evrin DAĞTEKİN<sup>1</sup>

<sup>1</sup>Eskisehir State Hospital, Cardiology Department, Eskisehir, Turkey

<sup>2</sup>Eskisehir State Hospital, Rheumatology Department, Eskisehir, Turkey

<sup>3</sup>Çanakkale Onsekiz Mart University Faculty of Medicine, Cardiology Department, Çanakkale, Turkey

\*Corresponding author; ozgeturgay@gmail.com

**Abstract:** Rheumatoid arthritis (RA) is a chronic, autoimmune inflammatory disorder which can also affect cardiovascular system. Cardiovascular system involvement can be seen in many forms such as pericarditis, myocarditis, coronary artery disease or heart failure. Diastolic dysfunction is especially important for preserved ejection fraction heart failure patients. With this study we aim to investigate echocardiographic diastolic dysfunction parameters in RA patients. 77 RA patients and 76 control subjects without coronary artery disease, heart failure, valvular heart diseases were included for the study and echocardiography was performed. Interventricular septum ( $p=0.041$ ), posterior wall diameter ( $p=0.008$ ), left ventricular mass index ( $p=0.037$ ) values were significantly higher and E wave ( $p=0.000$ ), E/A ( $p=0.000$ ), e' ( $p=0.018$ ) values were significantly lower in RA patients compared to control group. In conclusion echocardiographic diastolic dysfunction parameters were declined in RA patients.

Key words: Rheumatoid arthritis, Diastolic dysfunction, Echocardiography

### 1.Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune inflammatory disorder. Although RA primarily affects the peripheral joints, extra-articular involvement is also seen in this disorder. RA may affect many systems such as cardiovascular, ocular, neurological, hematological and pulmonary systems [1]. Early detection for cardiovascular involvement is very important because cardiovascular diseases are the major cause of mortality in RA patients [2,3]. Cardiovascular involvement can be seen in different forms such as pericarditis, myocarditis, coronary artery disease, heart failure and rhythm disorders [4]. Heart failure incidence is higher in RA patients and 13% of mortality is caused by heart failure [5,6]. The risk of coronary artery disease is two times higher in RA patients compared to normal population [7]. Autoimmunity and inflammation along with traditional risk factors contribute to the development of cardiovascular diseases [8]. This may explain the higher incidence in heart failure. Also amyloidosis or antirheumatic therapy may play roles for the development of heart failure [9].

Left ventricular diastolic dysfunction (LVDD) is associated with increased left ventricular filling pressure and left atrial volume [10]. Evaluation of LVDD is especially important for heart failure patients with preserved ejection fraction [11]. Since coronary artery disease and heart failure are more common in RA, detection of disrupted LVDD is especially important for this group of patients. With this study we aim to investigate the LVDD parameters via echocardiography in RA patients.

## 2.Methods

77 patients with diagnosis of RA according to the American College of Rheumatology criteria and 76 age and sex-matched control subjects were included for the cross-sectional study. All RA patients were under treatment and their diseases were not in active state. The patients below the age of 18, with severe valvular heart disease, heart failure or coronary artery disease were excluded. Brief anamnesis was conducted to obtain demographic data, duration of disease, history of chronic diseases. Weight and height data were collected while patients were wearing only their underwear.

The study was approved by the local ethics committee. Informed consent was obtained from each patient.

A 2-dimensional and Doppler echocardiography was performed at the admission to the clinic. Echocardiographic evaluation was performed according to guidelines of American Society of Echocardiography. Ejection fraction (EF), left ventricular end diastolic diameter (LVEDD), interventricular septal (IVS) thickness, posterior wall (PW) thickness, the ratio of peak velocity flow in early diastole to peak velocity flow in the late diastole (E/A), the ratio of E to early diastolic mitral annular velocity (E/e'), left atrium diameter, left atrium volume were examined. Left ventricular mass was calculated using Devereux formula and left ventricular mass index was calculated by left ventricular mass/body surface area [12].

Blood sample was taken in the morning after 8 hours of fasting to determine glucose, urea, creatinine, HDL-C, LDL-C, triglycerides, hemoglobin levels, leukocyte, neutrophil, C-reactive protein (CRP), PDW values.

Data were presented as mean  $\pm$  standard deviation (SD) and as proportions for categorical variables. The t-test or Chi-square test was used for comparisons of continuous and categorical variables, respectively. Distribution of the data for normality was tested by the Shapiro–Wilk test and homogeneity of group variances were tested by the Levene test. For the parameters which are not normally distributed, Mann Whitney U test was used. The data were analyzed using IBM SPSS ver. 22.0.

## 3.Results

A total of 153 patients were enrolled for the study. The study population included 77 patients with RA (50 males; mean age,  $53.1 \pm 7.6$  years) and 76 healthy subjects as controls (51 males; mean age,  $50.5 \pm 11.8$  years). The groups were similar in regards of age, gender, hypertension, diabetes mellitus, smoking status, weight, height, body-mass index, fasting blood sugar, urea, creatinine, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride and hemoglobin levels ( $p > 0.05$ ). There were significant differences in white blood cell ( $p = 0.003$ ), neutrophil counts ( $p = 0.003$ ) and CRP levels. Table 1 shows the patients' clinical data and laboratory results.

**Table 1.** Clinical and Biochemical Characteristics of Study Groups

	Rheumatoid Arthritis Patients (n=77)	Control Group (n=76)	p

Age, years	53.1 ± 7.6	50.5 ± 11.8	0.162
Gender, Male/Female	50/27	51/25	0.777
Hypertension, %	15 (19.5%)	20 (26.6%)	0.293
Diabetes Mellitus, %	15 (19.4%)	7 (9.2%)	0.070
Smoking, %	25 (32.5%)	26 (34.2%)	0.829
Weight, kg	74.2 ± 12.0	75.6 ± 13.5	0.494
Height, cm	164.8 ± 8.2	165.0 ± 8.7	0.871
BMI, kg/m <sup>2</sup>	27.3 ± 4.2	27.8 ± 5.1	0.504
Blood Examination			
FBG, mg/dl	101.5 ± 31.3	96.6 ± 23.8	0.283
Urea, mg/dl	13.1 ± 3.7	12.8 ± 4.2	0.707
Creatinine, mg/dl	0.7 ± 0.1	0.7 ± 0.1	0.328
HDL-C, mg/dl	48.9 ± 8.4	53.5 ± 12.7	0.166
LDL-C, mg/dl	116.4 ± 48.8	123.8 ± 32.6	0.577
TG, mg/dl	148.0 ± 57.6	144.4 ± 94.1	0.879
Hb, g/dl	13.6 ± 1.7	14.1 ± 1.7	0.078
WBC counts	9123.6 ± 3231.3	7782.5 ± 1973.6	0.003
Neutrophil counts	5844.6 ± 2699.7	4732.1 ± 1709.8	0.003
CRP, mg/dl	1.1 ± 1.6	0.6 ± 0.5	0.013

Abbreviations: BMI, body-mass index; CRP, C-reactive protein; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; Hb, hemoglobin; LDL-C, low-density lipoprotein cholesterol; RDW, red cell distribution width; TG, triglyceride; WBC, white blood cell.

Ejection fraction, LVEDD, left atrium diameter, left atrium volume, A wave and E/e' values were statistically similar between RA patients and control group ( $p > 0.05$ ). Interventricular septum ( $p = 0.041$ ), PW diameter (0.008), left ventricular mass index ( $p = 0.037$ ) values were significantly higher and E wave ( $p = 0.000$ ), E/A ( $p = 0.000$ ), e' (0.018) values were significantly lower in RA patients compared to control group (Table 2).

**Table 2.** Echocardiography results of the study population

Echocardiography Results	Rheumatoid Arthritis Patients (n=77)	Control Group (n=76)	p
Ejection fraction, %	58.0 ± 6.1	57.1 ± 2.8	0.299
LVEDD, mm	43.9 ± 4.8	44.5 ± 4.3	0.472
IVS diameter, mm	9.6 ± 1.8	8.9 ± 2.3	0.041
PW diameter, mm	8.9 ± 1.6	8.1 ± 1.8	0.008



Left atrium diameter, mm	33.8 ± 5.0	32.6 ± 3.8	0.085
Left atrium volume, cm <sup>3</sup>	28.2 ± 8.3	27.1 ± 8.9	0.451
Left ventricular mass index, g/m <sup>2</sup>	73.1 ± 18.2	66.5 ± 20.1	0.037
Diastolic Dysfunction parameters			
E, cm/s	60.4 ± 13.3	70.6 ± 15.0	0.000
A, cm/s	68.3 ± 15.2	65.4 ± 15.7	0.254
E/A	0.9 ± 0.3	1.1 ± 0.3	0.000
e', cm/s	8.3 ± 2.7	9.5 ± 2.8	0.018
E/e'	7.8 ± 2.4	8.0 ± 2.4	0.707

Abbreviations: A, mitral A wave; E, mitral E wave; e', average of lateral e' and septal e'; E/A, ratio of mitral E wave to mitral A wave; E/e', ratio of mitral E wave to average of lateral e' and septal e'; IVS, interventricular septum; LVEDD, left ventricular end diastolic diameter; PW, posterior wall.

#### 4. Discussion

We evaluated the diastolic dysfunction parameters with this study. We found out that diastolic dysfunction parameters such as E wave, E/A, e' were disrupted; IVS, PW diameters and left ventricular mass index are increased in RA patients compared to normal population.

Rheumatoid arthritis is a common rheumatological disorder worldwide. In RA, cardiovascular involvement can be seen and cardiac manifestations cause increased risk of mortality. Cause of death in 50% of RA patients is cardiovascular diseases [13].

Long term survival is shorter compared to normal population in RA patients [14]. Prevalence of congestive heart failure is higher and necropsy studies showed pericardial, myocardial and endocardial involvement in RA patients [15,16]. All-cause mortality is increased in isolated diastolic dysfunction patients [17,18]. In our study we evaluated echocardiographic diastolic dysfunction parameters in RA patients and compared the results with control group. In the study EF results were similar and the patients didn't have known heart failure or cardiovascular diseases. E wave, E/A ratio and e' values were disrupted and IVS and PW diameters were thicker in RA patients. Di Franco et al. also studied RA patients and found out E/A was disrupted but IVS, PW and other echocardiographic values were similar in RA patients and control group [19]. According to Erdem et al. [20] E wave, E/A, e', IVS and PW results were disrupted in RA patients and these results support our findings. The disruption in transmitral flow suggests myocardial involvement in RA patients [21]. We know that myocardium involvement can be seen as myocarditis or via ischemic heart diseases but in our study ejection fractions of the patients were normal and had no history of coronary artery disease [4]. So the changes in transmitral flow suggest a subclinical involvement of myocardium in RA patients.

Several studies investigating left ventricular mass index in RA patients has been conducted and the results were controversial. Rudominer et al. [22] found out that left ventricular mass index was higher in RA while Myasoedova et al. [23] found the opposite. In Myasodeova et al. study, it was emphasized that left ventricular mass index was lower in patients under corticosteroid therapy but it was not low in previous corticosteroid users. Midtbo et al. [24] compared active RA patients and patients in remission and found out that higher disease activity is associated with greater left ventricular wall

thickness. In the light of this result it is logical to think that left ventricular mass might be increased due to inflammation-induced vascular stiffening in RA patients and current medication might affect left ventricular mass index [22-24]. In our study, the majority of RA patients were under corticosteroid treatment. But we found out increased left ventricular mass index results which contradicts the results of Myasodeva et al. Further studies should be done to clarify the effect of corticosteroids on left ventricular mass index. In our study the disease and control groups were similar in terms of hypertension, body-mass index or other demographic characteristics so these basic characteristics should not cause the left ventricular mass index difference between the groups. C-reactive protein, white blood cell and neutrophil counts were increased in RA patients as a result of increased activity of inflammation which might be the cause of the increased left ventricular mass index.

## 5. Conclusions

In conclusion we showed that echocardiographic diastolic dysfunction parameters such as E/A, E wave, e' values were lower and IVS, PW diameters were higher in RA patients. Also left ventricular mass index was increased in RA patients compared to normal population. Main limitation of this study was small sample size. Further studies with larger sample size should be planned to confirm the results of our study.

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## THE EFFECT OF PUSHING TECHNIQUES ON DURATION OF THE SECOND LABOR STAGE, MOTHER AND FETUS: A RANDOMIZED CONTROLLED TRIAL

*Fatma Başar\*<sup>1</sup>, Seher Şeyma Hürata<sup>2</sup>*

<sup>1</sup> Kutahya Health Sciences University, Faculty of Health Sciences, Department of Obstetrics and Gynecology Nursing, Kutahya, Turkey.

<sup>2</sup> Community Health Center in Sırnak, Turkey.

\* Corresponding author; fatma.basar@ksbu.edu.tr

**Abstract:** *This study evaluated the effects of pushing techniques on the second stage of labor duration and maternal and fetal outcomes. The pregnant women were divided randomly into Valsalva pushing (n =20) or spontaneous pushing (n =20) groups. The experimental group received spontaneous pushing training in the latent phase. Interventions during labor as well as maternal and fetal complications and the duration of the second stage of labor were recorded. There was a significant difference in fetal Apgar scores and the duration of second labor stage between the two groups (p<0.005). Fetal distress, oxygen use, increase in oxytocin, operative intervention, perineal laceration, and postpartum hemorrhage were seen less in the spontaneous pushing group. However, no statistical difference was found between the groups (p>0.05). Spontaneous pushing is effective in shorter second stages of labor and higher Apgar scores. It should be included in maternal hospital protocols.*

**Key words:** *pushing techniques, labor second stage duration, maternal outcomes, fetal outcomes.*

### 1.Introduction

The second stage of labor is defined as the period from full dilatation of the cervix until expulsion of the fetus [1]. This stage includes frequent and regular pushing and women experience frequent vaginal rectal pressure and extreme pushing [2]. During the second stage of labor, spontaneous pushing (open glottis pushing while breathing out) or Valsalva maneuver techniques (closed glottis pushing while holding the breath) are used [3].

A common technique is to encourage women to use a closed-glottis pushing (holding breath while pushing) duration of 10 seconds or more, once the cervix has reached 10 cm dilation [4, 5]. In this procedure, women are coached to take a deep breath at the beginning of a contraction, then hold the breath as long and hard as possible and bear down towards the vagina throughout the contraction [5]. The process of taking a deep breath and holding it with a closed glottis is called the Valsalva Maneuver (VM). Several physiological findings oppose the use of the VM of 10 seconds or more, as this type of

directed pushing can negatively affect fetal acid-base balance, apgar scores and cerebral oxygenation. It can also interfere with the duration of the second stage of labour, increase maternal fatigue, cause damage to the maternal pelvic floor structures and impair bladder function [5, 6, 7, 8, 9]. A relationship has been observed between the Valsalva maneuver and reduction of oxygen supply to the fetus, maternal fatigue, and damage to the perineum. Recent scientific publications do not support the use of the Valsalva maneuver during the second stage of labor, and evidence suggests that it might be harmful [10, 11, 12].

In contrast, some authors argue that breathing control interventions should not be imposed during the expulsive stage and that rather than follow direct instructions for the VM, women should be free to follow their own instincts in response to the physiology of this stage in labour [5, 13]. This approach is known as ‘spontaneous or involuntary pushing’ and most of the respiratory effort to help in this type of bearing down occurs with an open glottis. [14]. Additionally, women who use spontaneous pushing begin at a resting respiratory volume, push three to five times per contraction and take several breaths between each bearing down effort. Spontaneous pushing occurs as a result of optimal obstetric conditions for fetal descent which includes fetal station of at least +1 and fetal position (approaching occipito anterior position. This condition evokes the Ferguson’s reflex, through increased oxytocin release, which augments maternal bearing down efforts by making them more effective and less fatiguing. The same uncertainty occurs in relation to the second-stage labour care of women [4, 5].

Spontaneous pushing is a method that is used in the management of the second stage of labor and suggested to be more physiological for the mother and infant [2]. However, this technique is less used [10].

There are no data to support a policy of directed maternal pushing. Despite several publications showing the adverse maternal and fetal effects from the use of the sustained VM, this choice of method is still common practice worldwide, and the scientific evidence base supporting the recommendation of breathing control for the expulsive stage is scant. The Valsalva pushing technique is used routinely in the second stage of labor and is accepted as standard obstetric management in Turkey, even though no research has been conducted in the country on the effects of pushing techniques.

The present study was planned to determine the effects of pushing techniques on the second stage of labor duration and maternal and fetal outcomes. This study will concentrate on all eligible studies using spontaneous versus directed pushing and delayed versus early pushing for bearing down during the second stage of labour.

## **2. Materials and Methods**

### **2.1. Design**

The study utilizes a randomized controlled trial design.

### **2.2. Setting and participants**

The study was conducted in the delivery room of Dumlupınar University Kütahya Evliya Celebi Training and Research Hospital. Sample acceptance criteria were: nulliparous women 18-35 years of age who were 38- 42 weeks pregnant with a single healthy fetus in vertex position, expected to have spontaneous vaginal delivery, without any pregnancy complications and in the latent phase of labor (0-4 cm).

### **2.3. Sampling and randomization**

The study population consisted of 192 nulliparous women who had applied for hospital delivery service a year prior to giving birth to their first child, who had vaginal deliveries and who did not have any communication problems. In this research, the sample size was subdivided into two medium-sized

independent groups. A t-test was applied, obtaining a rate of 80% in the power test and an alpha value of 0.05 with a 95% confidence level, which was calculated using estimation G-Power Software version 3.0.10. Pregnant women were randomly selected via a coin toss, and they were assigned to either the experimental or control group. The pregnant women were assigned alternately on one day to the experimental group and on the other to the control group. Attention was paid for the pregnant women who were taken into the practice at the same time to be monitored in different rooms. Thus, 40 pregnant women, 20 for experimental group and 20 for control group, participated in this study between November 2013 and March 2014.

## **2.4. Data Collection Tools**

The “Personnel Information Form” and “Labor Observation Form” were used to collect data and record information related to labor stages.

### **2.4.1. Personal Information Form**

Socio-demographical and obstetric characteristic questions were asked such as age of the pregnant women, willingness to become pregnant, and having information about labor.

### **2.4.2. Labor Observation Form**

Information regarding second, third, and fourth stages of labor were compiled as a result of a literature search. This form included questions about second (fetal distress, increase in oxytocin rate given to mothers, oxygen use, duration of second stage, and operative labor interventions), third (perineal lacerations), and fourth (postpartum hemorrhage and 5th minute Apgar score) stages of labor.

## **2.5. Data Collection Methods**

Pregnant women were followed during labor when cervical dilatation reached 4 cm. The fetus was assessed at delivery. The data were collected using face to face interviews. From the beginning of the study, doctors and midwives working in the labor room regularly assessed cervical dilatation. Pregnant women’s characteristics about second, third, and fourth stages of labor were recorded. Moreover, information from the second stage of labor was recorded on the Labor Observation Form.

## **2.6. Intervention**

The second stage of labor occurs during the period between cervical dilatation at 10 cm and delivery of the baby.

Women in both groups started pushing when

- Cervical dilatation was 10 cm.
- Strong uterine contractions occurred.
- Fetal head rotation was completed.
- Fetal head was at + 1 level in the pelvis at least.

The following applications for Valsalva Pushing and Spontaneous Pushing were used for participating pregnant women

- Meeting with pregnant women.
- Determination of the pregnant women who meet the criteria and agreed to participate in the study.
- Giving information about the aim of the study.
- Completing the personal information form through a face to face interview.
- Assessment and recording of fetal distress, increase in oxytocin, oxygen use, and operative labor interventions on the Labor Observation Form.
- Recording the duration of the second stage of labor on the Labor Observation Form.
- Assessing fetus and mother in terms of 5th minute Apgar score and hemorrhage control, perineal lacerations, and pads and recording it on the Labor Observation Form (Fig.1).

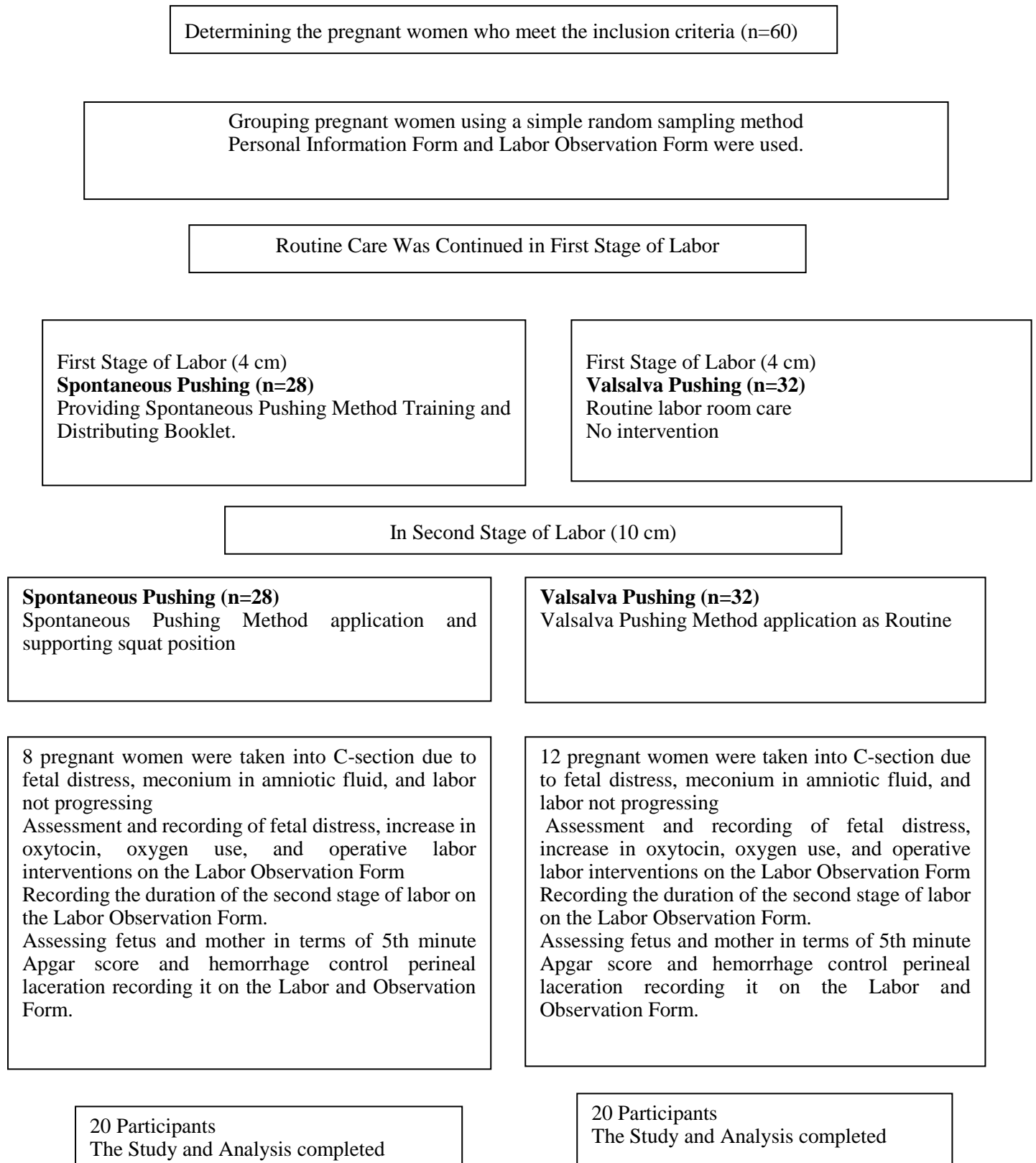


Fig. 1. Study Plan

### **Processes performed on Spontaneous Pushing Group:**

During the second stage of labor, women mostly stood in a squat position. Women were informed about spontaneous pushing and provided booklets during the active stage of dilatation (dilatation was 4 cm). Women were supported for spontaneous pushing and the women's desire to push was considered. Spontaneous pushing was applied as follows:

- Regular breathing until pushing feeling occurs when contractions start,
- Breathing and retraction of core muscles,
- Pushing gradually,
- Smoothly breathing out by pursing when pushing,
- Pushing for 5-6 seconds while breathing out,
- Breathing in and pushing while breathing out for 5-6 seconds smoothly and regularly,
- Regular breathing when contractions slow down

### **Processes performed on Valsalva Pushing Group:**

Pushing techniques were not taught to the pregnant women in the Valsalva pushing group. No intervention was made to these pregnant women except standard hospital practices, although they were observed during delivery. Valsalva pushing was applied as follow :

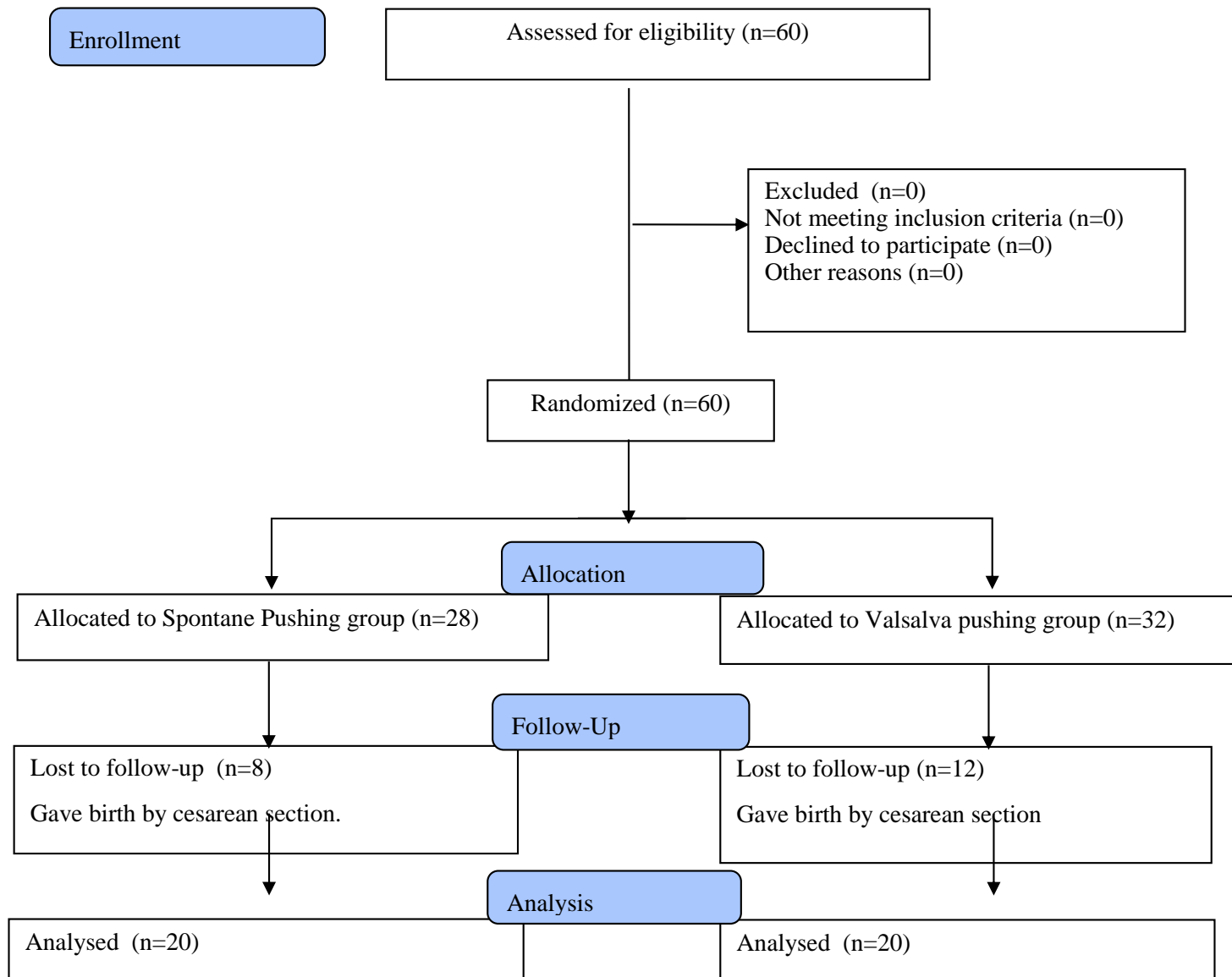
- Two regular breaths when contractions start
- Breathing deeply and holding breath
- Squeezing breath with diaphragm and abdominals
- Pushing as much as hard and long (10-15 seconds)
- Holding breath when pushing (closed glottis)
- Breathing out, breathing in deeply, holding breath
- Pushing hard for 10-15 seconds again
- Stop pushing when contractions ease
- Relaxing and resting until next contraction [15].

### **2.7. Data analysis**

The data were analyzed using SPSS 20.0 software. Number, percentage, Chi-Square test, and Fisher Exact Chi-Square test and A paired t test were used for data analysis.

### **2.8. Ethical considerations**

The purpose of the study was explained to each pregnant and their consent was obtained. The research permit was issued by the General Secretary of the Turkish Public Hospitals Agency of Kütahya Province under the Ministry of Health. Dumlupınar University ethics committee approved the study.



**Fig. 2.** Consort Flowchart

### 3. Results

During data collection, 60 pregnant women were randomly assigned to the experimental (spontaneous Pushing) and control groups (Valsalva pushing). 20 pregnant women were excluded from the research. The research was conducted with 20 pregnant women in the experimental group and 20 women in the control group (Fig. 2). Both groups are similar in terms of their socio-demographic and obstetric characteristics ( $p > 0.05$ ) (Table 1).

Of the pregnant women in the spontaneous pushing group, 40% whereas in the Valsalva pushing group 55% of pregnant women were aged between 20-24 ( $X^2=13.474$ ,  $p>0.05$ ).

Most of the pregnant women in the spontaneous pushing group (95%) and all pregnant women in Valsalva pushing group stated that they wanted the pregnancy ( $X^2=1.026$ ,  $p>0.05$ ). Many women (65% in both groups) stated that they had no information regarding labor ( $X^2=0.000$ ,  $p>0.05$ ) (Table 1).

**Table 1.** Sociodemographic ve obstetric history characteristics of the pregnant

Characteristics	Spontaneous Pushing (n=20)		Valsalva Pushing (n=20)		$X^2$	p
	No	%	No	%		
<b>Age (year)</b>						
15-19	2	10	4	20		
20- 24	8	40	11	55		
25-29	9	45	-	-	13.474	0.509*
30- 34	1	5	2	10		
35 years and up	-	-	3	15		
<b>Willingness to become pregnant</b>						
Yes	19	95	20	100	1.026	0.500*
No	1	5	-	-		
<b>Having information about labor</b>						
Yes	7	35	7	35	0.000	0.629*
No	13	65	13	65		

\* $p>0.05$

The duration of second stage of labor was 10-15 minutes and 10-20 minutes for 45 % of pregnant women both in the spontaneous pushing and Valsalva pushing groups, respectively. The duration of the second stage of labor in the spontaneous pushing group was statistically shorter than in the Valsalva pushing group ( $X^2=15.209$ ,  $p<0.05$ ) (Table 2).

**Table 2 .** Duration of the second stage of labor

	Spontaneous Pushing (n=20)		Valsalva Pushing (n=20)		$X^2$	p
	No	%	No	%		
<b>0-5 min</b>	3	15	-	-		
<b>5-10 min</b>	8	40	6	30		
<b>10-15 min</b>	9	45	4	20	15.209	0.004*
<b>15-20 min</b>	-	-	9	45		
<b>20 min</b>	-	-	1	5		

\* $p<0.05$  (Significant)

Of the pregnant women in the spontaneous pushing group, 35% had an oxytocin increase and 15% were given oxygen. Of the pregnant women in the Valsalva pushing group, 60% had an oxytocin



increase and 25% were given oxygen. Of the pregnant women in the spontaneous pushing group, 80% did not receive fundal pressure or a vacuum, whereas in the Valsalva pushing group 50% did not. There was no statistical difference between groups, although there was less intervention in the spontaneous pushing group ( $X^2=4.308$ ,  $p>0.05$ ) (Table 3).

Of the pregnant women, 95% in the spontaneous pushing group and 65% in the Valsalva pushing group had an episiotomy ( $X^2=5.925$ ,  $p>0.05$ ). In both groups, mostly mild postpartum hemorrhage occurred (spontaneous pushing=70%; Valsalva pushing=45%;  $X^2=2.572$ ,  $p>0.05$ ) (Table 3).

The mean apgar scores were  $9.86\pm 0.21$  for the spontaneous pushing group,  $9.37\pm 0.11$  for the valsalva pushing group ( $t=-4318$ ,  $p<0.05$ ). There was a statistically significant difference in the mean apgar scores among both groups (Table 3). The Apgar score was higher in the spontaneous pushing group ( $p<0.05$ ) and a statistically significant difference was found between them.

**Table 3.** Obstetric problems, management of the stages of labor and Apgar score

	Spontaneous Pushing (n=20)		Valsalva Pushing (n=20)		X <sup>2</sup> /t	p
	No	%	No	%		
<b>Fetal Distres</b>						
Occured	3	15	5	25	0.625	0.695
Did not occur	17	85	15	75		
<b>Increase in oxytocin dose</b>						
Increased	7	35	12	60	2.506	0.205
Not increased	13	65	8	40		
<b>Oxygen use</b>						
Used	3	15	5	25	0.625	0.347
Not used	17	85	15	75		
<b>Operative intervation</b>						
Yok	16	80.0	10	50	4.308	0.116
Fundal pressure	4	20.0	9	45		
Vacuum	-	-	1	5		
<b>Postpartum hemorrhage</b>						
Too little	2	10	4	20	2.572	0.276
Mild	14	70	9	45		
Middle	4	20	7	35		
<b>Apgar scoru (5min)</b>						
Mean $\pm$ SD	$9.86\pm 0.21$		$9.37\pm 0.11$		$t=-4318$	0.001*

\* $p<0.05$  (Significant)

#### 4. Discussion

In the present study, the duration of the second stage of labor was shorter in the spontaneous pushing group than in the Valsalva pushing group. Some studies have reported for a long time that Valsalva pushing shortens the second stage of labor. Koyuncu and Demirci [2] assessed the effect of pushing techniques on mother and fetus and showed the mean duration of the second stage of labor was significantly shorter in the Valsalva pushing group than the spontaneous pushing group. Another compilation by Prins et al. [12], which assessed 425 women, found the duration of the second stage of labor was shorter in the Valsalva pushing group. Vaziri et al. [11] found the labor duration of pregnant women in the spontaneous pushing

group was significantly higher than in the Valsalva pushing group. However, other studies showed that spontaneous pushing shortened the second stage of labor [3, 16, 17]. Bloom et al. [16] conducted a study on 320 women and found that the duration of second stage of labor was approximately 13 minutes shorter in the spontaneous pushing group. Jahdi et al. [17] found in their study on 191 women that the duration of the second stage of labor was significantly shorter in the spontaneous pushing group. According to a study by Mohamed and AbdElati [18], the duration of the second stage of labor was significantly shorter in the spontaneous pushing group than the Valsalva pushing group. The results are parallel to the present study results.

There was an increase in oxytocin rate in the spontaneous pushing group but no significant difference was found between the groups. In a compilation of 9 randomized controlled studies also found no difference in oxytocin use between groups [10]. Yıldırım and Beji [3] determined the effects of pushing techniques during the second stage of labor on mother and fetus and found no difference between Valsalva pushing and spontaneous pushing in oxytocin use increase. In parallel to the present study, previous studies support that pushing techniques do not affect oxytocin use [3, 6].

Although the intervention (forceps, fundal pressure, or vacuum) rate in the spontaneous pushing group was less in the present study, no significant difference was found between the two groups. Yıldırım and Beji [3] also found no difference in oxygen use between Valsalva pushing and spontaneous pushing group. Although the intervention incidence (forceps, Valsalva maneuver and vacuum) was less in intervention made to labor in spontaneous pushing group, the difference between them was not significant. A study by Schaffer et al. [6] performed with 128 women showed there was no difference between Valsalva pushing and spontaneous pushing in episiotomy and forceps use. A compilation by Barasinski et al. [19] assessed 7 randomized controlled studies and 2 meta-analysis studies and found no difference between the spontaneous pushing and Valsalva pushing groups in episiotomy incidence. In a compilation by Prins et al [12] that assessed 425 women found no difference between groups in interfered birth rates. The literature shows that pushing techniques do not affect operative labor techniques, which supports the present study results [2, 3, 5, 16].

A study by Mohamed and AbdElati [18] found that perineal lacerations were significantly less in the spontaneous pushing group than the Valsalva pushing group. In the present study, there was no difference between the two groups while perineal laceration was seen significantly less in the present study. Another compilation by Prins et al. [12] that assessed 425 women found no difference in perineal recovery. A study by Koyuncu and Demirci [2] performed to assess the effects of pushing techniques on mother and fetus found no significant difference between Valsalva pushing and spontaneous pushing groups in perineal-cervical laceration. Some results in the literature are parallel to the present study results and support that pushing techniques do not affect perineal trauma rates [3, 5, 10, 16, 19].

Although the hemorrhage incidence was less in spontaneous pushing group, there was no significant difference between the groups. In a compilation by Tayrac and Letouzey [10] that assessed 9 randomized controlled study found no difference between groups in postpartum hemorrhage. Previous studies were parallel to the present study results and supported that pushing techniques do not affect postpartum hemorrhage [3, 12].

Fetal distress frequency in this study was less in the spontaneous pushing group, but there was no statistically significant difference between two groups. Fetal distress occurs more in the Valsalva pushing group than the spontaneous pushing group [20]. In this study, the 5th minute Apgar score of the spontaneous pushing group was higher than the Valsalva pushing group. A study by Mohamed and AbdElati [18] found that mean Apgar score of spontaneous pushing group are higher than the Valsalva pushing group. A study by Yıldırım and Beji [3] conducted to determine the effects of pushing technique on mother and fetus in second stage of labor found that the neonate mean Apgar score was significantly higher in the spontaneous pushing group than the Valsalva pushing group. Results of previous studies were parallel to the present study results. However, there are studies that report no difference in Apgar scores. Jahdi et al. [17] found in their study on 191 women that there was no difference in 1st and 5th minute Apgar scores between pushing groups. Vaziri et al. [11] also found no significant difference in 5th minute mean Apgar scores between the spontaneous and Valsalva pushing groups.

## 5. Conclusions

Spontaneous pushing training given during the second stage of labor is effective for completing labor with requiring less intervention, and delivering in a shorter time and increased the fetal Apgar score. Spontaneous pushing during the second stage of labor should be included in maternal hospital protocols.

## 6. Limitations

There are some limitations of this study. Application of treatment routines (oxytocin, dolantin, and epidosin) to all pregnant women did not allow the researchers to limit the effects of these factors. Taking pregnant women into C-section prolonged the duration of the study. A separate pain room was used to do the practice. Therefore, some pregnant women felt alone and abandoned. Some problems occurred because environmental simulators were not controlled sufficiently.

## Conflict of interest

The authors declared no conflict of interest.

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## **FOSTER PARENT'S MOTIVATIONS REGARDING FOSTER CARE: A CROSS-SECTIONAL STUDY FROM SOUTH INDIA**

*Kurian Jose<sup>1</sup>, Sheeba Mumtaz<sup>2</sup>, P.J. Anjali<sup>3</sup>, N.A. Uvais<sup>4</sup>*

<sup>1</sup>PhD scholar, TATA institute of social sciences (TISS), Mumbai, India

<sup>2</sup>District Child Protection Officer, Social Justice Department, Government of Kerala

<sup>3</sup>ICDS Supervisor, Social Justice Department, Government of Kerala

<sup>4</sup>Department of Psychiatry, Iqraa International Hospital and Research Centre, Calicut, Kerala, India

\* Corresponding author: [druvaisna@gmail.com](mailto:druvaisna@gmail.com)

**Abstract:** *Institutionalized children's foster care is getting more momentum in India recently. Perceptions and motivations regarding foster care among foster parents are an area unexplored and the current study is indeed an attempt to look into it. Initial assessment of the sample population was done at home and their socio-demographic data was collected. After taking informed consent, the participants were given an open ended question, what motivated you to apply for foster care? to answer in detail in writing. Qualitative content analysis, a process designed to condense raw data into categories or themes based on valid inference and interpretation was used to analyse the data. The sample population consisted of 36 foster parents. The mean age of husband was  $51.66 \pm 6.58$ , mean age of wife was  $44.83 \pm 5.64$  and average number of children in the family was  $1.58 \pm 1.02$ . Analysis of sociodemographic variables showed that out of 36 foster parents, 21 was belonging to Hindu religion, 8 belonging to Islamic religion and 7 belonging to Christian religion. Most of them belongs to upper middle class and resides in semi urban regions of Kozhikode district. The major motivational themes came out in the qualitative interview were altruism, deprivation, social response, sympathy, empathy, religious beliefs, prestige of the family and a way of meeting parental needs. The present study explored motivations regarding foster care among foster parents. The study found altruism as the most important factor motivating foster care among studied population. Further researches are needed to understand how different motivations affect the quality and continuity of foster care in the Indian context, so that an ideal foster assessment can be made by the concerned authority before entrusting the care of a child to the foster parent.*

**Keywords:** *Foster care, perceptions, motivations, foster parent*

## 1. Introduction

The concept of foster care is getting expanded worldwide and research shows that each year the total number of foster placement increases. But, the total number of foster parents does not increase at the same rate and over 57% of foster parents quit within five years from fostering [1]. Motivations of foster parents are known to predict the success or failure of foster care in terms of the total number of children fostered the number of years fostered and the development of secure attachments [2]. Motivations to foster arise from a person's theories about how life is and how life should be and if the foster care experience corresponds to that theory, the foster care experience is most likely to be good. Otherwise, foster parents can adjust their theory or quit fostering [3]. One of the ways to identify more parents with 'high foster care potential' in order to meet the growing need is by carefully studying the motivations of parents for fostering in different populations. Research has shown that the motivation for fostering varies in different countries and generally an intrinsic, child-centered and self-oriented motivations for fostering were associated with positive outcomes [4]. The concept of foster care system is in its infancy in India. There is a conscious effort from the government bodies like, The Central Adoption Resource Authority, to put priority on domestic and safe adoptions of children over institutional care and it has given the authority to states to expand their child protection laws, and to implement non-institutional care. The motivations that influence Kerala foster parents to enroll in foster care are not known.

## 2. Material and Methods

This cross-sectional study was conducted at Kozhikode district of Kerala state, India. The sample population was chosen from 300 odd applicants applied for foster care of children from Government Children's Home, Kozhikode, where District Child Protection office arranged summer foster care for the first time in 2016.

Initial assessment of the sample population was done at home and their socio-demographic data was collected. After taking informed consent, the participants were given an open ended question, "*what motivated you to apply for foster care?*" to answer in detail in writing.

Qualitative content analysis, a process designed to condense raw data into categories or themes based on valid inference and interpretation was used to analyze the data [5]. During this process the researcher(s) scrutinize and compare the data. In this study, it involved reading, rereading and summarizing the initial data. Recurring words and phrases were identified and placed into categories, which were assigned descriptive titles, and emergent themes were identified.

## 3. Results

The sample population consisted of 36 foster parents. The mean age of husband was  $51.66 \pm 6.58$ , mean age of wife was  $44.83 \pm 5.64$  and average number of children in the family was  $1.58 \pm 1.02$ . The findings are summarized in Table 1.



**Table 1.** Socio demographic variables ( Continuous)

Variables	Mean $\pm$ S.D	Minimum	Maximum
Age husband (In years)(no=36)	51.66 $\pm$ 6.58	42.00	68.00
Age of wife ( In years) ( no=36)	44.83 $\pm$ 5.64	30.00	55.00

Analysis of sociodemographic variables showed that out of 36 foster parents, 21 was belonging to Hindu religion, 8 belonging to Islamic religion and 7 belonging to Christian religion. Most of them belongs to upper middle class and resides in semi urban regions of Kozhikode district. The findings are summarized in Table 2.

**Table 2.** Socio demographic variables ( Categorical)

Variables		Sample population (n=36)	
Religion	Hindu	21 (58.33 %)	
	Muslims	8 (22.22 %)	
	Christians	7 ( 19.44%)	
Socioeconomic Status:	Upper Middle	32 ( 89.44%)	
	Lower Middle	3 ( 8.33 %)	
	Upper Lower	1 ( 2.78%)	
Residence	Rural	16 ( 44.44%)	
	Semi Urban	18 ( 50.00%)	
	Urban	2(5.56%)	

### 3.1 What motivated you to apply for foster care?

The qualitative interview with foster parents revealed multiple, varied and interesting themes that motivated them towards fostering children of children's home, Kozhikode. The major emerging motivational themes for considering foster care were described below:

### 3.1.1. Altruism

Altruism is considered as one of the leading motivating factor for the foster care [6]. By definition, altruism is a helping behavior that benefits the recipient but provides no benefits and may incur costs to the provider [7].

For many respondents the altruistic behaviour was inculcated from the childhood as they saw the suffering in the society especially in the context with the children. It got ‘nurtured up’ as they matured and a ‘sacrificial life’ they wanted to offer to the people who suffer.

“From the childhood I used to feel that I must keep aside a part of my life for children in distress. I was keeping up that spirit always in one corner of my mind”.

The personal gain of the altruistic behavior is often mental satisfaction, which was gained through the gratitude of the person who benefit from the particular help or support, as participants mentioned:

“..... used to show gratitude to me which would make me happy, so I thought of going ahead with the decision of foster care”.

“--By helping parentless children in their education, I could feel their love and gratitude intensified and those thoughts made us to think about foster care”

But what facilitate altruism is a matter of further research.

### 3.2. Deprivation as a factor promoting altruism:

Childhood experiences could shape motivation for care and protection of vulnerable children. Although the respondents haven’t disclosed all their painful experiences at childhood, such as abuse, neglect or dependency, such experiences might have positively motivated a good number of respondents towards foster care.

“My bitter childhood experience (which I hesitate to disclose) motivated me to take the decision of bringing a foster child to home for summer holidays.”

Unpleasant experience of childhood days turn this decision making process. Poverty ridden life in the childhood along with the deprivation of basic necessity was found to be an attribution for the foster care. For some the combination of factors such as neglect, poverty, struggles of life for material deprivation, might motivate to support the other fellow being in struggle. “My father left us during our childhood days and all of us (children ) at family struggled a lot”.

### 3.3 Social response or social consciousness / Common Group Identity

Some of the respondents felt that it is their social responsibility to support those children who are uncared by their parents. They felt the arrival of a new child to their homely atmosphere like adding

one more child to their children. Some of the helping activities by the respondents in the past provided them with ‘new insight’ to go ahead with further supporting the socially deprived and denied with facilities of ‘smooth’ life. Such initial help and support are also seen as ‘added responsibility’ and the ‘societal expectations’ further compel them to look for such activities.

“ When I saw the paper news about summer foster care, I felt happy to give love and affection to an “Orphan child” for few days. Above all the child (foster) would be a company to my kids at home”.

The statement has two things in its interpretation. The common perception of institutionalized children being ‘Orphan’ is a ‘normalized’ thought for many and could be a part of labeling. The gain for some of the respondents out of the foster care as a companionship for one’s own children. It might mutually benefit, over and above the vacation is the time for the parents on heavy duty do not get free time in Indian scenario ( Especially those employees under government senior staff, since it was the time for the state elections to be yet to complete and the duty hours and responsibilities are normally increased, posing a threat upon the reduced attention to the children who are already on vacation ). Respondents also used to denote the children at the institutions as ‘Orphan’, ‘ such kids’ and they felt it’s their social responsibility to provide ‘ Love’ and ‘affection’ towards such children.

### **3.4 Sympathy and empathy**

Sympathy and empathy was identified as factors motivating foster care. The two terms was used interchangeably by the respondents in order to express their feelings while opting for the foster care. “...felt sympathy for those children in the institutions. So I wanted to support them”. “I felt sad about those children who have no place to go and I perceived the psychological trauma they are undergoing as my own, as if it is happening to my kids”.

### **3.5 Religious teaching**

Religious beliefs and teachings influences the lives of the majority of the people and it was identified as a motivating factor for foster care. For those who are motivated by religious beliefs, fostering a child can be seen as an act of fulfilment of what they ‘studied’ or ‘were taught by sages’ or ‘learned in the scriptures’ and they express it as an act of ‘thanks giving for the benefits/blessings they received from God’. The respondents who had formal religious studies either in the childhood or early adult hood wanted to keep up the spirit of their religious beliefs through foster care.

### **3.6 Prestige and pride of family**

Family prestige and pride was also identified as a motivating factor for foster care. Certain families in certain localities are powerful and they often want to play a wider role in the society by protecting cultural values and promoting charitable activities. But, in the current social scenario they often find difficulties in finding proper channels to express their good intentioned activities. Furthermore, due to the socio-economic development of the population of Kerala at large, very few people approach traditionally powerful families for help, which some families view as a sign of their reduced power over the society.

“...supporting others in need is a powerful tool to maintain family prestige. But, no one approach us these days. We saw foster care as an opportunity to keep up the lost prestige and pride of our family”. Such motivations also reflect the underlying paradigm shifts in the mindset of the society at large as the charitable behaviour has become wider, which initially was restricted to people belonging to the same community or same locality and used as a tool in extending influences over the society.

### **3.7 Satisfying the parental demand**

Satisfying the parental demands to reduce loneliness and boredom was also identified as a factor, which motivated parents to foster children. The foster child was expected to change home atmosphere positively by meeting one of the unmet needs.

“ We leave home regularly in the morning for work and children attend school all the day. We usually return in the evening. Our parents and grandparents remain home throughout and they often feel lonely and bored. Hence, we thought of foster care. We felt that the foster child can reduce their loneliness and boredom.”

## **4. Discussion**

The sociodemographic profile of parents who were motivated for foster care, their perception regarding foster care and different themes that motivate them towards foster care were explored in the current study. Different varied and interesting motivational themes came out through this study from altruistic behaviour to meeting unmet parental needs.

Why people become foster parents can be explained by the resource theory, which suggests that the more resources possessed by a person, the more likely they are to be given to others [8]. Therefore, as shown in our study, families with more resources (higher education, higher income, being married, having time, having parenting experience, having social support and working in a helping profession) are more likely to start fostering.

Foster parents report multiple reasons to become a foster parent, broadly grouped into intrinsic and extrinsic motivations. Intrinsic motivations come from within the individual, such as values, standards and personal traits. Motivations driven by an anticipated reward or by the fulfilment of expectations from others are called extrinsic motivations [9]. Another categorization of motivation for foster care is into child-centered and self-oriented motivations. Child-centered reasons focus on the child's needs. Self-oriented reasons are centered on the foster parents' needs [9]. Studies in American foster parents mainly reported child-centered reasons such as wanting to help a child, wanting to provide a child with love and a good home, wanting to provide a home to a child who would otherwise be in an institution, which is consistent with the current study [9]. Around 50% of the American foster parents also believe foster care is a way to do something for the community [9].

For a majority of the current study population, the motive behind foster care was altruism. The foster care workers gave foster parents with motivation as altruism (child- and society-oriented) a high performance rating in foster care [10]. Certain emotionality arises all of a sudden when encountering suffering of others, motivates people to act selflessly to relieve suffering, which can be termed as

altruistic motivation, which remain sustained for a long period and might also lead to empathy in long run [11]. From the study results, it can be argued that certain emotional actors leading to empathy is essential in producing altruistic motivation and it might act as an important mediator resulting in helping and other prosocial behaviours [12]. Feelings such as sympathy and empathy also motivate people to work towards relieving the suffering of vulnerable sections of the society, also thought to result in altruistic behaviours [13]. Furthermore, the mental reward of helping someone in need, in the form of satisfaction, often reinforce altruistic behaviour [14]. Socialisation is another factor leading to altruistic behaviour, as literature found socially excluded people less empathetic than people with socialisation [15]. Responding to the social cause and terming it as one's responsibility could be a part of the social norms, and act as a compelling force towards altruistic behaviour.

The study also found that most of the study population belongs to middle-age. Consistent with the existing literature, our study also shown that altruistic behaviour is more often found among the middle-aged people [16].

Religious beliefs and adherence to religious practices were also found as a motivational theme in our study. The literature suggests that, though no direct linkage was found between religiosity and helping behaviours, it could act as a motivating factor promoting prosocial behaviours [17].

The study also found satisfying the parental demands to reduce loneliness and boredom as a factor which motivated parents to foster children, which is a self-oriented motivation. Literature suggest that such self-oriented motivations were related to worse out-comes in foster care. When parental motivations were 'wanting companionship' or 'wanting to be loved by a child' and related to other foster parental needs, it realised in fewer foster placements and resulted in more placement disruptions and movements [9].

As a society, the population of Kerala, participated in various reforms targeted at helping the vulnerable sections of the society, which might have inculcated helping behaviours into the current generation from early childhood from elders in the family, leading to empathetic attitude towards underprivileged sections of the society, including children of children's home [14]. The current study also showed that the people of urban and semi-urban areas provide more helping hands towards foster care than those at the rural areas [18]. But the level of information regarding the summer foster care reaching the remote rural areas and the reasons for the lack of motivations among the rural population needs to be studied further. Furthermore, apart from altruistic behaviour, rewards also motivate people towards prosocial activities such as foster care. But, does proper care and protection of children happen in a reward oriented atmosphere is a question needs to be studied.

## 5. Conclusion

The present study explored perceptions and motivations regarding foster care among foster parents. The study found altruism as the most important factor motivating foster care among studied population. Further researches are needed to understand how different motivations affect the quality and continuity of foster care in the Indian context, so that an ideal foster assessment can be made by the concerned authority before entrusting the care of a child to the foster parent.

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## CANCER RISK FACTORS AND PREVENTION IN TURKEY

**Ahmet OZDEMIR<sup>1</sup> Emine KAPLAN SERIN\*<sup>2</sup> Mümin SAVAS<sup>1</sup>**

<sup>1</sup>Department of Nursing, School of Health Adiyaman University, Adiyaman, Turkey

<sup>2</sup>Department of Nursing, School of Health Munzur University, Tunceli, Turkey

\*Corresponding author: [emineserin@munzur.edu.tr](mailto:emineserin@munzur.edu.tr)

**Abstract:** *All over the world, the prevalence of cancer is increasing day by day with the increasing incidence of cancers and cancer-related mortality rates in Turkey. Cancer is one of the most important health problems due to frequent occurrence, high cost of treatment with mortality and morbidity, side effects that it creates. Taking precaution responsibilities against cancer is important among the health professionals, especially nurses. It is known that many well-known risk factors such as smoking, infections, avoidance of exposure to radiation, as well as healthy lifestyle behaviors such as healthy eating and physical exercise are effective in protecting from many types of cancer. Therefore, cancer risk factors and ways of protection should be known and publicized by health professionals.*

**Key words:** *Cancer, Risk, Nurse, Cancer Prevention*

### 1. Cancer Risk Factors in Turkey

Cancer is a disease that develops through the alteration of the cells in the body, is independent of environmental factors and can multiply uncontrollably and metastasize at different times. There are more than 100 different types of cancer that have different names depending on the organ and the cell type they are from. Cancer is a disease caused by uncontrolled proliferation of cells in the body. With the increasing frequency of cancers and cancer-related death rates all over the world, the importance of cancer is increasing day by day [1].

The distribution of cancer cases around the world occurs in more than 60% of Africa, Asia and Central-South America, which account for about 70% of cancer deaths. Lung, breast, prostate and colorectal cancers are the major cancers in high or very high income countries. In 2012, 14 million people have cancer and 8 million people have lost their lives because of cancer. The five most common malignancies among males worldwide in 2012 are lung, prostate, colorectal, stomach, and liver cancers [2]. In Turkey, lung cancer was the most common cancer in men and 52.5% according to the 2016 annual health statistics. Lung cancer is followed by prostate, colorectal, bladder and stomach cancer respectively. In women, the most common cancer with 43% was breast cancer. Breast cancer is followed by thyroid, colorectal, uterine corpus and lung cancer respectively [3]. Cancer is one of the most



important health problems due to high mortality and morbidity as well as cost of treatment, duration and side effects [4]. Many types of cancer can be safeguarded from common risk factors such as smoking, infections, avoidance of exposure to radiation [5]. Therefore, protection from cancer is a priority issue. The risk factors should be considered in the primer prevention [6]. Risk factors can be grouped into four groups:

### 1.1. Behavioral Risk Factors

Insufficiency in physical activity, obesity, unbalanced nutrition, alcohol and tobacco use are interchangeable factors and are risky behaviors for all cancers. It is stated that these factors cause more than half of all cancers [7]. Erdem et al. (2017) conducted a study conducted by the most important cause of cancer is cigarettes [8].

**Alcohol:** Boffetha and Hashibe (2006) reported that 3.6% of all cancer cases were alcohol-related. This situation changes in populations due to the consumption frequency [9]. For example, in Canada, a population-based, case-control study found that the relative risk of various types of cancer (esophagus, stomach, colon, liver, pancreas, lung, prostate) was higher in alcohol consumers than in those who did not or occasionally consume alcohol [10].

**Diet:** Overfeeding with fatty foods, alcohol use, post-menopausal weight gain increase breast cancer risk [11]. Breast cancer is more common in the postmenopausal period in overweight or obese women. However, the risk in premenopausal overweight women, is lower than those without [12].

### 1.2. Biological Risk Factors

Physical characteristics such as age, sex and race. Whether physical and biological properties are risk factors for cancer depends on the type of cancer.

**Gender:** Some types of cancer are associated with gender. For example, because prostate gland is only in men, prostate cancer is seen in men. Breast cancer can be seen in both men and women, but women are at higher risk of developing breast cancer [13]. According to the Health Statistics Yearbook (2016), breast cancer is the most common cancer among women, while men are much lower in rate. In males, breast cancer is usually seen after 60 years of age. However, men are late diagnosed because they are later aware of this condition. For this reason, the disease progresses and the treatment becomes difficult [14].

**Age:** Older age is the most important risk factor for many types of individual cancers. According to the current data from the National Cancer Institute's Surveillance, Epidemiology and End Results program, the median age of cancer is 66 years. 25% of the cancer cases are diagnosed in people aged 65 to 74 years [15]. The likelihood of breast cancer is 65 years old, six times more likely to be 35 years old [16]. The study conducted by Aydoğan et al. (2013) found that the average age of the patients in the breast cancer group was 47.99 [17].

**Race:** Certain types of cancers are more common in some races. For example, in Afro-Americans prostate cancer is more common when compared to individuals with white race. It is stated that the mortality rates due to prostate cancer are 2-3 times higher than those of black race to white race [18].

**Skin:** Skin cancer is more common in blondes [19]. Adele et al. (1998) reported that a large proportion of the skin cancer type Actinic keratosis was seen in blond individuals [20]. Frost et al. (1998) reported that blond individuals had a higher incidence of skin cancer in their study in Queensland Australia [21].

### 1.3. Environmental Risk Factors

**Asbestos:** Places or working environment can be a risk factor for cancer development. Some substances found at home or at work such as asbestos, radon, UV radiation, cigarette exposure increase cancer risk. One of the most important environmental risk factors is the exposure to asbestos gas used in the industrialized world of developing countries, despite its being stopped in developed countries [22]. According to World Health Organization data, 125 million individuals are exposed in this gas workplace. In 2004, 107,000 deaths from asbestos-related lung cancer (mesothelioma) and exposure to asbestos in the workplace, along with this 1,523,000 Disability Adjusted Life Years were detected. In addition, exposure to asbestos outside the workplace may be associated with many deaths [23].

Another environmental risk factor is the diet. Some foods taken with the diet increase the risk of developing cancer, while others can be protective [13]. Studies by Chao et al. Have shown that long-term consumption of red meat may increase the risk of large bowel cancer, while consumption of chicken and fish may reduce the risk of large bowel cancer [24]. In addition, intaking dietary genetically modified organisms (GMOs) are among the causes of cancer formation. As a result of the fact that GMO feeding cannot be fully evaluated on humans in terms of ethics for the growth of cancer, rats are used differently from humans in studies [25]. When the results obtained from them are considered; GMOs have been reported to be damaging to many systems in the organism such as adversely affecting RNA synthesis, causing hyperplasia in the digestive system, impairing the immune system and reproductive genes [26–28].

Merdin et al. (2013) in terms of environmental factors may cause cancer in the study: From the perspective of consumer products; cigarettes (31%), hormone foods (27%), nutrition with burned foods (14%), alcohol (16%), and cola drinks (7%); in terms of lifestyle; stress (32%), mobile phone use (19%), environmental pollution (16%), skin overexposure to sun (15%) and obesity (12%) [29].

### 1.4. Genetic Risk Factors

Genetic risk factors are associated with genes inherited from the family. Individuals whose family members are diagnosed with cancer at a young age are at higher risk than others in the community when they have the same type of cancer story in three or more generations. Individuals with three or more cancer cases by their parents or those with different types of cancer in one or both family members are at a higher risk of developing cancer than the other individuals. In the presence of these conditions, genetic screening tests should be performed if cancer is suspected to be hereditary [13].

**Hormones:** Estrogen hormone in women increases breast cancer risk. The removal of the estrogen hormone reduces the growth of the tumor. Early menstruation (before 12 years of age), late menopause (after 55 years of age) and giving birth reduce the risk of breast cancer. Nevertheless, having no birth or giving first birth after 35 years increases the risk of breast cancer [11].

**Obesity:** A study by Oxman et al. (2005) reported that 14% of cancer deaths in men and 20% of women are associated with overweight and obesity. In men, obesity causes increased mortality from prostate and stomach cancers. Obesity increases deaths from breast (postmenopausal), endometrium, cervix, uterus and ovarian cancers in women. In males and females, kidney (renal cell), colon, esophagus (adenocarcinoma), pancreas, gall bladder and liver cancer are increased by obesity [30].

**Immunosuppression:** After any organ transplantation, it is important to use immunosuppressive treatment to resist graft rejection, decrease the graft rejection process, and reduce the effect of the organism's immune mechanism against foreign substances [31]. Silverberg et al. (2018) reported that the rate of cervical cancer was higher in women with HIV who had previously undergone solid organ transplantation and immunosuppressive therapy compared to other groups [32].

**Infectious agents:** Some infectious agents, including viruses, bacteria and parasites, can cause cancer or increase the risk of cancer. Some viruses can disrupt signals that normally regulate cell growth and proliferation. In addition, some infections weaken the immune system and cause the body to be less able to fight other cancers [33].

**Radiation:** The radiation emitted by a particular wavelengths, called ionizing radiation, has energy that damages DNA and causes cancer. It has been found that low energies from mobile phones and electromagnetic fields do not damage DNA and cause cancer [34]. Exposure to radiation increases the risk of breast cancer, especially during the period when the breast is actively developing, between 10 and 14 years of age. However, radiation or radiotherapy after forty-five years does not affect the risk of breast cancer [11].

## 2. Protection From Cancer Risk Factors

It is important to raise public awareness in order to prevent cancer risks. Precautions are provided under the following headings.

### 2.1. Nutrition

Nutrition is reported that effective in 70% of all cancers and 40% in cancer-related deaths [35]. In the study conducted by Sinha et al., meat cooking methods and consumption of red meat has been examined in relation to colorectal cancer. As a result of the study, it was reported that the consumption of 80 g meat per week, colorectal cancer risk 11.0%, very cooked meat 29.0%, high-temperature meat cooking 26.0% for every 10 g meat consumption per day, and cooking of red meat grill or barbecue by 15.0% increased [36]. In some studies it has been shown that red meat exacerbation increases the risk of breast cancer 5 times a week [37,38]. A meta-analysis found that individuals who regularly drink coffee have a 18% lower risk of pancreatic cancer and 14% lower rates of drinkers with low and moderate drinking, compared to those who drink no coffee or rarely drink coffee per day. In the subgroup

analyzes, coffee drinking was associated with decreasing pancreatic cancer in men, but women did not have such a relationship. This meta-analysis reveals that there is an inverse relationship between coffee drinking and pancreatic cancer [39].

## **2.2. Screening methods**

Early recognition of cancer is important in reducing mortality. In Turkey since 2008, "National Cancer Control Program" is implemented. Within this program, breast, cervix and colorectal cancer screenings are performed. Breast and cervical cancer screenings are performed only on women, while colorectal cancer screenings are performed on both genders [35]. Although breast cancer is the second most common cause of cancer among all cancers, it occurs at an earlier age than other cancers. The National Turkish Manual recommends first screening at the age of 40 and mammography every two years until the age of 69. Coverage rate of breast cancer screening in Turkey is at 20-30%. The etiopathogenesis of cervical cancer is the only cancer that can be diagnosed and prevented. Cervical cancer screening differs from country to country. However, the final recommendation is; a woman, at least once in her life, 30-65 years of age in a suitable way to have cancer screening. Cervical cancer; it is important to be screened because it is a preventable disease, 100% can be treated if it is diagnosed early, 10-20 years carcinogenesis process and treatment of cases that will turn into cancer at this stage. If colorectal cancer is diagnosed at an early stage, it can be treated to a great extent. Early diagnosis of colorectal cancer reduces mortality and morbidity as well as treatment costs. colorectal cancer screening in Turkey are between the ages of 50 and 70 [40]. The execution of cancer screening in Turkey CEDSEC (Cancer Early Diagnosis, Screening and Education Center)'s are the main institutions. Knowing CEDSECs by the individuals to be scanned is the most important step in the success of the screening programs. In the study conducted by Pirinççi et al., it was stated that 82.4% of the patients who applied to a health institution did not know KETEM [41]. In study conducted by Şeker et al., it was determined that approximately one out of five of the nurses (19,2%) did not know KETEM [42]. It is conjectured that the lack of information on cancer screening by health care professionals is not negligible. This group, which enables people to become aware of cancer, needs to be aware and informed first.

## **2.3. Smoking and Alcohol**

90% of lung cancer due to smoking in Turkey is emerging. Depending on the use of tobacco products, one out of every three children under the age of 10 is exposed to passive smoking, and 300 individuals lose their lives generated by illness due to cigarettes every day. With effective tobacco control, approximately 110,000 people would survive each year. Smoking is responsible for 3 to 15% of lung cancers [40]. Alcohol causes cancers of the esophagus, larynx and liver [43]. In an individual who consumes alcohol and tobacco together, the risk of esophageal cancer is 100 times higher than that of a person who consumes alcohol or cigarettes alone [44].

## Conclusion

Cancer is complex and the disease is increasing in frequency. Nurses have important duties in the prevention and treatment of cancer, which has behavioral and environmental etiologic factors. Nurses provide comprehensive, co-ordinated and comprehensive health services to individuals, families and society in various cultures. These key features enable nurses to play a key role in protecting and improving health, as it gives them the ability to become health professionals who have frequent, close and long-term relationships with individuals. For these reasons, the knowledge of healthy life style changes of nurses should be increased. They should know the risk of cancer develop and should suggest healthy lifestyle behaviors that are important to protect from cancer.

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## CHANGABLE ENVIRONMENTAL RISK FACTORS IN AUTISM: VITAMIN D AND FOLIC ACID

*Nalan Hakime NOGAY*<sup>1</sup>

<sup>1</sup> Erciyes University Faculty of Health Sciences, Department of Nutrition and Dietetics, Kayseri

\* Corresponding author; nalanhakime@gmail.com

**Abstract:** *Autism Spectrum Disorder (ASD) is a severe neuro-developmental disorder which generally starts during infancy as well as mostly in the first 3 years of life. ASD is characterized by social, behavioral, and communication symptoms. Genetics and certain environmental factors may play a role in the pathogenesis of autism, although the etiology of the disease is unknown. Maternal nutrition is important for development of the fetal brain. The mother's nutritional condition before and during pregnancy may affect the risk of ASD incidence. Vitamin D deficiency is taken into consideration as a possible risk factor for development of ASD. Compared to healthy peers, children with ASD were indicated to have lower levels of vitamin D. However, it is not clear yet if this condition was influenced by the fact that whether patients with ASD are born with lower levels of vitamin D or they are exposed to sunlight lesser. Also folic acid supplementation during pregnancy and blood folate levels in children with autism are environmental factors contributing to autism incidence through dietary intake. The aim of this study is to explain the relationship between vitamin D, folic acid and ASD.*

**Key Words:** Autism, Folic acid, Vitamin D

### 1.Introduction

Autism Spectrum Disorder (ASD) is a severe neuro-developmental disorder which generally starts during infancy as well as mostly in the first 3 years of life [1]. ASD is characterized by social, behavioral, and communication symptoms [2]. It has been recently shown that prevalence of ASD has increased dramatically [3].

Genetics and certain environmental factors may play a role in the pathogenesis of autism, although the etiology of the disease is unknown. Exposure to prenatal teratogens, alcohol, and infections are factors that trigger autism incidence [4].

Maternal nutrition is important for development of the fetal brain. Insufficient maternal nutrition is related to an increase in negative neurodevelopmental results such as neural tube defect, autism spectrum disorder (ASD), and schizophrenia. The fetal brain's structural and functional development is affected by nutrient balance and need. Therefore, the mother's nutritional condition before and during pregnancy may affect the risk of ASD incidence [5]. Along with neurological disorders, metabolic disorders such as phenylketonuria, histidinemia, mitochondrial dysfunction, chronic constipation, stomachache,

malabsorption, gluten intolerance, and allergies are observed. Besides gastrointestinal symptoms, children with autism have nutrition problems such as preferring specific tastes, disgusting certain textures, preferring soft and sweet foods. Thus, nutritional deficiencies play a role in autism [6].

Photolabile and photosynthetic vitamins lead to a higher autism risk by altering genetic and epigenetic interactions. During pregnancy, folic acid and Vitamin D, which are photolabile vitamins, are quite important [7].

Folic acid supplementation during pregnancy and blood folate levels in children with autism are environmental factors contributing to autism incidence through dietary intake. Plasma phosphate concentration is an important determiner of homocysteine levels and a negative correlation exists between them. Serum homocysteine levels are higher in patients with ASD than in their healthy peers. In addition, vitamin B<sub>12</sub> is essential for metabolism of homocysteine [4].

Vitamin D deficiency is taken into consideration as a possible risk factor for development of ASD [8]. Compared to healthy peers, children with ASD were indicated to have lower levels of vitamin D. However, it is not clear yet if this condition was influenced by the fact that whether patients with ASD are born with lower levels of vitamin D or they are exposed to sunlight lesser [2]. Vitamin D deficiency is one of the most critical risk factors of ASD due to several reasons. Firstly, epidemiologic information indicates that vitamin D deficiency is a risk factor for ASD. Secondly, decreased levels of serum vitamin D are associated with alexithymia seen in ASD. Thirdly, vitamin D takes part in DNA repair. Vitamin D can reduce severity of ASD by showing an anti-inflammatory and autoimmune effect and also increasing the number of T-regulatory cells [9]. The aim of this study is to explain the relationship between vitamin D, folic acid and ASD.

## **2. VITAMIN D**

### **2.1. Vitamin D and risk of ASD**

Vitamin D is a steroid hormone that can be taken by diet. However, vitamin D synthesized from sunlight in the skin is the essential resource of vitamin D. Production of vitamin D by the skin is extraordinarily strong and fast. For example, light-skinned people produce vitamin D more than 20000 IU in a time shorter than 30 min when whole of their bodies are exposed to sun in the summer [10]. While Serum 25(OH) D concentration of < 25 nmol/L is defined as vitamin D deficiency, the concentration of 25-49.9 nmol/L is defined as vitamin D insufficiency [11]. The best known role of vitamin D is that it facilitates absorption of calcium and phosphate in the intestine [12]. It also plays role in neurodevelopment, immunological modulation, antioxidant mechanisms, and gene regulation. Positive effects of vitamin D on the human body, particularly on the brain, are known well. Vitamin D deficiency poses a major health problem for numerous societies [13]. Factors such as exposure to sunlight, skin pigmentation, season of delivery, and location of residence affect level of vitamin D [1]. It was reported that risk of developing ASD in further life was higher in children whose mother became pregnant in winter months compared to those whose mother became pregnant in summer months [11]. In a related study, risk of ASD stated to increase by 6% in children whose mother became pregnant in winter season in California between 1990 and 2002 compared to summer season [14]. Another issue focused by scientists is the relationship between season of delivery and ASD risk. Despite the fact that different results were obtained from previous studies, the season in which child is born is considered to be likely associated with ASD risk [11]. A study on vitamin D level of mother and risk of ASD for her child revealed that lower 25(OH) D levels in pregnancy were associated with occurrence of more mental

and psychomotor problems in child to be born [15]. On the other hand, in another study, no relationship was found between maternal 25(OH) D concentration and psychological health and intelligence of the child at the age of 9 months and 9 years [16]. Obtaining different results from the studies is thought to be arising from differences in timing of blood samples taken during pregnancy. In addition, these studies show that different parts of infants' brains may be affected depending on timing of exposure to low level of vitamin D during pregnancy and this leads to cause different neurodevelopmental and cognitive outcomes [11].

Vitamin D levels of 13 children with ASD and 14 healthy children without any medical or psychiatric disorder, aged between 3 and 12 years, were measured and it was revealed that there was no difference between two groups and no relationship between vitamin D level and autism [8]. In an study conducted with 237 children with ASD and 243 healthy children in order to determine the effect of VDR polymorphism on serum 25(OH) D level, significant correlation was determined between VDR (vitamin D receptor) polymorphism and ASD supporting the hypothesis that 25(OH) D plays role on pathology of autism [1]. Vitamin D affects development of the brain through endocrine functions such as stress-mediated agents, inflammation mediated cytokines, and regulation of extracellular calcium. Vitamin D also has direct effects on the brain. Vitamin D has an effect on the brain development via regulation of calcium and glucocorticoids in embryonic neurons, regulation of neurotrophic factors in embryonic brain, embryonic neuronal differentiation, regulation of reactive oxygen species in embryonic non-neuronal cells, and anti-inflammatory effect on developing brain [17].

## **2.2. The action mechanism of vitamin D in ASD**

Some possible mechanisms of therapeutic and preventative effects of vitamin D in ASD have been discussed. One of these is to make contribution to vitamin D for DNA repair. Vitamin D deficiency takes place in numerous *de novo* gene mutation. Reactive oxygen species are a part of normal metabolic function of somatic cells and regularly contribute to DNA damage. Therefore, human genome needs to repair itself [11]. Researchers have reported that vitamin D deficiency is associated with DNA damage and sufficient levels of vitamin D are critical for preventing DNA damage [10]. The second one is the major role of vitamin D in immune system. Evidences show occurrence of neuroglial activation and neuroinflammation of the brains of patients with ASD [2]. Recent studies indicate that children with ASD have lower levels of glutathione and glutathione peroxidase. Oxidative stress and reduced antioxidant capacity were revealed to result in chronic inflammatory response, mitochondrial dysfunction, DNA damage, and clinical characteristics of autism [11]. Vitamin D increases production of antioxidants such as thioredoxin, glutathione, and superoxide dismutase [2]. Glutathione protects nerve cells against toxins. Thirdly, in ASD, the existence of maternal antibodies in fetal brain tissue was shown. Level of these autoantibodies was thought to be directly associated with severity of autism. Vitamin D has a stimulatory effect on T regulatory cells. T regulatory cells suppress reactions by other autoimmune cells in order to prevent body to attack its own tissues [10]. Thus, vitamin D may have a role to protect fetus and decrease autoimmune conditions by stimulating T regulatory cells [2]. In a study conducted about this topic, it was reported that 73.3% of children with autism had T regulatory cell deficiency [18].

ASD, also, is an inflammatory disease. While Vitamin D increases protective immune response, it decreases inflammation. Calcitriol regulates various immune cells such as monocytes, macrophages, and T and B lymphocytes. In studies on patients with ASD, proinflammatory molecules like MCP-1,

TNF- $\alpha$ , were observed to increase. Vitamin D, on the other hand, has a decreasing effect on these molecules [10].

Neurotrophins are the proteins stimulating nerve and brain cells to survive, develop, and function [1]. It was indicated that levels of several neurotrophic factors such as nerve growth factor (NGF) and brain derived neurotrophic factor (BDNF) were abnormal in some individuals with ASD [11]. Vitamin D takes part for regulation of neurotrophins. Mitochondrial disorder is seen in 1 out of every 20 people with ASD. Vitamin D is considered to recover mitochondrial damage [10].

Seizure is observed in more than 25% of patients with ASD. In a previous study, vitamin D deficiency was determined in 8 of 13 patients suffering seizures and these individuals were administered 40000-200000 IU vitamin D for once, and then they were continued to be administered 2000-2600 IU/day for 3 months. As a result of the study, seizures were detected to decrease by 40% [19].

Another effect of vitamin D is on serotonin. While active form of vitamin D decreases peripheral TPH1, it increases central TPH2; this condition explains serotonin paradox in ASD, that is peripheral serotonin is high but central serotonin is low [3]. Vitamin D regulates serotonin synthesis in the brain through tryptophan hydroxylase 2 (TPH2). Therefore, low vitamin D levels result in abnormal serotonin synthesis causing abnormalities in brain development. Low vitamin D levels may result in insufficient TPH2 expression during fetal and neonatal development and lead to low serotonin concentration in the developing brain [20].

### **2.3. The use of vitamin D for treating and preventing ASD**

It has been hypothesized that gestational vitamin D deficiency contributes the cause of autism. Vitamin D supplementation during pregnancy and early childhood is also considered to decrease prevalence of autism in newborn siblings. In a related study, mothers of children with ASD were given 5000 IU/day vitamin D during pregnancy and their newborns were given 1000 IU/day until the age of 3 years, and only 1 of 19 children followed up was diagnosed with ASD. It was concluded in the study that vitamin D administered to infants and toddlers during pregnancy and after birth could decrease incidence of autism [2].

Vitamin D supplementation is thought to decrease behavioral problems of children with ASD. In a related study, 37 of 215 children with ASD were administered with 150000 IU once a month and 400 IU/day for 3 months and it was observed that 25(OH) D levels of all children increased and their behavioral problems recovered at the end of 3 months [13]. In another study, individuals with ASD, having averagely 31.5 nmol/L of baseline 25(OH) D level were administered with daily 1600-4000 IU D<sub>3</sub> and the depression was recovered [21]. 106 children with ASD, possessing serum 25(OH) D concentration of < 75 nmol/L, were administered 300 IU/kg vitamin D for 3 months in such a way not to exceed 5000 IU per day, and behaviors such as irritability, stereotypic behavior and hyperactivity considerably recovered [22]. In a study including 60 children with ASD and control group, aged between 4 and 10 years, 78.3% of children with ASD and 33.3% of control group were observed to have sleep disorders. In the same study, it was observed that group with serum 25(OH) D concentrations of 20-29 nmol/L was administered daily 5000 IU(D<sub>2</sub>), the group with < 20 nmol/L received weekly 50000 IU(D<sub>2</sub>) and vitamin D supplementation had a positive effect on total duration of sleep [23].

Vitamin D is a potential preventative agent for ASD due to its effects such as anti-inflammatory effects, anti-autoimmune activities, and stimulation of antioxidant pathways and provided that daily safe intake level is not exceed, its use in higher doses could be therapeutic in ASD. Targeted blood level is 50 ng – 80 ng/ml to treat vitamin D deficiency in children with ASD [1].

### **3. FOLIC ACID**

#### **3.1. Folate Metabolism**

Folates include a family of compounds chemically related to folic acid. All tissue folates are in the polyglutamate form. Metabolizing the polyglutamate forms of the folates is necessary for their biological activities. Polyglutamate forms are far more effective substrates for dependent enzymes than monoglutamate forms. It is the active coenzyme structure of the tetrahydrofolate vitamin [24]. Folate is necessary for normal metabolic processes as the methyl group donor. It also plays an important role in methionine syntheses. A sufficient amount of folate prevents excessive accumulation of serum homocysteine levels [25].

Folate has many roles as a coenzyme. Its function is to transfer and accept carbon units. The functions of folate in mammals are generally to retrieve mono carbon units from serine and transfer it to purines and pyrimidine biosynthesis. Therefore, folate enzymes are essential for DNA synthesis. Folate coenzymes are necessary for the synthesis of methionine and other cellular compounds [5]. Different genetic polymorphisms occurring in folate pathway key enzymes are related to autism. These abnormalities cause deterioration in the production of folate cycle metabolites, a decrease in 5-methyltetrahydrofolate production, and transmission of folate across the blood-brain barrier [26]. As a result, folic acid is necessary for CpG methylation and gene expression. Low folate levels reduce genomic methylation and negatively affect gene expression during developmental processes such as cell growth [7]. Genetic polymorphisms in methylenetetrahydrofolate reductase and dihydrofolate reductase as well as a reduction in folate transmission are related to autism [26].

#### **3.2. The role of folate in autism occurrence**

Folic acid supplementation may be related to some abnormalities in children. Lymphoblastoid cells exposed to folic acid supplementation may cause changes in gene expression [27]. In addition, epigenetic changes during gestational development may affect DNA methylation levels in the fetus resulting in various neuropsychiatric situations affecting brain development due to the changes in gene expression [28]. There are significantly different methylated areas in the cerebral hemispheres of young mice that had higher maternal folic acid exposure than the ones with lower maternal folic acid exposure [29]. Abnormalities in the frontal lobe may affect brain development and ASD [30].

Dietary folic acid supplementation during pregnancy is a successful community health program instituted to prevent neural tube defects. However, encouraging folic acid intake with supplementation before and during pregnancy and enriching certain grains with folic acid highly increases folic acid levels [25]. Some epidemiological studies show that folic acid supplementation protects against ASD, whereas others report that it increases ASD risk and prevents neurocognitive development in children whose mothers used synthetic folic acid. One study determined the effect of high folic acid intake on cerebral hemisphere genes in rats. One week before mating and during pregnancy, female rats were given 20 mg/kg (control group) or 20 mg/kg folic acid. On the first postnatal day, cerebral hemisphere tissues were obtained and assessed. Pups whose mothers received high levels of folic acid had sex-specific changes in gene expression [31]. Another study found that gene expression in the cerebral hemisphere changed in mouse pups exposed to high levels of folic acid during pregnancy and behavioral disorders such as anxiety and hyperactivity were observed [32].

A comparison of the autism incidence rate published in a study conducted between 1976 and 1997, the prescription rate of vitamins containing 1 mg folic acid, and the prescription rate of any pediatric vitamin containing folic acid was assessed. A significant correlation between autism incidence



and prenatal vitamin use and a weak correlation with pediatric vitamin use was found. The same study showed that very little or high consumption of folic acid may damage nerve tissue [33].

Human dihydrofolate reductase (DHFR) expression is relatively low and has a variable nature in liver. The highest reliable level of folic acid which is tolerable is 1000 mcg/day. High intake of folic acid may result in non-metabolized folic acid in the blood. A dose-related effect occurs when the intake level exceeds 200 mg/day. More than 1 mg folic acid intake results in non-metabolized folic acid, although there were breaks between dosages. Non-metabolized high serum folic acid levels have harmful effects on dihydrofolate enzyme expression, folic acid intake regulation in kidney and intestinal epithelium, neural tissues, and mental health [25].

Neural development is sensitive to maternal metabolic conditions. A high amount of folic acid supplementation in a pregnant woman's diet causes changes in brain synaptic transmission and increased crisis risks [34]. In pups born from mice with high folic acid intake, gene expression in the cerebrum changed and these pups showed cognitive changes such as anxiety and hyperactivity [32]. Another study found that high folic acid nutrition during pregnancy caused altered regulation in gene expression of ASD-related and neurodevelopmental genes [35]. Mean levels of folic acid are reliable markers of health problems, however high levels may alter the epigenetic network [25].

Folate and bipterin pathway members interact. Product levels from both pathways and cerebrospinal fluid bipterin levels may change, which can be treated with tetrahydrobiopterin, a critical component in serotonin, dopamine, and neurotransmitter synthesis [7]. Folate and folic acid are essential for basic cellular processes including DNA replication and protein methylation. Therefore, folic acid intake has an impact dependent on time and dosage. There are different hypotheses to explain the relationship between folic acid and autism. One hypothesis is that serum folate receptor alpha (FR $\alpha$ ) autoantibodies (FRAs) block the folate binding area of the membrane-linked folate receptors on choroid epithelial cells [5]. FRAs are related to developmental diseases including fetal abnormalities and cerebral folate deficiency [36]. Another study assessed the effects of FR $\alpha$  antibody exposure before and after weaning on subsequent behaviors during pregnancy in rats. The study found that the anxiety level of the rats exposed to FR $\alpha$  antibodies before weaning were high, whereas the rats exposed to FR $\alpha$  antibodies in later stages did not show behavioral disorders [37].

Metabolic abnormalities regarding folate metabolism are seen in most ASD studies [25]. Cerebral folate deficiency (CFD) syndrome is a neurometabolic disorder characterized by low 5-methyltetrahydrofolate (5MTHF) levels in cerebrospinal fluid, despite normal levels of systematic folate. CFD distorts the transmission of folate across the blood-brain barrier. Although the biological mechanism between ASD and CFD is not fully known, it can be explained by some symptoms observed in autism such as folate deficiency in the central nervous system, DNA methylation in the brain, and oxidative stress. Some children with CFD showed relief in autism symptoms with folic acid treatment [38].

One of the most important abnormalities regarding ASD is the presence of autoantibodies against FR $\alpha$ . Energy reliant receptors are used for the transportation of folate to the blood-brain barrier. Autoantibodies can bind to these receptors and inhibit their function [26]. A control group was consisted of 75 patients with autism and 30 patients without autism. The blocked FR $\alpha$  auto antibody percentage was 47% in the patients with autism and 3% in the control group [39]. Another study showed that high dosage of folic acid treatment significantly ameliorated the linguistic area of children with ASD such as oral communication, receiver and enunciative fields. According to a study, FRAs were found in

75.3% of 93 children with autism whose serum folate antibodies were measured. Interestingly, an amelioration in oral communication, receptive and expressive language, attention, and repetitive behaviors of children with FRAs treated with oral leucovorin (folinic acid) calcium for approximately 4 months was observed. The authors recommended all children with autism have an FRA test [38]. Similarly, communication, learning, and cognitive disorders occurred in rats exposed to FRAs during pregnancy, which could be prevented by folinic acid treatment [36]. Another study found that rat pups exposed to FR $\alpha$  antibodies during pregnancy and lactation showed intensive behavioral problems [37]. Genetic polymorphisms are often observed in the enzymes necessary to metabolize folate in autism. The MTHF reductase (MTHFR) enzyme is used in folic acid methylation to turn it into a usable form. The survival rate of children with the MTHFR C677T polymorphism can be increased by boosting maternal folic acid intake. These children have reduced enzyme activity and increased neurological recession and autism without folic acid supplementation. Therefore, mutations in the MTHFR enzyme are related to autism. According to proposed hypotheses, the increase in folic acid supplementation boosts the birth rate of children who had mutations in the MTHFR enzyme. Normal or reduced levels of folic acid in a fetus with reduced level of MTHFR enzyme increase the miscarriage risk. Thus, it is necessary to provide children with folic acid to compensate for the reduced enzyme activity after birth. If folic acid supplementation for the children whose MTHFR enzymes are mutated does not occur, it poses a risk for autism development [40].

Excessive folic acid can change behavioral characteristics during cerebral development by changing gene expression. C677T-MTHFR interacts with dietary folate to change the balance between DNA and methionine biosynthesis. Due to insufficiencies in the diet, reductions in genomic methylation capacity can negatively affect gene expression. Low folate levels can affect methionine and S-adenosyl-methionine and change methyl group synthesis [7].

#### 4. Conclusions

Sufficient levels of folate before and at the early stages of pregnancy has a general protective effect. However, high levels can cause undesired effects on DNA methylation during periods of rapid cell division, such as prenatal development. Non-metabolized folic acid can directly change the behaviors of the neurons in certain neural cycles during development. High folic acid supplementation changes genomic functions. One must be careful because folic acid supplementation with folic acid enriched grains can have harmful effects causing excessive folic acid accumulation.

Low levels of vitamin D during pregnancy, postnatal period and early childhood are considered to be a risk factor for ASD which is one of neurodevelopmental disorders. Exposure to vitamin D deficiency in early period may contribute etiology of ASD by interacting with other factors. Vitamin D may directly influence main symptoms of ASD. Therefore, vitamin D supplementation may be beneficial for reducing symptoms seen in patients with ASD. It should be a part of treatment procedure for ASD to routinely assess serum vitamin D level and to supplement sufficient vitamin D. However, conducting long-term controlled clinical studies with large sample size will help to understand potential role of vitamin D and folic acid.



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