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The role and importance of galectin-3 in colon carcinoma metastasis

Galektin-3'ün kolon karsinom metastazındaki yeri ve önemi

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ABSTRACT

Aim: Galectin-3 is an endogenous β -galactoside binding protein which is an S-type lectin family member with intracellular and extracellular localization and has certain tasks for controlling cell adhesion, growth, proliferation, differentiation, migration, and apoptosis. In this study we aimed to elucidate the role of galectin-3 expression in metastasis biology and its role in predicting tumor metastasis in colon carcinomas.

Materials and Method: In this research, 80 cases with colon adenocarcinoma containing the transition of the normal mucosa-tumor tissue were included. The expression of galectin-3 in these cases was investigated immunohistochemically.

Results: There was no significant relationship between Galectin-3 expression and age, gender, and histological type, but there was a significant increase in the amount of galectin-3 expression while the histological grade increased. Galectin-3 expression of the adjacent normal mucosa and tumor was found to be significantly higher in patients with metastases than patients without metastases. There was also a correlation between the presence of vascular invasion and the increase of galectin-3 expression. The mean galectin-3 expression in metastatic foci was higher than that of the tumor area. These findings suggest that the cells with metastatic phenotype express a higher amount of galectin-3 and also galectin-3 has an indirect role in the pathogenesis of metastasis even if its place could not be determined currently.

Conclusion: In our study, it was concluded that the expression of galectin-3 may play a role in the metastatic process of colon carcinomas.

Keywords: Colon Adenocarcinomas, Metastasis, Galectin-3

Öz

Amaç: Galektin-3, hücre içi ve hücre dışı yerleşimli, hücre adezyonu, büyümesi, çoğalması, farklılaşması, göçü ve apoptozu kontrol etmek ve aralarındaki ilişkiyi düzenlemek gibi görevleri olan S tipi bir lektin ailesi üyesi olan endojen bir β -galaktozid bağlayıcı proteindir. Bu çalışmada galektin-3 ekspresyonunun metastaz biyolojisindeki rolünü ve kolon karsinomlarında tümör metastazını öngörmedeki rolünü aydınlatmayı amaçladık.

Gereç ve Yöntem: Bu çalışmaya normal mukoza-tümör dokusunun geçişini içeren kolon adenokarsinomu bulunan 80 olgu dahil edildi. Bu vakalarda galektin-3 ekspresyonu immünohisto-kimyasal olarak araştırıldı.

Bulgular: Galektin-3 ekspresyonu ile yaş, cinsiyet, histolojik tip arasında anlamlı bir ilişki olmadığı ancak histolojik derece arttıkça galektin-3 ekspresyon miktarında anlamlı bir artış olduğu görüldü. Komşu normal mukoza ve tümörün galektin-3 ekspresyonu, metastazı olan hastalarda metastazı olmayan hastalara göre anlamlı derecede yüksek bulundu. Vasküler invazyon varlığı ile galektin-3 ekspresyonunun artışı arasında da bir korelasyon tespit edildi. Metastatik odaklardaki galektin-3 ekspresyonunun ortalaması, tümör alanınınındakinden daha yüksek bulundu. Bu bulgular metastatik fenotipli hücrelerin daha yüksek miktarda galektin-3 ekspresyonu ettiğini ve galektin-3'ün metastaz patogenezinde henüz yeri belirlenememiş olsa da dolaylı olarak rolü olduğunu düşündürmektedir.

Sonuç: Çalışmamızda galektin-3 ekspresyonunun kolon karsinomlarının metastatik sürecinde rol oynayabileceği sonucuna varıldı.

Anahtar Kelimeler: Kolon Adenokarsinomları, Metastaz, Galektin-3

Introduction

Tumor metastasis is a complex process involving interactions between tumor cells, host cells, connective tissue components, and blood vessels with a step wise nature. Thus, all the steps involved in the metastatic process also guide the development of targeted therapies.

The galectins are a family of mediators that have crucial roles for the immune response and thus they have the capacity to regulate inflammatory processes. This regulatory impact can be both inflammatory and anti-inflammatory depending on the localization (1, 2). Galectin-3 is an endogenous β -galactoside-binding protein with intracellular and extracellular localization that belongs to the S-Type lectin family. Its' main functions can be elaborated as cell growth, adhesion, proliferation, differentiation, migration, and apoptosis (1, 2, 3). Galectin-3 is an Ig E binding protein, also known as CBP 35, CBP 30, MAC-2, RL-29, L-29, hL-31, IL-34, or LBP. It is a member of the β -galactoside-binding protein family that recognizes N-acetylglucosamine structures of various glycoconjugates (3 – 7). Galectin – 3 is expressed in various diseases such as diabetes mellitus (8, 9, 10), cardiac diseases (11 – 17), neurodegenerative diseases (18 – 23) and tumor formation (24 – 33).

Galectin – 3 is expressed by the tumor cells and may contribute to the aggressiveness, progression and metastasis of tumor tissue (34 – 40). These are called tumor derived galectins and deteriorate the immune functions while enhancing inflammation. Regarding this fact one can state that the tumor-derived galectins have bipotential consequences on both tumor and immune cells (39). In a tumor tissue the most prevalent immune cells are macrophages, and they are called tumor-associated macrophages (TAMs) (40, 41, 42). In previous literature the increased number of tumor-associated macrophages has been interpreted as an indicator of poor prognosis. These macrophages secrete galectin – 3 into and leverage tumor tissue progression as galectin – 3 facilitates tumor angiogenesis by regulating vascular endothelial growth factor (43). At this stage it should be mentioned that macrophages are not the only galectin – 3 expressing cells but this expression is also performed by tumor stroma. This secretion ratio may be in favor of tumor cells in the progressed neoplasms.

Galectin – 3 is abundant in the cell surface and in biological fluids such as serum and urine. It is also secreted by tumor cells, tumor-associated macrophages and inflammatory cells which make it both a diagnostic and prognostic biomarker (25 – 28, 30, 31). Galectin – 3 has been utilized as a biomarker to detect glioma tumorigenesis (24).

In previous studies the association between tumor presence, prognosis and galectin -3 levels have been identified thus this situation has been tumor type dependent. The expression of galectin – 3 is up-regulated in many types of cancers (37) and new therapeutic strategies may

be designed to facilitate the use of galectins as biological response modifiers to either tumor cells or immune cells (38, 39, 40).

In this study we aimed to elucidate the role of galectin-3 expression in metastasis biology and its role in predicting tumor metastasis in colon carcinomas.

Materials & Method

Hematoxylin-eosin stained sections of 80 adenocarcinoma cases that were previously reported by the Istanbul Training and Research Hospital pathology clinic were re-examined under a Olympus BX51 light microscope. They were re-evaluated in terms of *histological type, histological grade, stage, lymph node and distant metastasis, and vascular invasion*. Grading was accomplished using the three values. TNM staging was re-evaluated according to American Joint Committee on Cancer (AJCC) 8th Edition.

We have chosen a representative colon adenocarcinoma containing the transition of the adjacent normal mucosa-tumor tissue block from each tumor for immunohistochemical analysis. Immunohistochemical study was also performed on one metastatic lymph node and distant metastasis section in all metastatic cases. We have utilized a 4 µm section from each formalin-fixed, paraffin-embedded tissue block and mounted on to positively charged slides. The slides were stained with Galectin-3 (*NCL-Gal3 Clone: 9C4*) mice monoclonal antibody (*Novo Castra Laboratories*) with the streptavidin-avidin-biotin method. The immune-histochemically stained sections were examined and scored by two different pathologists with light microscopy.

Both staining intensity and staining percentage were assessed for Galectin-3 in the center and invasive margin of the tumor, in the metastatic focus in the lymph node, and distant metastatic focus. According to the staining intensity, negative staining was evaluated as *Category 0*, mild staining as *Category 1*, moderate staining as *Category 2* and strong staining as *Category 3*. The percentage of staining was evaluated as the ratio of the stained area to the total tumor area. The following formula was used to calculate the mean staining density score for each assessed compartment. Mean staining density score: $(0 \times \text{percentage of the negatively stained area}) + (1 \times \text{percentage of the weakly stained area}) + (2 \times \text{percentage of the moderately stained area}) + (3 \times \text{Percentage of the strongly stained area})$ (10).

Statistical Analysis

SPSS (*Statistical Package for the Social Sciences*) Windows 10.0 Software package was used for statistical analyses. Student's t-test, Mann Whitney U test, and Kruskal -Wallis test were utilized for comparisons. Pearson test was performed for correlation analysis. A p level less than 0,05 was considered statistically significant.

Results

The samples to be examined have been collected from 80 individuals. Of the 80 patients 47.5% ($n=38$) were male, 52.5% ($n=42$) were female. The mean age of the patients was 57.12 years (*ranging from 28 to 89 years*). The mean age of the cases without metastasis was 55.6 ± 11.02 and the mean age of the patients with metastasis was 58.72 ± 10.50 . No statistically significant relationship has been detected between age and metastasis. ($p=0.205$).

No significant difference have been observed between genders in terms of normal mucosa, tumor, invasion, and lymph node metastasis galectin score. There was no statistically significant difference between classical NOS and mucinous type adenocarcinoma in terms of galectin score values of normal mucosa, tumor, and invasive margin (*Table 1*). The number of signet ring cells and undifferentiated carcinoma cases was insufficient for further statistical analysis.

Table 1: Relationship between histological type of tumor neighboring mucosa, tumor, invasive margin, and lymph node metastasis galectin score

Histological type	NOS	Mucinous	<i>p</i> value
Neighboring mucosa galectin score	2.77 ± 0.39	2.81 ± 0.24	0.776
Tumor galectin score	1.57 ± 0.65	1.81 ± 0.66	0.359
Invasive margin galectin score	2.09 ± 0.82	2.31 ± 0.39	0.478
Lymph node metastasis galectin score	2.43 ± 0.47	2.76 ± 0.39	0.138

Data expressed as mean \pm SD

SD: Standard deviation

NOS: Not otherwise specified

The mean galectin scores of the invasive margin of the tumor with metastasis (*Stage III, IV, V*) were significantly greater than those of the cases without metastasis (*Stage I, II*) ($p=0.003$). In addition, the galectin score of the neighboring mucosa was significantly greater in subjects with metastasis compared to those without ($p=0.001$). There was no significant difference between the subjects with or without metastasis with respect to the tumor galectin score in the whole tumor area ($p=0.83$) (*Table 2*). Lymph node metastases had a mean galectin score of 2.44.

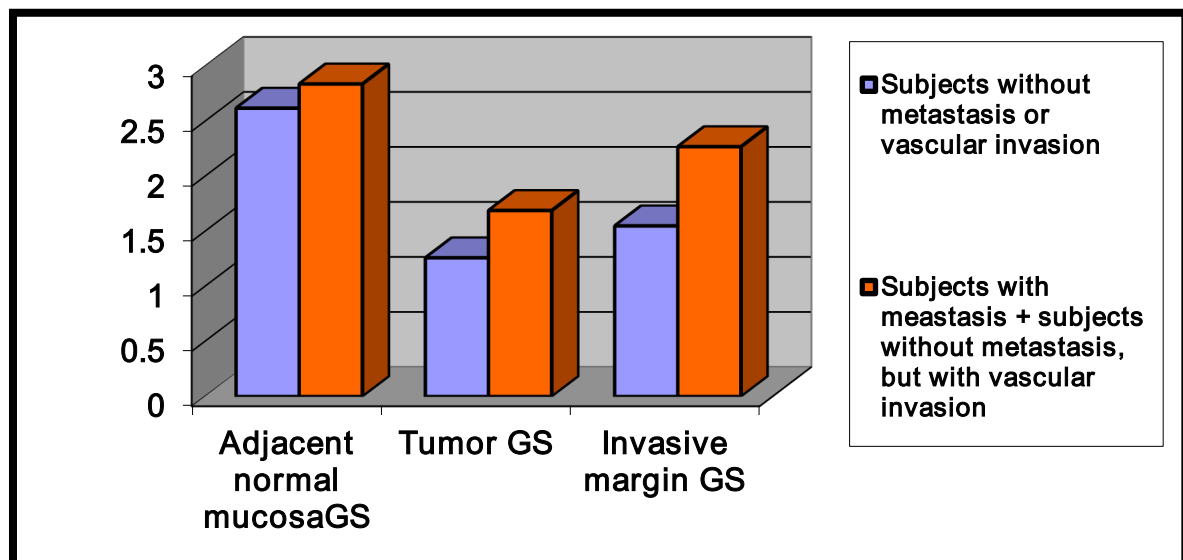
Table 2: Comparison of the adjacent normal mucosa, tumor, and invasive margin galectin scores of the subjects without metastasis with those of the "subjects with metastasis+subjects without metastasis but with vascular invasion" group.

Presence of metastasis Stage	Subjects without metastasis Stage I, II	Subjects with metastasis Stage III, IV, V	<i>p</i> value
Adjacent normal mucosa galectin score	2.64±0.46	2.90±0.22	0.001
Tumor galectin score	1.43±0.63	1.69±0.68	0.083
Invasive margin galectin score	1.77±0.80	2.30±0.76	0.003

Data expressed as mean ± SD

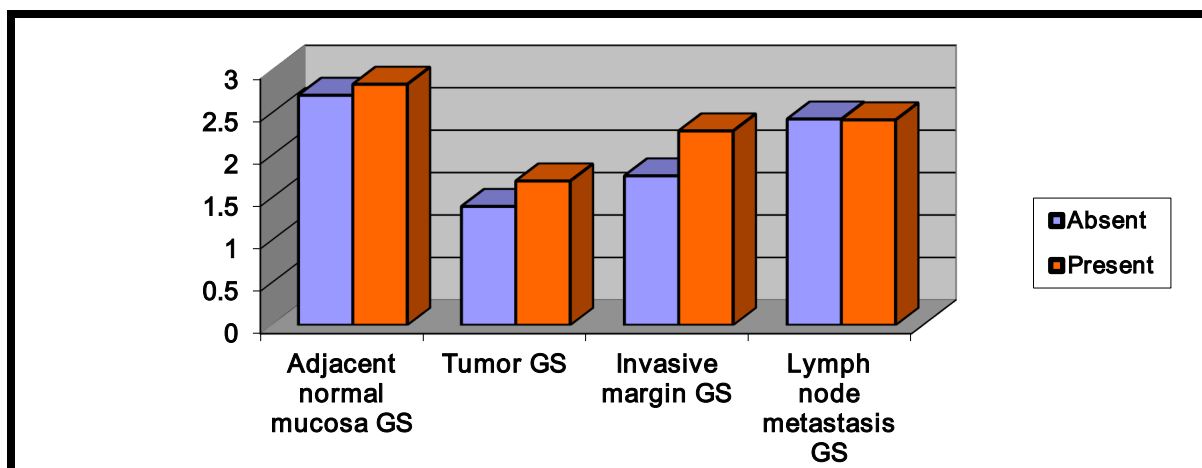
SD: Standard deviation

Crossover of the subjects with vascular invasion from the group of subjects without metastasis to those with metastasis led to a significantly greater normal mucosa, tumor, and invasion area galectin scores in subjects with metastasis than those without ($p=0.016$, $p=0.008$, $p<0.001$) (Figure 1). The tumor and invasive margin galectin scores were significantly greater in the subjects with vascular invasion compared to the subjects without vascular invasion ($p=0.048$, $p=0.004$) (Figure 2).



GS: Galectin score

Figure 1: Graphical comparison of the adjacent normal mucosa, tumor, and invasive margin galectin scores of the subjects without metastasis with those of the "subjects with metastasis+subjects without metastasis but with vascular invasion" group



GS: Galectin score

Figure 2: Comparison of the mean galectin scores of adjacent normal mucosa, tumor, invasive margin and lymph node metastasis between the subjects with and without vascular invasion.

The adjacent normal mucosa galectin scores of *Grades 2, and 3* cases were significantly higher than *Grade 1*. Tumor, invasive margin, and lymph node galectin score did not significantly differ with respect to tumor grade (*Table 3*).

A strong cytoplasmic and strong nuclear staining for galectin-3 was observed in the upper parts of normal mucosa while there was weak nuclear staining for galectin-3 in the basal part. At the transformation zone from normal mucosa to adenoma, the galectin-3 expression was reduced, which was increased again in areas of dysplasia in parallel with the grade of dysplasia. The galectin-3 expression was greater in areas of carcinoma than adenomatous areas with dysplasia, with the greatest staining being in the deep invasion areas.

Table 3: Comparison of the mean galectin scores of adjacent normal mucosa, tumor, invasive margin and lymph node metastasis between the subjects with and without vascular invasion.

GRADE	GRADE 1	GRADE 2	GRADE 3	<i>p</i> value
Adjacent normal mucosa galectin score	2.55±0.59	2.78±0.34	2.91±0.19	0.012
Tumor galectin score	1.51±0.56	1.51±0.72	1.69±0.63	0.512
Invasive margin galectin score	1.86±0.79	1.98±0.90	2.31±0.66	0.156
Lymph node metastasis galectin score	2.32±0.36	2.41±0.42	2.46±0.64	0.863

Data expressed as mean ± SD

SD: Standard deviation

A correlation analysis showed that the adjacent normal mucosa galectin score was correlated to tumor stage and grade. Invasive margin galectin score showed a positive correlation with stage at the same time, invasive margin galectin score also had greater than adjacent normal mucosa and tumor galectin scores. The lymph node metastasis score was also correlated to invasion and tumor galectin score (*Table 4*).

Table 4: Correlation coefficients (r)

	Age	Stage	Grade	Histological Type	Adjacent Normal Mucosa galectin score	Tumor galectin score	Invasive margin galectin score
Adjacent normal mucosa galectin score	0.009	0.359	0.321	0.115			
Tumor galectin score	-0.002	0.169	0.073	-0.074	0.189		
Invasive margin galectin score	0.080	0.316	0.149	-0.166	0.245	0.711	
Lymph node metastasis galectin score	0.099	0.135	-0.038	-0.256	0.050	0.306	0.516

A comparison of the sensitivities and specificities of adjacent normal mucosa, tumor, and invasive margin galectin scores based on the stage revealed that the invasive area galectin score had the greatest sensitivity. When adjacent normal mucosa, tumor, invasive margin galectin score values are compared according to stages in terms of sensitivity and specificity; the invasive margin galectin score value is the parameter with the highest sensitivity. Even after adding vascular invasion to the cases without metastasis, the invasive margin galectin score still had the greatest sensitivity (*Figure 3*).

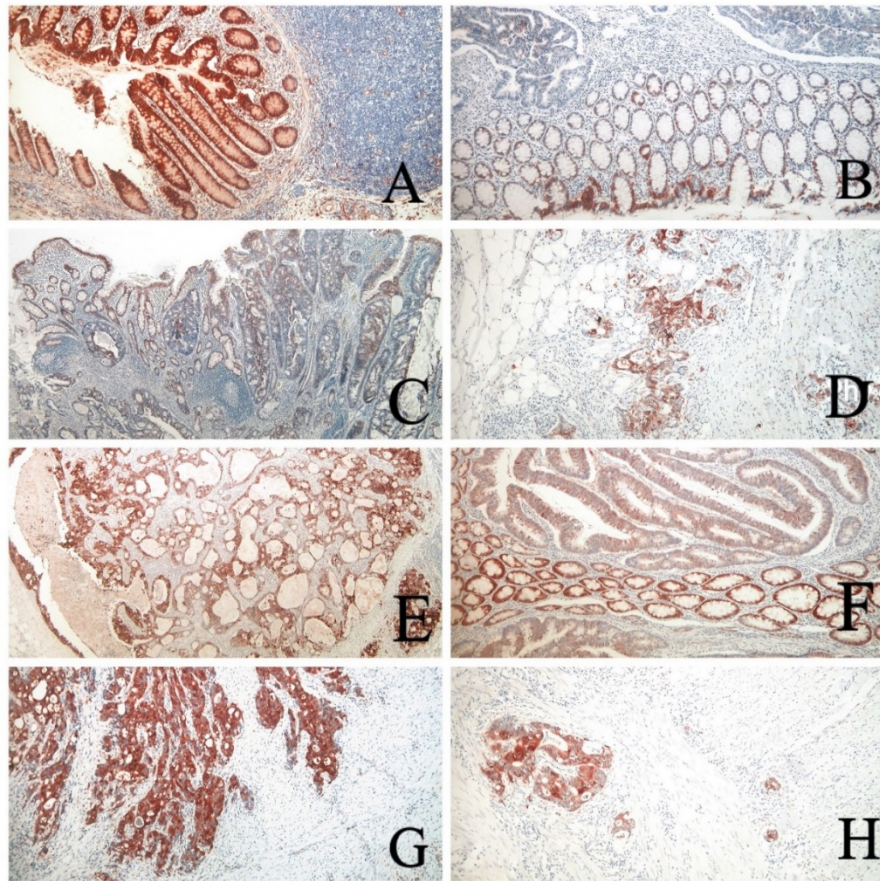


Figure 3: Galectin-3 immunohistochemical results. A: Score 3 galectin-3 expression, more severe and cytoplasmic, on the crypt surface in normal colonic mucosa. In addition to the epithelium, strong expression is also observed in some lymphocytes, stromal cells, and endothelial cells (IHKX4). B: Tumor galectin-3 expression score of 0,4 and normal mucosa galectin-3 staining pattern in a case without metastasis (IHKX4). C: Score 1,6 galectin-3 expression on the tumor surface in a patient with metastasis. Normal mucosa tumor transition area and generally superficial tumor area are observed (IHKX4). D: Score 2,6 galectin-3 expression in the invasive margin in the same case as in C (IHKX4). E: Score 2,8 galectin-3 expression in lymph node metastasis of the same patient as in C (IHKX20). F: Score 1,9 galectin-3 expression in the superficial tumor area in a patient without metastasis but with vascular invasion (IHKX4). G: Invasive margin galectin-3 expression score of 3, which was the strongest staining (IHKX4). H: Score 2,8 galectin-3 expression in the invasive tumoral area and vascular invasions in the same case as in F (IHKX10).

Discussion

Galectin-3 is a carbohydrate-binding protein that belongs to the S-type lectin group and has an affinity for β -galactoside sugars. Disorders on the cell surface or in glycoproteins to which galectin-3 is bound, such as mucins, play an important role in carcinogenesis in the gastrointestinal system (25). Increased galectin-3 levels have been reported in some neoplasms and this finding has been suggested to relate to disorders of cell growth, transformation, and metastasis (26).

Although the biological functions of galectin-3 have not been fully elaborated, it has been found to induce tumor progression and metastasis by means of carbohydrate-mediated homotypic aggregation and inhibition of apoptosis (1,2,27).

Most colorectal adenocarcinomas develop on the basis of adenomas, rather than de novo development (28). Furthermore, only part of the cells in a tumor possesses metastatic phenotype and a heterogeneous cell population is formed within a tumor. Considering this, a score encompassing the whole tumor area may not reflect the actual galectin-3 expression. Thus, we separately scored the invasive margin of the tumor area with the highest metastatic potential (30). As a result, overall galectin-3 expression detected in a tumor did not show a significant correlation to its metastatic capacity, while an expression in the invasive component showed a positive correlation to the presence of metastases. This was considered to be a result of a heterogeneous population within the tumor (29).

In very early stages of galectin research promising data have been published by various investigators. Iramura and Lee have reported in separate studies that there existed a direct relation between galectin-3 expression and tumor stage (44,45). Similarly, Schoeppner et al. showed that galectin-3 expression was increased in proportion to an increase in stage and was correlated with reduced survival (46), hence, studies on some malignancies other than colorectal carcinomas have reported opposite results. Lotan et al. showed in gastric carcinomas (47) and Vandenbrule et al. showed in ovarian carcinomas (48) that metastatic properties and the clinical course did not correlate to galectin-3 levels. Unlike the studies on colon carcinomas, Lotz et al. found that reduced galectin 3 expressions were associated with tumor progression (49). Invasion of vascular structures by tumor cells is one of the metastasis steps (26,28). The cases having no metastasis in the resection material, namely the cases in stage I and II were included in the group with vascular invasion in the metastatic process to form a separate case group. When we separately analyzed that group, we observed a more significant relationship between galectin-3 and metastasis.

Taking vascular invasion as a single parameter, the significant association between vascular invasion and tumor invasion and galectin scores can be explained by the increased cell population that can invade vessels during the metastatic process. This significant relationship, however, also suggests a role of galectin-3 in the heterotypic-homotypic aggregation of tumor cells with each other and thrombocytes during the entry into the vessel lumen and tumor embolization (30, 31).

It has been reported that there was generally a strong galectin-3 staining in the upper 2/3 of the normal colonic mucosa and negative or weak staining in the base of crypts, and the staining was usually nuclear in the basal part and cytoplasmic and nuclear on the surface (34, 35, 38). The sole presence of nuclear staining in the basal part may be linked to a higher rate of cellular proliferation and an increased nuclear galectin-3 concentration as a component of ribonucleoprotein particles during cellular proliferation (37). The galectin-3 expression on the surface may be attributed to a greater mucin content in the crypt surface as well as the presence of galectin-3 as an anti-receptor of mucins in glycoprotein structure (9,10).

Since colorectal carcinomas were among the best examples of malignancies to identify the adenoma-dysplasia-carcinoma they provide a unique opportunity for carcinogenesis studies (39). Some of our subjects clearly demonstrated the typical morphogenetic transformation from normal mucosa to carcinoma. While a reduction in expression was observed in the areas of adenoma, dysplasia, and carcinoma compared to normal mucosa, a strong cytoplasmic expression similar to normal mucosa was noted in the deepest and least differentiated infiltration areas of the tumor. Similar findings have also been observed in areas of deep myometrial invasion in endometrial adenocarcinomas. This was the result of the accumulation of cells with metastatic ability through genetic mutations at the deepest site, by virtue of their potential for degrading the extracellular matrix and inhibiting cellular adhesion and migration. In this study there was no significant relationship between age, gender, histological type, histological grade, and galectin-3 expression level; but as the grade increased, the amount of normal mucosal galectin expression increased significantly.

Some studies have examined the use of galectin-3 in the differential diagnosis of some malignancies such as thyroid carcinoma and anaplastic large cell lymphoma, albeit with conflicting results (40, 43). Galectin-3 expression may occur as a result of malignant transformation, but malignant transformation may also induce galectin-3 expression (41, 42). In our study, normal mucosa galectin score correlated with the increase in tumor stage and grade. This finding may be due to the normal mucosa from the periphery of the tumor undergoing some mutational changes that would lead to the development of a high-grade tumor. The mean galectin-3 expression was higher in the metastatic foci than in other tumoral regions, suggesting that cells with metastatic phenotype express a greater amount of galectin-3 and galectin-3 indirectly plays an important role in the pathogenesis of metastasis.

Conclusion

Exploring tumor markers that can predict tumor metastasis and prognosis is important for effective treatment guidance. Galectin-3 may predict prognosis in some solid tumors. In

targeted treatment of cancer patients, anti-invasion and anti-metastatic agents can be improved by identifying inhibitors capable of preventing apoptosis escape, cell adhesion, growth, differentiation, and angiogenesis, such as anti-galectin 3.

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Competing interests

The authors declare that they have no competing interests.

Ethics Statement

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23/09/2022

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Authorship Contributions

Concept: UK, MK, Design: UK, MK, Supervising: MK, HD, Financing and equipment: UK, MK, HD, Data collection and entry: MK, HD, Analysis and interpretation: MK, HD, Literature search: UK, Writing: UK, Critical review: MK, HD

Abbreviations:

AJCC: *American Joint Committee on Cancer*

NOS: *Not otherwise specified*

SD: *Standard deviation*

SPSS: *Statistical Package for the Social Sciences*

TAM: *Tumor-associated macrophages*

TNM: *Tumor Nodes and Metastasis*

GS: *Galectin score*

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Hemşirelik öğrencilerinin algıladıkları sosyal destek düzeyleri ile stres ve stresle baş etme davranışları arasındaki ilişki

The relationship between the perceived social support levels of nursing students and their stress and stress coping behaviors

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Öz

Amaç: Bu çalışma hemşirelik öğrencilerinin algıladıkları sosyal destek düzeyleri ile stres ve stresle baş etme davranışları arasındaki ilişkinin belirlenmesi amacıyla gerçekleştirildi.

Gereç ve Yöntem: Araştırma tanımlayıcı ve ilişki arayıcı desende yürütüldü. Araştırmanın verileri bir üniversitenin hemşirelik bölümünde 2021-2022 bahar yarıyılında öğrenim gören 254 öğrenci aracılığıyla ve yüz yüze görüşme tekniği kullanılarak toplandı. Verilerin toplanmasında tanımlayıcı bilgi formu, Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ), Hemşirelik Öğrencileri için Algılanan Stres Ölçeği (HÖASÖ) ve Hemşirelik Öğrencileri için Stresle Baş Etme Davranışları Ölçeği (HÖSBDÖ) kullanıldı. Verilerin değerlendirilmesinde tanımlayıcı istatistikler ile ölçek puan ortalamalarının karşılaştırılmasında korelasyon analiz testleri kullanıldı.

Bulgular: Araştırmaya katılan öğrencilerin yaş ortalamasının 20.72±1.85, %68.9'unun kadın ve %55.1'inin gelir düzeyinin gidere eşit olduğu belirlendi. Çalışmaya katılan öğrencilerin %69.3'ü akademik başarı durumlarının orta olduğunu bildirdi. Araştırmada ölçek puan ortalamaları ÇBASDÖ, HÖASÖ ve HÖSBDÖ için sırasıyla 50.75±17.75, 59.59±24.35 ve 39.74±9.77 olarak saptandı. ÇBASDÖ ile HÖSBDÖ toplam puanları arasında pozitif yönde $r=.207$ düzeyinde ve istatistiksel olarak anlamlı bir ilişki tespit edildi ($p=0.001$). HÖASÖ ile HÖSBDÖ toplam puanları arasında pozitif yönde $r=.233$ düzeyinde ve istatistiksel olarak anlamlı bir ilişki tespit edildi ($p=0.000$).

Sonuç: Araştırmanın sonucunda öğrencilerin algıladıkları sosyal destek düzeyleri ile stresle baş etme davranışları arasında pozitif yönlü anlamlı bir ilişki olduğu bulundu. Hemşirelik öğrencilerinin algıladıkları yüksek stresle etkin baş etme stratejilerini kullanabilmeleri adına desteklenmeleri gerektiği düşünülmektedir.

Anahtar Kelimeler: Algılanan Sosyal Destek; Hemşirelik Öğrencileri; Stres; Stresle Baş Etme

ABSTRACT

Aim: This study was carried out to determine the relationship between the perceived social support levels of nursing students and their occupational stress and coping behaviors.

Material and Method: The research was conducted in a descriptive and correlational design. The data of the study were collected by using face-to-face interview technique through 254 students studying in the nursing department of a university in the spring semester of 2021-2022. A descriptive information form, the Multidimensional Scale of Perceived Social Support (MSPSS), the Perceived Stress Scale for Nursing Students (PSSNS), and the Scale of Coping Behaviours of Stress for Nursing Students (SCBSNS) were used to collect data. In the evaluation of the data descriptive statistics, and correlation analysis tests for comparing the scale mean scores were used.

Results: It was determined that the mean age of the students participating in the study was 20.72±1.85, 68.9% were female, and 55.1% had an income level equal to expenditure. 69.3% of the students who participated in the study reported that their academic achievement was moderate. In the study, the mean scores of the scale were determined as 50.75±17.75, 59.59±24.35, and 39.74±9.77 for MSPSS, PSSNS, and SCBSNS, respectively. A positive and statistically significant correlation at the level of $r=.207$ was found between MSPSS and total scores of SCBSNS ($p=0.001$). A positive and statistically significant correlation was found at the level of $r=.233$ between the total scores of PSSNS and SCBSNS ($p=0.000$).

Conclusion: As a result of the research, it was found that there was a positive and significant relationship between the students' perceived social support levels and their stress coping behaviors. It is thought that nursing students should be supported in order to use effective coping strategies with perceived high stress.

Keywords: Perceived Social Support; Nursing Students; Stress; Coping With Stress

Giriş

Stres, bireyin hayatında karşılaştığı farklılıklara uyum sağlayabilme çabası; uyum sağlanamadığı durumlarda da fiziksel ve ruhsal dengede bozulmayla sonuçlanabilen bir süreç olarak tanımlanmaktadır (1). Hemşirelik öğrencilerinin öğrenim gördükleri süreçte deneyimledikleri stres düzeyinin oldukça yüksek olduğu ifade edilmektedir (2). Bu stresi tetikleyen ya da etkileyen pek çok faktör sıralanmaktadır. Özellikle hastanın ağrı deneyimi ya da hayatını kaybetmesi, acil müdahale gereklilikleri, meslek derslerine yönelik teorik bilgi ya da pratik uygulamalarda beceri yetersizliği, hastaya zarar verme korkusu gibi konular öğrencilerde stresin artmasına neden olabilmekte ve öğrenciler yaşanan bu stres faktörleri ile baş etmeye çalışmaktadır (2,3). Öğrencinin hemşirelik eğitimi sürecini başarılı bir şekilde tamamlayarak, mesleğe yönelik istenilen seviyede bilgi ve beceri kazanımı için yaşanan stresin yönetimi önemlidir. Etkili biçimde yönetilemeyen stresin öğrencinin profesyonel kimlik süreci üzerindeki kötü etkileri bildirilmektedir (4). Hemşirelik öğrencileri üzerinde yapılan araştırmalar, etkili başa çıkma stratejilerine sahip olmayan öğrencilerin stresli durumlarda psikiyatrik belirtiler gösterme riski taşıdığını ortaya koymaktadır (5,6).

Sosyal destek, bireylerin aile ve arkadaşları ile olan ilişkilerini kapsayan temel bir ihtiyaç olarak görülmektedir (7). Sosyal destek, bireyde stres oluşturan yaşam olaylarının algılanan önemini azaltmakta ve bireyin bu duygusal gerginliğin üstesinden gelmesine yardımcı olmaktadır. Stresi önlemenin ve algılanan stresle başa çıkabilmenin en etkin yollarından biri, bireyin yaşamın bütün alanlarında yeterli sosyal desteğe sahip olmasıdır (8). Öğrencilerin yeterli sosyal destek alınması ile birlikte karşılaştıkları sorunları erken evrede çözerek öğrenim hayatlarında önemli kazanımlar elde edebileceği ifade edilmektedir. Yeterli sosyal desteğin öğrencilerin zihinsel sağlık düzeyleri ile akademik başarı düzeylerinde olumlu bir etki oluşturduğu bildirilmektedir (9). Bu bilgiler doğrultusunda öğrencilerin algıladıkları sosyal destek düzeyinin ve karşılaşılan sorunların çözümünde destek kaynaklarından yararlanma düzeyinin belirlenmesi önem taşımaktadır. Literatürde bulunan çalışmalar incelendiğinde hemşirelik öğrencilerinin sosyal destek düzeyleri ile algıladıkları stres ve stresle baş etme davranışlarını birlikte ele alan herhangi bir araştırmaya rastlanmamıştır. Bu çalışma hemşirelik öğrencilerinin algıladıkları sosyal destek düzeyleri ile mesleğe yönelik stres ve stresle baş etme davranışları arasındaki ilişkinin belirlenmesi amacıyla gerçekleştirildi.

Gereç ve Yöntem

Bu araştırma tanımlayıcı ve ilişki arayıcı desende, 14.02.2022-01.12.2022 tarihleri arasında gerçekleştirildi. Araştırmanın evrenini 2021-2022 bahar yarıyılında Adıyaman Üniversitesi Sağlık Bilimleri Fakültesi Hemşirelik Bölümünde öğrenim gören 435 öğrenci oluşturdu. Örneklem sayısının hesaplanmasında evreni bilinen örneklem hesaplama yöntemi kullanıldı ($n = Nt^2pq/d^2(N-1) + t^2pq$). Buna göre; $N=435$; $t=1,96$; $p=0.50$; $q=0.50$; $d=0.05$ (\pm %5 örnekleme hatasını kabul edildiğinden) olarak yerleştirildiğinde araştırmada ulaşılması gereken minimum örneklem sayısı 204 olarak hesaplandı. Araştırmada örneklem seçimi rastgele sayılar tablosu kullanılarak yapıldı. Bu kapsamda bölümden öğrenci listesi alınarak, bu listede rastgele sayılar tablosu sıralamasına uygun öğrencilere anket formu uygulandı. Araştırma 254 öğrenci ile tamamlandı.

Araştırmaya Dahil Edilme Kriterleri:

- Belirlenen tarihte ilgili fakültenin hemşirelik bölümünde aktif öğrenim görüyor olmak,
- Araştırmaya katılmaya gönüllü olmak şeklinde belirlendi.

Verilerin Toplanması

Araştırmanın verileri araştırmacılar tarafından veri toplama formu kullanılarak yüz yüze görüşme tekniği ile toplandı. Verilerin toplanmasında tanımlayıcı bilgi formu, Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ), Hemşirelik Öğrencileri İçin Algılanan Stres Ölçeği (HÖASÖ) ve Hemşirelik Öğrencileri İçin Stresle Baş Etme Davranışları Ölçeği (HÖSBDÖ) kullanıldı.

Tanımlayıcı Bilgi Formu: Tanımlayıcı bilgi formu araştırmacılar tarafından oluşturulmuştur. Bu form katılımcıların bazı özelliklerini (yaş, cinsiyet, bulunduğu sınıf, ailenin gelir düzeyi, akademik ortalama) belirlemeye yönelik altı sorudan oluşmaktadır.

Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ): Zimet ve arkadaşları tarafından 1988 yılında geliştirilen ölçeğin Türkçe geçerlik ve güvenilirliği Eker ve arkadaşları (2001) tarafından yapılmıştır. Ölçeğin Cronbach alpha değeri 0.89 olarak belirlenmiştir. 12 maddeden oluşan ölçek Aile, Arkadaşlar, Özel insan şeklinde üç alt boyuttan oluşmaktadır. Ölçekten alınabilecek toplam puan 12-84 arasındadır. Elde edilen puanın yüksek olması bireyler için o boyutta algılanan sosyal desteğin yüksek olduğunu göstermektedir (10). Araştırmamızda Cronbach alpha katsayısı 0.915 olarak belirlenmiştir.

Hemşirelik Öğrencileri İçin Algılanan Stres Ölçeği (HÖASÖ): Sheu ve arkadaşları tarafından (2002) geliştirilen ölçeğin Türkçe geçerlik ve güvenilirlik çalışması Karaca ve

arkadaşları (2015) tarafından yapılmıştır. Beşli likert tipte olan ölçekten alınabilecek puanlar 0–116 arasında değişmektedir. Ölçeğin alt boyutları mesleki bilgi ve beceri eksikliğinden kaynaklanan stres; hastaya bakım verirken yaşanan stres; ödevlerden ve iş yükünden kaynaklanan stres; öğretim elemanları ve hemşirelerden kaynaklanan stres; ortamdan kaynaklanan stres; akranlardan ve günlük yaşamdan kaynaklanan stres şeklindedir. Yüksek puan, stres derecesinin yüksekliğini göstermektedir. Ölçeğin Cronbach alpha katsayısı yapılan geçerlik ve güvenirlik çalışmasında 0.85 olarak belirlenmiş (11), bizim araştırmamızda bu değer 0.964 olarak saptanmıştır.

Hemşirelik Öğrencileri İçin Stresle Baş Etme Davranışları Ölçeği (HÖSBDÖ): Sheu ve arkadaşları tarafından (2002) geliştirilen ölçeğin Türkçe geçerlik ve güvenirlik çalışması Karaca ve arkadaşları (2015) tarafından yapılmıştır. 19 maddeden oluşan ölçek; iyimser kalma, transfer, sorun çözme ve kaçınma alt boyutlarından oluşan beşli likert tiptedir. Bir faktörde görülen yüksek skor, bu baş etme stratejisini diğer stratejilerden daha sık kullandığı anlamına geldiği bilinmelidir. Hangi alt boyutun puanı yüksek olursa öğrencinin o baş etme stratejisini daha sık kullandığı anlamına gelmektedir. Ölçeğin Cronbach alpha katsayısı 0.76 şeklinde bulunmuştur (11,12). Araştırmamızda Cronbach alpha katsayısı 0.772 olarak saptanmıştır.

Verilerin Değerlendirilmesi

Çalışmadan elde edilen bulguların istatistiksel analizinde için SPSS (Statistical Package for Social Science) 22 paket programı (IBM Corporation, Armonk, NY) kullanıldı. Verilerin değerlendirilmesinde; sayı, yüzdelik, aritmetik ortalama (\bar{X}) ve standart sapma (SS) gibi tanımlayıcı istatistikler kullanıldı. Tüm ölçeklerin puan ortalamalarının karşılaştırılmasında korelasyon analiz testleri uygulandı.

Araştırmanın Etik Boyutu

Çalışmanın yapılabilmesi için Adıyaman Üniversitesi Sosyal ve Beşeri Bilimler Etik Kurulundan etik kurul onayı alındı (Karar tarihi ve no: 30.12.2021-180). Bunun yanında çalışmanın yürütüldüğü kurum olarak Adıyaman Üniversitesi Sağlık Bilimleri Fakültesi Hemşirelik Bölümünden kurum izni alındı. Dahil edilme kriterlerini karşılayan öğrencilere araştırmanın amacı ve süreci açıklanarak, gönüllü olanlar çalışmaya dâhil edildi. Araştırmada yer alan katılımcılardan gönüllü bilgilendirilmiş onam formu kullanılarak yazılı onamları alındı.

Bulgular

Araştırmaya katılan hemşirelik öğrencilerinin yaş ortalamasının 20.72 ± 1.85 , %68.9'unun kadın, %55.1'inin gelir düzeyinin gidere eşit olduğu belirlendi. Öğrencilerin %31.1'i birinci sınıf, %18.1'i ikinci sınıf, %30.7'si üçüncü sınıf ve %20.1'i dördüncü sınıfta öğrenim görmekteydi. Çalışmaya katılan öğrenciler akademik başarı durumlarını; %9,1'i kötü, %69.3'ü orta ve %21.7'si iyi olarak bildirdi.

Araştırmada ÇBASDÖ toplam puan ortalaması 50.75 ± 17.75 olup; aile, arkadaş ve özel insan alt boyut puan ortalamaları sırasıyla; 19.54 ± 6.73 , 17.72 ± 7.38 ve 13.48 ± 8.19 olarak belirlendi.

HÖASÖ toplam puan ortalaması 59.59 ± 24.35 olarak saptandı. Mesleki bilgi ve beceri eksiliğinden kaynaklanan stres alt boyutu puan ortalaması 6.02 ± 2.87 , hastaya bakım verirken yaşanan stres alt boyutu puan ortalaması 15.98 ± 7.19 , ödevlerden ve iş yükünden kaynaklanan stres alt boyutu puan ortalaması 10.27 ± 4.66 , öğretim elemanları ve hemşirelerden kaynaklanan stres alt boyutu puan ortalaması 12.58 ± 5.46 , ortamdan kaynaklanan stres alt boyutu puan ortalaması 6.36 ± 2.62 , akranlardan ve günlük yaşamdan kaynaklanan stres alt boyutu puan ortalaması 8.36 ± 3.75 olarak bulundu.

HÖSBDÖ toplam puan ortalaması 39.74 ± 9.77 olarak saptandı. İyimser kalma alt boyutu puan ortalaması 7.47 ± 2.81 , transfer alt boyutu puan ortalaması 6.77 ± 1.95 , sorun çözme alt boyutu puan ortalaması 11.22 ± 3.69 , kaçınma alt boyutu puan ortalaması 14.25 ± 4.39 'dur (Tablo 1).

Tablo 1. Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ), Hemşirelik Öğrencileri İçin Algılanan Stres Ölçeği (HÖASÖ), Hemşirelik Öğrencileri İçin Stresle Baş Etme Davranışları Ölçeği (HÖSBDÖ) Alt Boyut ve Toplam Puan Ortalamaları			
Alt Boyut ve Toplam Puan Ortalamaları		Ort±SS	Min-Maks
ÇBASDÖ	Aile	19.54 ± 6.73	4-28
	Arkadaş	17.72 ± 7.38	4-28
	Özel İnsan	13.48 ± 8.19	4-28
	Toplam	50.75 ± 17.75	12-84
HÖASÖ	Mesleki bilgi ve beceri eksikliğinden kaynaklanan stres	6.02 ± 2.87	0-12
	Hastaya bakım verirken yaşanan stres	15.98 ± 7.19	0-32
	Ödevlerden ve iş yükünden kaynaklanan stres	10.27 ± 4.66	0-20
	Öğretim elemanları ve hemşirelerden kaynaklanan stres	12.58 ± 5.46	0-24
	Ortamdan kaynaklanan stres	6.36 ± 2.62	0-12
	Akranlardan ve günlük yaşamdan kaynaklanan stres	8.36 ± 3.75	0-16
	Toplam	59.59 ± 24.35	0-116
HÖSBDÖ	İyimser kalma	7.47 ± 2.81	0-16
	Transfer	6.77 ± 1.95	0-12
	Sorun çözme	11.22 ± 3.69	0-24
	Kaçınma	14.25 ± 4.39	0-24
	Toplam	39.74 ± 9.77	0-76

Öğrencilerin algılanan stres düzeyi ile algılanan sosyal destek düzeyi ve stresle baş etme davranışları arasındaki korelasyon bulguları Tablo 2’de sunulmuştur. Tablo incelendiğinde; HÖASÖ ile ÇBASDÖ arasında negatif yönde bir ilişki olduğu ($r=-.047$), ancak bu ilişkinin istatistiksel olarak anlamlı olmadığı tespit edildi ($p>0.05$). HÖASÖ ile HÖSBDÖ toplam puanları arasında pozitif yönde $r=.233$ düzeyinde ve istatistiksel olarak anlamlı bir ilişki tespit edildi ($p=0.000$).

Tablo 2. Algılanan Stres Düzeyi ile Algılanan Sosyal Destek Düzeyi ve Stresle Baş Etme Davranışları Arasındaki İlişki				
	ÇBASDÖ		HÖSBDÖ	
	r	p	r	p
HÖASÖ	-.047	0.454	.233	0.000
r: Korelasyon Katsayısı; p: anlamlılık düzeyi				

Öğrencilerin algılanan sosyal destek düzeyi ve alt boyutları ile stresle baş etme davranışları ve alt boyutları arasındaki korelasyon bulguları Tablo 3’te sunulmuştur. Tabloya göre; HÖSBDÖ iyimser kalma alt boyutu ile ÇBASDÖ özel insan alt boyutu arasında anlamlı bir ilişki bulunurken, HÖSBDÖ transfer alt boyutu ile ÇBASDÖ tüm alt boyutları arasında anlamlı bir ilişki saptandı ($p<0.05$). HÖSBDÖ sorun çözme alt boyutu ile ÇBASDÖ ve tüm alt boyutları arasında anlamlı bir ilişki bulunmazken ($p>0.05$), HÖSBDÖ kaçınma alt boyutu ile ÇBASDÖ tüm alt boyutlar arasında anlamlı bir ilişki bulundu ($p<0.05$). ÇBASDÖ ile HÖSBDÖ toplam puanları arasında pozitif yönde $r=.207$ düzeyinde ve istatistiksel olarak anlamlı bir ilişki tespit edildi ($p=0.001$).

Tablo 3. Algılanan Sosyal Destek Düzeyi ile Stresle Baş Etme Davranışları Arasındaki İlişki								
	Aile		Arkadaş		Özel İnsan		ÇBASDÖ	
	r	p	r	p	r	p	r	p
İyimser kalma	.023	0.720	.032	0.610	.136	0.031	.084	0.180
Transfer	..212	0.001	.172	0.006	.146	0.020	.219	0.000
Sorun çözme	-.016	0.804	-.011	0.859	.099	0.114	.035	0.576
Kaçınma	.330	0.000	.160	0.011	.192	0.002	.280	0.000
HÖSBDÖ	.191	0.002	.111	0.077	.192	0.002	.207	0.001
r: Korelasyon Katsayısı; p: anlamlılık düzeyi								

Tartışma

Hemşirelik öğrencileri öğrenim hayatları boyunca pek çok stresle karşılaşmaktadır. Süreç boyunca karşılaştıkları bu stresle aktif baş etme yöntemlerinin kullanılması fiziksel ve ruhsal sağlığın sürdürülebilmesi adına önemlidir (8). Hemşirelik öğrencilerinin algıladıkları sosyal destek düzeyleri ile algılanan stres ve stresle baş etme davranışları arasındaki ilişkinin belirlenmesi amacıyla gerçekleştirilen bu araştırmanın sonucunda öğrencilerin algılanan sosyal destek düzeyi ile algılanan stres düzeyi arasında herhangi bir ilişki olmadığı ancak algılanan sosyal destek düzeyi ile stresle baş etme davranışları arasında anlamlı bir ilişki olduğu bulundu.

Araştırmamızda HÖASÖ puan ortalaması 59.59 ± 24.35 'tir. Hemşirelik öğrencilerinin algıladıkları stres düzeyini değerlendiren farklı çalışmalarda belirlenen puanlar farklılık göstermektedir. Ergin ve Çevik'in (2017) çalışmasında bu değer 49.07 ± 22.11 olarak ifade edilirken, Bozyılan ve Güngörmüş'ün (2021) çalışmasında 57.06 ± 23.53 şeklinde bulunmuştur (12,13). Bu farklılıklar bazı demografik değişkenlerle ilişkili olabileceği gibi eğitim öğretim deneyimlerindeki farklılıklardan da kaynaklanabilir.

Hemşirelik öğrencilerinin karşılaştıkları stresli durumlarda etkin baş etme stratejilerini kullanmaları önemlidir (8). Ürdün'de yapılan iki farklı çalışmada hemşirelik öğrencilerinin stresle baş etme yöntemi olarak problemi çözme, iyimser kalma şeklindeki aktif baş etme stratejilerini kullandıkları belirlenmiştir (14,15). Ülkemizde yapılan bir çalışmada ise hemşirelik öğrencilerinin stresle baş etmede daha sık sorun çözme davranışını kullandıkları ifade edilmiştir (12). Araştırma bulgularımızda HÖSBDÖ alt grupları incelendiğinde en sık kullanılan baş etme stratejisinin kaçınma olduğu görülmektedir. Kaçınma stratejisinin stresle baş etmede kullanılacak problem odaklı bir yöntem olmadığı bilinmektedir. Ancak öğrencilerde algılanan stres düzeyinin yüksekliği etkin bir baş etme stratejisinin kullanımını sınırlandırabilir. Zira yapılan çalışmalarda da hemşirelik öğrencilerinin algıladıkları stres düzeyi arttıkça kaçınma stratejisini daha sık kullandıkları bildirmiştir (16,17). Araştırmamızda da öğrencilerin stres düzeyinin literatüre kıyasla yüksek olması kaçınma yönteminin daha sık kullanımıyla ilişkilendirilebilir.

Araştırmamızda öğrencilerin algılanan sosyal destek düzeyleri ile stresle baş etme davranışları arasında anlamlı ilişki olduğu saptandı. Ancak bu ilişkinin öğrencilerin algıladıkları sosyal destek düzeyleri ile iyimser kalma ya da sorun çözme stratejilerinin kullanımından ziyade transfer ve kaçınma stratejilerinin kullanımıyla ilişkili olması dikkat çekicidir. Yani algılanan sosyal destek arttıkça öğrencilerin baş etme davranışlarında artış olsa

da etkin stratejilerin kullanılmasında yetersizlikler olduğu görülmektedir. Üstündağ, Bostancı ve Aydoğan (2019) çalışmasında da araştırma bulgularımıza benzer şekilde algılanan sosyal destek düzeyi ile stresle baş etme davranışları arasında anlamlı bir ilişki olduğu tespit edilmiştir. Aynı çalışmada aile ve arkadaş desteği düzeyi ile stresle başa çıkmada aktif/etkili tarz olan kendine güvenli yaklaşım, iyimser yaklaşım düzeyi arasında pozitif yönde ve yüksek düzeyde ilişki olduğu ifade edilmiştir (8). Aydın, Kahraman ve Hiçdurmaz (2017) hemşirelik öğrencileriyle yaptıkları çalışmada öğrencilerin algılanan sosyal destek düzeyi arttıkça psikolojik iyilik durumlarının da arttığı bulunmuştur (18). Bu sonuç da algılanan sosyal desteğin psikolojik iyi oluşluk üzerindeki etkisinin stresle baş etme davranışını dolaylı olarak etkileyebileceğini düşündürmektedir.

Sonuç

Araştırmanın sonucunda öğrencilerin algıladıkları stres düzeyleri ile stresle baş etme davranışları arasında pozitif yönlü orta düzeyde anlamlı bir ilişki olduğu bulundu. Algılanan sosyal destek düzeyi ile algılanan stres düzeyleri arasında herhangi bir ilişki bulunmazken; algılanan sosyal destek düzeyi ile stresle baş etme davranışları arasında pozitif yönlü orta düzeyde anlamlı bir ilişki olduğu bulundu.

Hemşirelik öğrencilerinin sosyal destek algılarının geliştirilmesinin, deneyimledikleri stresle etkili baş etmeleri konusunda katkı sağlayacağı düşünülmektedir. Ancak yine de algılanan sosyal desteğin artmasının etkin baş etme stratejisiyle ilişkili olmayabileceği dikkate alınmalıdır. Hemşirelik öğrencileri algıladıkları yüksek düzeydeki stresle etkin baş etme stratejilerini kullanabilmeleri adına desteklenmelidir.

Bildirimler

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An Investigation of Diabetes Mellitus and Vitamin D Deficiency in Patients Presented to Internal Medicine Outpatient Clinic

Dahiliye Polikliniğine Başvuran Hastalarda Diyabetes Mellitüs ve Vitamin D Eksikliğinin Değerlendirilmesi

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ABSTRACT

Introduction: Vitamin D deficiency plays a role also in the occurrence of autoimmune diseases, including heart disease, cancer, inflammatory bowel diseases, diabetes, and rheumatological diseases. In addition, vitamin B12 deficiency, one of the autoimmune diseases, can also be seen in cases of Vitamin D deficiency. Furthermore, Vitamin D is also associated with insulin secretion and increased insulin sensitivity in target cells, and relevant studies reported Vitamin D deficiency at the initial stage of diabetes mellitus (DM). Accordingly, the present study aimed to investigate the relationship between Vitamin D, DM, Vitamin B12, and ferritin in patients presented to the internal medicine outpatient clinic.

Materials and Methods: The data from adults aged 18 years and over, who presented to the Internal Medicine Outpatient Clinic of the Mersin City Training and Research Hospital between 01 June 2021 and 31 December 2021 were retrospectively investigated.

Results: 476 (95.2%) patients had vitamin D levels below 30 ng/ml, 20 (4.0%) had vitamin B12 levels below 200 pg/ml, and 319 (63.8%) patients had ferritin levels below 20 ng/ml. There was a significant decrease in ferritin in female gender ($p<0.01$), advanced age patients with DM ($p<0.01$), and patients without DM ($p=0.01$).

Conclusion: Vitamin D deficiency plays an important role in the occurrence of many diseases, including DM and Vitamin B12 deficiency. Ferritin, an inflammatory marker, has been shown to be associated with a number of diseases. As a result of the present study, there was a significant decrease in ferritin in advanced age patients with DM, female sex, and patients without DM, and a higher rate of Vitamin D deficiency. Further long-terms studies including post-treatment follow-up periods are required to diagnose the above diseases in an earlier period, prevent complications, and prevent diseases by means of vitamin deficiency treatments.

Keywords: Vitamin D deficiency; Diabetes Mellitus; Ferritin; Vitamin B12

ÖZ

Giriş: D vitamini (vit-D) eksikliği kalp hastalıkları, kanser, inflamatuvar barsak hastalıkları, diyabet, romatolojik hastalıklar gibi otoimmün hastalıkların gelişiminde de rol aldığı tespit edilmiştir. Ayrıca ottoimmün hastalıklardan olan vitamin B12 (vit-B12) eksikliği, vit-D eksikliğinde görülebilmektedir. Bunların yanı sıra vit-D insülin sekresyonunun da ve insülinin hedef hücrelerde duyarlılığının artırılmasında da önemli bir role sahip olup, yapılan çalışmalarda diyabetes mellitüsün (DM) başlangıç aşamasında vit-D eksikliği gözlenmiştir. Bu nedenle bu çalışmamızda dahiliye polikliniğine başvuran hastalarda vit-D, DM, vit-B12 ve ferritin arasındaki ilişkiyi değerlendirmeyi hedefledik.

Materyal ve Metod: 18 yaş ve üzeri erişkin, 01 Haziran 2021 ile 31 Aralık 2021 tarihleri arasında Mersin Şehir Eğitim ve Araştırma Hastanesi dahiliye polikliniğine başvuran hastaların verileri retrospektif olarak değerlendirildi.

Bulgular: Hastaların 476 (%95.2)'sinde vitamin D seviyesi 30 ng/ml altında, 20 (%4.0) B12 vitamin seviyesi 200 pg/ml altında, 319 (63.8) ferritin seviyesi 20 ng/ml altında tespit edildi. Kadın cinsiyet ($p<0.01$), ileri yaş ($p<0.01$) DM olanlarda; DM olmayan grupta ferritin düşüklüğü ($p=0.01$) anlamlı tespit edilmiştir.

Sonuç: Vit-D eksikliği DM ve vit-B12 eksikliği gibi bir çok hastalığın oluşumu sürecinde önemli bir rol oynamaktadır. İnflamatuvar bir marker olan ferritinde bir çok hastalık ile ilişkisi gösterilmiştir. Biz bu çalışmamızda DM ile ileri yaş ve kadın cinsiyet, DM olmayanlarda ferritin düşüklüğü anlamlı olup, vit-D eksikliğini yüksek oranda tespit ettik. Bu hastalıkların erken dönemde tespit edilebilmesi, komplikasyonların önlenmesi veya vitamin eksikliği tedavileri ile hastalıkların önlenmesi için daha uzun dönem, tedavi sonrası takipleri de içeren çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Vitamin D eksikliği; Diyabetes Mellitüs; Ferritin; Vitamin B12

Introduction

Vitamin D is a fat-soluble vitamin produced on the skin exposed to sun rays. It has a key role in the calcium and phosphorus metabolism in our body. (1) Furthermore, the fact that there are Vitamin D receptors on immune system cells, suggests its involvement in the regulation of the immune system. Accordingly, involvement of Vitamin D deficiency has been reported in the occurrence of autoimmune diseases, including heart diseases, cancer, inflammatory bowel diseases, diabetes, and rheumatological diseases.(2,3) In addition, vitamin B12 deficiency, one of the autoimmune diseases, can also be seen in cases of Vitamin D deficiency.(4) Furthermore, Vitamin D is also associated with insulin secretion and increased insulin sensitivity in target cells, and relevant studies reported Vitamin D deficiency at the initial stage of diabetes mellitus (DM).(5,6) Individuals with vitamin D deficiency exhibited a 48 percent reduction in insulin secretion compared to individuals with optimal levels of vitamin D. Thus, indicating that vitamin D stimulates the pancreas to produce insulin.(7)A short-term experimental study suggested that vitamin D supplementation leads to an improvement in pancreatic beta cell functioning and marginally lowers patients' HbA_{1c}.(8)Recent studies on the early diagnosis of DM and its complications suggested that the increase in serum ferritin levels might serve as an inflammatory marker.(9)

Accordingly, the present study aimed to investigate the relationship between Vitamin D, DM, Vitamin B12, and ferritin in patients presented to the internal medicine outpatient clinic.

Materials and Methods

The data from adults aged 18 years and over, who presented to the Internal Medicine Outpatient Clinic of the Mersin City Training and Research Hospital between 01 June 2021 and 31 December 2021 were retrospectively investigated. The patients were screened for age, gender, and comorbid diseases (diabetes mellitus, hypothyroidism).

Vitamin D, Vitamin B12, and Ferritin levels were analyzed (Siemens Healthcare Diagnostics Inc, Laboratory Diagnostics, Advia Centaur XPT, Erlangen, Germany, produced in Ireland). Individuals with vitamin D levels of >30 ng/ml were considered normal, where individuals with vitamin D levels of <30 ng/ml were considered Vitamin D deficient (8); individuals with vitamin B12 levels of <200 pg/ml were considered Vitamin B12 deficient (9), individuals with ferritin levels of <20 ng/ml were considered ferritin deficient, where

individuals with ferritin levels of >220 ng/ml were considered ferritin high. Patients aged over 18 years, who presented to the internal medicine outpatient clinic between June and December 2021 were included in the study. Patients with chronic diseases, including bone diseases and metabolic diseases, and patients, who received Vitamin D treatment in the last 3 months, were not included in the study.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) Ver. 21.0 (IBM Corp., Armonk, NY, USA) software. The hypothesis of the normal distribution of the variables was tested by the Kolmogorov-Smirnov test. Numerical variables were expressed in median \pm SD (standard deviation), where categorical variables were expressed in numbers and percentages. The t test and Mann-Whitney U were used in comparisons between the two groups by numerical variables; where Chi-squared or Fisher exact Chi-squared tests were used for the categorical variables. Required permission for the conduct of the study was obtained from the Non-interventional Clinical Ethics Committee of the Mersin University. (23.02.2022-150)

Results

The mean age of the 500 patients presented to the internal medicine outpatient clinic was 48.4 ± 15.4 , where 326 (65.2%) of the patients were female. Diabetes mellitus was the most common comorbid disease in 119 (23.8%) patients. The demographic data of the patients are shown in Table 1.

Table 1. Demographic data		
Features	n: 500	
	n	(%)
Age mean\pmSD	48.4 \pm 15.4	
Gender		
Male	174	(%34.8)
Female	326	(%65.2)
Comorbidity		
Diabetes Mellitus	119	(%23.8)
Hypothyroidism	31	(%6.2)
Both of them	5	(%1.0)
No	345	(%69.0)
Vitamin D ng/ml median (min-max)	13 (4-87)	
Vitamin B12 pg/ml median (min-max)	350 (125-954)	
Ferritin ng/ml median (min-max)	33 (1-639)	

476 (95.2%) patients had vitamin D levels below 30 ng/ml, 20 (4.0%) had vitamin B12 levels below 200 pg/ml, 319 (63.8%) patients had ferritin levels below 20 ng/ml, and 0 (0%)

patients had ferritin levels above 220 ng/ml. The relationship between vitamin D and age, gender, ferritin, vitamin B12, and diabetes mellitus is provided in Table 2.

Table 2. The relationship between vitamin D and age, gender, ferritin, vitamin B12, diabetes mellitus					
Features	Vitamin D<30ng/ml n:476		Vitamin D>30ng/ml n:24		P
Age mean±SD	48.4±15.5		48.6±14.1		0.9
	n	%	n	%	
Female	307	(%61.4)	19	(%3.8)	0.1
Ferritin<20 ng/ml	303	(%60.6)	16	(%3.2)	0.8
Vitamin B12<200 pg/ml	20	(%4.0)	0	(%0)	0.6
Diabetes Mellitus	115	(%23.0)	4	(%0.8)	0.4

There was no significant relationship between vitamin D levels and age, gender, ferritin, vitamin B12, and having diabetes mellitus disease. The relationship between Diabetes Mellitus and age, gender, vitamin D, ferritin, and vitamin B12 is provided in Table 3

Table 3. The relationship between Diabetes Mellitus and age, gender, vitamin D, ferritin, and vitamin B12					
Features	Diabetes Mellitus (+) n:119		Diabetes Mellitus (-) n: 381		P
Age mean±SD	57.9±11.7		45.4±15.4		<0.01
	n	%	n	%	
Female	65	(%13.0)	261	(%52.2)	<0.01
Vitamin D<30 ng/ml	115	(%23.0)	361	(%72.2)	0.4
Ferritin<20 ng/ml	65	(%13.0)	254	(%50.8)	0.01
Vitamin B12<200 pg/ml	4	(%0.8)	16	(%3.2)	0.8

It was significant in female gender ($p<0.01$) and advanced age patients with Diabetes Mellitus ($p<0.01$). In addition, there was significant decrease in ferritin ($p=0.01$) in the non-Diabetic Mellitus group.

Discussion

65.2% of the patients, who participated in the study, were female, where the mean age was 48.4 ± 15.4 . In a 2004 study by Akman et al. , 77.7% of the patients presented to the general internal medicine outpatient clinic were female, with a mean age of 50 ± 14.20 , where Zülfinaz et al. reported in 2020 that 73.9% of their subjects were female with a mean age of 41.76 ± 15.27 (12,13). The data in our study are indicative of the fact that the rate of women's presentation to

hospital was higher compared to men consistent with the relevant literature.

The prevalence of DM across the world is 7.7%, where according to the TURDEP-1 study the same rate is 7.2% (14,15) in Turkey, and the most common comorbid disease in the present study was DM (23.8%). The present study was designed as a cross-sectional study, and therefore, our rates were high since the assessment was based on the patients, who presented to the outpatient clinic.

In 2020, a meta-analysis by Mahmood et al. reported that 64.6% of healthy people had Vitamin D levels of <30 ng/mL below (16). Pakistani studies reported the vitamin D deficiency ranged from 95.2% to 84.3%, and female individuals account for the 86.4-62.3% (17,18). In the present study, 95.2% of the patients had vitamin D deficiency, where 61.7% were women. A literature review indicated that most of the studies on Vitamin D were conducted in Pakistan. There were higher rates of lower Vitamin D levels associated with women's inadequate exposure to sunlight due to the attire, which covered the entire body, as required by the social norms, lower socioeconomic levels, and sedentary life (19). Given to the similarity of the social norms between Turkey and Pakistan, consistent with the relevant literature the Vitamin D deficiency was more prevalent in women in the present study due to the inadequate exposure to sunlight. It is also important to remember the effect of lower socioeconomic levels and sedentary life on Vitamin D deficiency.

In a study by Jumaa and colleagues, it was revealed that the levels of vitamin D were significantly lower in patients with DMT2 as compared to non-diabetics(20) Sacerdote et al. reviewed the literature extensively to find evidence indicating a correlation between vitamin D deficiency and DMT2. The study reported that current evidence suggests that there is an association between DMT2 and insulin disorders with vitamin D status; however, further studies are warranted(21).

It was reported that there was a relationship between inflammatory markers and DM (22). Besides, certain studies suggested a positive relationship between ferritin, an inflammatory marker, and DM (23). In the present study, there were significantly lower ferritin levels in the non-DM group. A 2021 study in Turkey reported the incidence of iron deficiency anemia as 20.3%, which was considered high (24). In the present study, due to the fact that anemia incidence in Turkey is high, the ferritin decreased to normal levels even it was high, there was no relationship between low ferritin in non-DM individuals.

Neal ES et al. established a female rat model of dietary B₁₂ deficiency and identified that four weeks of dietary B₁₂ deficiency, promoted glucose intolerance and delayed peak plasma insulin levels following a glucose load, decreased anaplerosis and increased ketogenesis in the liver, depleted hepatic stores of other B vitamins involved in glucose homeostasis, mitochondrial function and one-carbon metabolism and altered liver one-carbon metabolism, leading to changes in methylation capacity and amino acid homeostasis (25).

The limitations of the present study include the fact that it was designed as a cross-sectional study, which included patients, who presented to the outpatient clinic, within a certain time interval, that there was no data with respect to exposure to sunlight, no demographic data, including socioeconomic level, no control group, and lack of long-term post-treatment follow-up. The high number of patients, simultaneous examination of certain parameters, including Vitamin D, DM, Vitamin B12, and ferritin constitute the powerful aspects of the present study.

Conclusion and Recommendations

Vitamin D deficiency plays an important role in the occurrence of many diseases, including DM and Vitamin B12 deficiency. Ferritin, an inflammatory marker, has been shown to be associated with a number of diseases. In the present study, there was a significant decrease in ferritin in advanced age patients with DM, female sex, and patients without DM, and a higher rate of Vitamin D deficiency. Further long-term studies including post-treatment follow-up periods are required to diagnose the above diseases in an earlier period, prevent complications, and prevent diseases by means of vitamin deficiency treatments.

Conflict of interest:

The authors declared no conflict of interest

Support Resources

No financial support was received for the study

Ethical Declaration

Required permission for the conduct of the study was obtained from the Non-interventional Clinical Ethics Committee of the Mersin University. (23.02.2022-150)

Authorship Contributions

Concept: DG, SME Design: DG, SME, Supervising: DG, SME, Financing and equipment: DG, SME, Data collection and entry: DG, SME, Analysis and interpretation: DG, SME, Literature search: DG, SME, Writing: DG, SME, Critical review: DG, SME

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Evaluation of acute stress disorder after pregnancy loss

Gebelik Kaybı Sonrası Akut Stres Bozukluğunun Değerlendirilmesi

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ABSTRACT

Aim: Our study aimed to assess and prevent acute stress disorder in women with pregnancy loss.

Materials And Methods: Pregnant women presenting to the Department of Obstetrics and Gynecology at level 2 centers between March 2019 and March 2021 were included in the study. Women with pregnancy loss of fewer than 21 weeks were assigned to the "pregnancy loss group" and women with healthy pregnancies were assigned to the "control group." After the questionnaire, patients were asked to complete the post-traumatic stress disorder (PTSD) scale. In the study, 91 (35%) were in the pregnancy loss group and 156 (65%) were in the control group. Statistically, $p < 0.05$ was considered significant.

Results: The mean age of the patients with pregnancy loss was 27.52 ± 5.60 years, whereas the pregnant women in the control group were 26.43 ± 5.44 years old. The mean age of the two groups was similar ($p = 0.656$). The PTSD score of the participants was 33.10 ± 9.3 (min=15, max=49). The mean PTSD score of the cases who suffered pregnancy loss was 36.23 ± 9.49 and 31.12 ± 7.34 in the control group. The PTSD score of the group with pregnancy loss was significantly higher than that of the control group ($p = 0.003$).

Conclusion: symptoms of acute stress disorder were found to be more common in women who experienced pregnancy loss. Couples who have suffered pregnancy loss should receive social and psychological support. Psychological support and counseling are very important for the couple's psyche. In this way, the woman's disorder can be prevented from developing into post-traumatic stress disorder.

Keywords: Acute Stress; Pregnancy Loss; Miscarriage

ÖZ

Amaç: Çalışmamızın amacı gebelik kaybı olan kadınlarda akut stres bozukluğunu değerlendirmek ve önlemektir.

Gereç ve Yöntem: Mart 2019-Mart 2021 tarihleri arasında 2. basamak merkezlerde Kadın Hastalıkları ve Doğum Kliniğine başvuran gebeler çalışmaya dahil edildi. 21 haftadan daha az gebelik kaybı olan kadınlar "gebelik kaybı grubu"na, sağlıklı gebelikleri olan kadınlar ise "kontrol grubu"na ayrıldı. Anketin ardından hastalardan travma sonrası stres bozukluğu (TSSB) ölçeğini doldurmaları istendi. Çalışmada gebelik kaybı grubunda 91 (%35), kontrol grubunda 156 (%65) hasta yer aldı. İstatistiksel olarak, $p < 0,05$ anlamlı kabul edildi.

Bulgular: Gebelik kaybı olan hastaların ortalama yaşı 27.52 ± 5.60 iken kontrol grubundaki gebelerin yaşı 26.43 ± 5.44 idi. İki grubun yaş ortalaması benzerdi ($p = 0.656$). Katılımcıların TSSB puanı 33.10 ± 9.3 'tür (min=15, max=49). Gebelik kaybı yaşayan olguların ortalama TSSB puanı 36.23 ± 9.49 ve kontrol grubunda 31.12 ± 7.34 idi. Gebelik kaybı olan grubun TSSB puanı kontrol grubuna göre anlamlı olarak yüksekti ($p = 0.003$).

Sonuç: Gebelik kaybı yaşayan kadınlarda akut stres bozukluğu belirtilerinin daha sık olduğu saptanmıştır. Gebelik kaybı yaşayan çiftler sosyal ve psikolojik destek almalıdır. Psikolojik destek ve danışmanlık çiftlerin psikolojisi için çok önemlidir. Bu şekilde kadındaki rahatsızlığın travma sonrası stres bozukluğuna dönüşmesi engellenebilir.

Anahtar Kelimeler: Akut Stres; Gebelik Kaybı; Düşük

Introduction

During pregnancy, women experience psychological, social, and physical changes, and pregnant women try to adapt to this process. Termination of a pregnancy before 20 weeks gestation is called miscarriage and is the most common cause of pregnancy loss(1). Termination of a pregnancy before 20 weeks gestation is called a miscarriage and is the most common cause of pregnancy loss(2). The rate of pregnancy loss is 14-29% in women aged 25-30 years and 75% in women aged 45-48 years. Pregnancies that end in the first 12 weeks account for 10-20% of all pregnancies(1-3). Psychiatric disorders occur in 45%-50% of women after spontaneous abortion(1, 4). While the incidence of major depression in the general population is 3-10%, this rate has been found to increase to 12-50% in women who have had an abortion(5). It has been found that 25-40% of women suffer from anxiety disorders after early abortion and 35% develop post-traumatic stress disorder (PTSD)(6). The aim of this study was to assess and prevent acute stress disorder (ASD) after abortion in women.

Material And Methods

Pregnant women presenting to the Department of Gynecology and Obstetrics at level 2 centers between March 2019 and March 2021 were included in this study. Patients with pregnancy loss (< 21 weeks) after enrollment in the study formed the "pregnancy loss group" and those with a healthy pregnancy formed the "control group." Those who volunteered to participate in the study were informed before the study, and those who gave consent were enrolled in the study. The questionnaire prepared by the researchers was administered to the participants during face-to-face interviews. The first part of the questionnaire asked for the participants' sociodemographic data, and the second part asked for their obstetric history. Patients were also asked to complete the post-traumatic stress disorder (PTSD) scale. Of the 247 patients who completed the questionnaire, 91 (35%) were included in the pregnancy loss group and 156 (65%) in the control group. Women who had experienced pregnancy loss were included in study 2-28 days after pregnancy loss. In the post-traumatic stress disorder (PTSD) scale, symptoms in the questions are graded between 1 and 5 depending on the severity. The literature states that the 50-point PTSD score is the cut-off value for ASD. Statistical analysis was performed using the SPSS 25.0 program. For data analysis, mean, frequency, and standard deviation were calculated, and to show the difference between the two groups, parametric

values were evaluated with Student's t-test and nonparametric values with Mann Whitney U-test. Statistically, $p < 0.05$ was considered significant. Ethics committee approval was obtained for this study in accordance with the Declaration of Helsinki.

Results

The mean age of participants was 26.82 ± 5.26 (min=17, max=48). The mean age of patients who lost their pregnancy was 27.52 ± 5.60 years, and that of patients whose pregnancies continued was 26.43 ± 5.44 years. The mean age of the two groups was similar ($p=0.754$). The economic income level ($p=0.359$), occupation ($p=0.224$), place of residence ($p=0.367$), and education level ($p=0.591$) of the "pregnancy loss group" and the "control group" had similar characteristics. The sociodemographic data of the groups can be found in the table.(Table 1).

Table 1. Sociodemographic data of the participants

Variables	Total		Group experiencing pregnancy loss		Control Group		p
	n	(%)	n	(%)	n	(%)	
Income	<5000	157 (61.1)	62 (68.2)	97 (62.2)	0.359		
	5000-10000	43 (17.4)	14 (15.4)	28 (17.8)			
	10000-15000	17 (7)	6 (6.5)	10 (6.5)			
	>15000	30 (14)	9 (9.9)	21 (13.5)			
Education level	Primary	148 (59.9)	57 (62.6)	93 (59.6)	0.09		
	secondary	59 (23.8)	19 (20.8)	33 (21.1)			
	High school	40 (16.3)	15 (16.6)	30 (19.3)			
Residential area	Rural	149 (60.3)	58 (63.7)	94 (60.2)	0.325		
	Urban	98 (39.7)	33 (36.3)	62 (39.8)			

It was found that 15 of the participants (6%) had gestational hypertension, 9 (3.6%) had gestational diabetes mellitus, and 223 (91.4%) had no disease. It was found that 10 (10.9%) of the patients in the pregnancy loss group had gestational hypertension, 3 (3.2%) had gestational diabetes mellitus, and 78 (85.9%) had no disease. In the control group, 7 (4.4%) had gestational hypertension, 5 (3.2%) had gestational diabetes mellitus, and 144 (92.4%) had no diagnosed disease. The disease history of the two groups was similar ($p=0.05$).

It was found that women in the pregnancy loss group experienced an average of 9.24 ± 4.78 weeks of pregnancy, while the average week of pregnancy in the control group was 9.11 ± 5.18 . The mean age at marriage among women was 21.14 ± 4.20 years (min=16, max=35). The mean age at marriage was 19.48 ± 3.20 years in the pregnancy loss group and 20.11 ± 3.42 years in the control group. The mean age at marriage of the two groups was similar ($p=0.325$). The mean total number of pregnancies in the cases was found to be 2.53 ± 1.42 . The mean number of pregnancies in the pregnancy loss group was 3.69 ± 2.35 , while in the control group it was 2.78 ± 1.90 . The mean total number of pregnancies was significantly higher in the pregnancy loss group than in the control group ($p=0.003$).

The mean PTSD score of the participants was 33.10 ± 9.3 (min=15, max=49). The mean PTSD score of the cases in the pregnancy loss group was 36.23 ± 9.49 and 31.12 ± 7.34 in the control group. It was found that the PTSD score of the group that suffered pregnancy loss was significantly higher than that of the control group ($p=0.002$). It was found that 77 (84.6%) of the 91 cases who had suffered pregnancy loss had a score below the scale cut-off score (< 50) and 14 (15.4%) had a score above the scale cut-off score (≥ 50). It was found that all members of the control group ($n=156$) scored below the scale cut-off value. It was found that the cases who had pregnancy loss were significantly above the cut-off value compared to the control group cases ($p=0.0001$).

In the pregnancy loss group, it was found that all 14 patients whose PTSD scores were above the cut-off value had three or more previous miscarriages or stillbirths. Of the other cases in the pregnancy loss group, 19 (24.6%) had no history of miscarriage or stillbirth, 18 (23.4%) had one, 24 (31.2%) had two, and 16 (20.8%) had three or more. He reported having a history of multiple miscarriages or stillbirths. There was a significant association between a previous miscarriage or stillbirth and a score above the PTSD cut-off value ($p=0.001$).

Cases in the pregnancy loss group that were above or below the PTSD cut-off had similar values: educational level ($p=0.513$), place of residence ($p=0.601$), income level ($p=0.177$), medical history (0.119), and occupational characteristics ($p=0.257$).

Discussion

In our study, participants were assumed to be diagnosed with ASD based on the scores they received for PTSD. In the study by Kersting et al, 50 points or more for PTSD was accepted as the cutoff for ASD(7). Previous studies have shown that 57-83% of cases with ASD later develop PTSD and that ASD is a risk factor for PTSD(6). In our study, it was found that the average PTSD score of women who had experienced pregnancy loss was significantly higher than that of healthy controls. In addition, our study found that 12% of women met criteria for ASB 2-28 days after pregnancy loss. In a similar study by Slade et al, 1370 women were studied after pregnancy loss, and they reported that the rate of meeting PTSD criteria was 25% after one month and 4% after four months(8). However, they attributed the decrease in PTSD rate to the fact that there were patients who could not complete the study and stated that the PTSD rate should be between 4-10%(8). Another study found that the rate of ASB was 10% one week after pregnancy loss and 1% one month later(9). Another study found that 15% of women met criteria for ASB at week 3 after early pregnancy loss. Our study contains similar findings to other studies(10). The introduction of psychological and social support mechanisms for those who have experienced pregnancy loss is important for the health of these individuals(11).

In our study, the age, educational level, place of residence, and socioeconomic status of the participants were similar in both groups. It was found that there was no significant difference between the mean PTSD scores in the patient group by age, education level, place of residence, and socioeconomic status. In reviewing the literature, many studies have shown that there is no association between age, marital status, social class, and psychiatric morbidity after pregnancy loss. Our study is consistent with other studies.

In our study, it was found that 14 patients who met the criteria for ASD and scored above the cut-off on the PTSD scale had three or more previous miscarriages. A significant association was found between the miscarriage or stillbirth in the participants' history and the mean score they achieved on the PTSD scale. Examining data from two population-based cross-sectional studies, Szepietowska et al. found that pregnancy loss and risk for psychiatric

disorders increased in their study(12). In addition, earlier pregnancy loss has been shown to negatively affect mood and psychological well-being, particularly in young women(13). In addition, they reported that depressive symptoms and depressive disorders were more common in women with a history of pregnancy loss(14). Considering this situation, these women need to seek psychiatric help after pregnancy loss and during their new pregnancies, both for their health and that of their baby(14).

In our study, the mean pregnancy loss was found to occur at 9.24 ± 4.78 weeks, and the mean PTSD score was significantly higher than that of healthy controls. Many studies of perinatal loss suggest that maternal attachment to the fetus is related to the duration of pregnancy, and it has been shown that there is an association between experiencing more grief after pregnancy loss and the duration of pregnancy. However, there are conflicting results in studies of pregnancy loss. Some studies show a positive association between gestational age and more intense and prolonged depressive symptoms, while some studies report more depression with early pregnancy loss (< 16 weeks)(15). On the other hand, no association was found between the duration of pregnancy and psychiatric morbidity after pregnancy loss.

There are numerous limitations to this study. First, the results are based on a small sample and self-report scales. Second, the PTSD scale was used because there is no scale for assessing ASD in Turkey. Third, only acute stress symptoms were investigated and other common psychopathologies were not examined in the study.

Conclusion

In our study, symptoms of acute stress disorder were found to increase after pregnancy loss. Families affected by pregnancy loss need to receive social and psychological support, which is very important for family well-being. Effective implementation of support mechanisms in cases of increased acute stress, such as pregnancy loss, will prevent individuals from developing post-traumatic stress disorder.

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Support Resources: No support resources

Ethical Declaration: Local ethics committee approval was obtained

Authorship Contributions

Concept: MB, KS, MS, Design: MB,NKB, EG,HK Supervising: MB, MS, Financing and equipment: KS, NKB,EG,HK, Data collection and entry: MB, KS,NKB,MS Analysis and interpretation: MS, EG,HK Literature search: MB,MS Writing: MB,KS,MS Critical review: KS, EG,HK

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