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Prevalence of Obesity in Rheumatologic Diseases and Its Relationship with Disease Activity

Romatolojik Hastalıklarda Obezite Prevalansı ve Hastalık Aktivitesi ile İlişkisi

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Abstract

Objective: Obesity is a common health problem and a complex disease that is defined as overly fat deposition in adipotic tissue. Studies conducted in our country (Turkey) have reported prevalence of obesity between 12 and 22 percent. Obesity has been shown to be associated with several rheumatic diseases and inflammation. The aim of this study is to assess the prevalence of obesity in rheumatologic diseases, and possible relationships between disease activity and accompanying obesity.

Method: A total of 1064 newly patients diagnosed with osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), fibromyalgia (FM), gout, Behçet's disease (BD), vasculitis, polymyalgia rheumatica (PMR), Sjögren's syndrome (SS), Familial Mediterranean fever, polymyositis, and systemic sclerosis (SSc) were included in the study. Age, gender, disease activity scores, and laboratory and clinical findings were all recorded.

Results: Obesity incidences were found to be 4.5% in RA, 3.2% in SLE, 1.6% in AS, 40.1% in OA, 11.2% in FM, 19.7% in gout, 1.8% in BD, 15% in vasculitis, 13.7% in PMR, 8% in SS, and 8.3% in SSc. Obesity and OA were revealed to have a statistically significant association. Disease activity scores were statistically significantly higher in obese FM patients compared to non-obese patients ($p<0.001$). We found a low rate of obesity in inflammatory rheumatic diseases, and we could not find a relationship between obesity and disease activity.

Öz

Amaç: Obezite adipoz dokuda fazla yağ depolanması olarak tanımlanan kompleks bir hastalık ve genel sağlık sorunudur. Ülkemizde yapılan araştırmalarda obezite prevelansı %12-22 olarak bildirilmiştir. Obezitenin çeşitli romatizmal hastalıklar ve enflamasyonla ilişkisi gösterilmiştir. Bu çalışmanın amacı romatolojik hastalıklarda obezite prevelansını ve hastalık aktivitesi ile ilişkisini araştırmaktır.

Yöntem: Çalışmaya yeni osteoartrit (OA), romatoid artrit (RA), ankilozan spondilit (AS), sistemik lupus eeritamatosus (SLE), fibromiyalji (FM), gut, Behçet hastalığı (BH), vaskülit, polimiyalji romatika (PMR), Sjögren sendromu (SS), Ailevi Akdeniz ateşi, polimiyozit ve sistemik skleroz (SSc) tanısı almış 1064 romatoloji hastası dahil edilmiştir. Hastaların yaş, cinsiyet, hastalık aktivite skorları, laboratuvar ve klinik bulguları kaydedilmiştir.

Bulgular: Obezite insidansları RA'da %4,5, SLE'de %3,2, AS'de %1,6, OA'de %40,1, FM'de %11,2, gutta %19,7, BH'de %1,8, vaskülitte %15, PMR'de %13,7, SS'de %8, ve SSc'de %8,3 olarak tespit edildi. Obezite ve OA arasında istatistiksel olarak kuvvetli ilişki saptandı. Hastalık aktivite skorları ise obez FM hastalarında obez olmayanlara göre istatistiksel olarak anlamlı düzeyde yüksek bulundu ($p<0,001$). Enflamatuvar romatizmal hastalıklarda obezite oranı düşük bulunurken, obezite ile hastalık aktivitesi arasında bir ilişki bulunmadı.

Sonuç: Yapılan son çalışmalarda obezite ve enflamasyon arasında ilişki gösterilse de bizim çalışmamızda ilginç olarak obezitenin OA ve FM hastalarıyla ilişkisi ortaya konmuş ancak enflamatuvar romatizmal

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Conclusion: While recent studies have associated obesity with inflammation, interestingly, in our study, obesity was found to be related to OA and FM, but was not associated with inflammatory rheumatic diseases. The relationship with OA may be explained by mechanical factors, but more comprehensive studies are needed on the relationship with obesity and inflammatory rheumatic diseases.

Keywords: Ankylosing spondylitis, disease activity, obesity, osteoarthritis, rheumatoid arthritis, rheumatological diseases

hastalıklar ile arasında ilişki gösterilememiştir. OA ve obezite arasındaki ilişki mekanik faktörlerle açıklanabilir, ancak FM ve diğer enflamatuvar romatizmal hastalıklar ve obezite ilişkisini açıklayabilmek için daha kapsamlı ileri çalışmalara ihtiyaç duyulmaktadır.

Anahtar kelimeler: Ankilozan spondilit, hastalık aktivitesi, obezite, osteoartrit, romatoid artrit, romatizmal hastalıklar

Introduction

Inflammatory rheumatic diseases (IRD) which comprise diverse conditions are chronic inflammatory diseases that usually affect the musculoskeletal system, and also cause systemic involvement (1). Obesity is described as a systemic disease with known metabolic and cardiovascular complications, but also has a role in the development of inflammatory diseases and reported to be highly prevalent in IRD (2).

The assumed mechanisms for the relationship between pain and obesity include mechanical, structural, metabolic and behavioral changes, and most likely the combination of factors is effective and can contribute differently depending on the disorder. Increased pressure on the joints from the increase of body weight, various metabolic alterations, and lifestyle changes due to restricted movements may facilitate diseases characterized by pain, and they may worsen the existing diseases of obese people. A positive correlation has been found between musculoskeletal system disorders and obesity grades (3). Studies in the literature have demonstrated that obesity is associated with low back and neck pain, fibromyalgia (FM), osteoarthritis (OA), some soft tissue diseases (carpal tunnel syndrome, plantar fasciitis), and connective tissue disease, such as gout and rheumatoid arthritis (RA) (4).

Obesity is also associated with inflammation (5). The link between obesity and inflammation was explained by the release of bioactive proteins named adipokines from white adipose tissue, which are potential mediators playing a role in the modulation of inflammatory response (6). Adipokines, and the leptin and adiponectin hormones, promote metabolic homeostasis and play a role in the release of inflammatory factors such as IL-12p40 and IL-16 (5,6).

The relationship between obesity and rheumatologic diseases has been defined in the literature, and studies have shown the relationship between obesity and OA, RA, systemic lupus erythematosus (SLE), gout, and FM (2). However, studies showing the relationship between obesity and ankylosing spondylitis (AS), polymyalgia rheumatica (PMR), Sjogren disease (SSc) and vasculitis, have been limited. Similarly, there have been no adequate studies on the relationship between obesity and systemic sclerosis (SS), Behçet's disease (BD) and Familial Mediterranean fever (FMF). Our study is the first to demonstrate the prevalence of obesity and its relation to disease activity within a wide range of rheumatologic diseases.

The aim of this study is to assess the prevalence of obesity in rheumatologic diseases, and possible relationships between disease activity and accompanying obesity.

Materials and Methods

Our study had cross-sectional design, our study group consisted of 1,064 patients of rheumatic disease with or without obesity. The study was carried out between 01.01.2015 and 31.12.2015 by scanning the patient files. These patients were diagnosed with rheumatologic diseases according to the relevant criteria. Body weight was measured in kilograms (kg) with a scale, and height was evaluated in meters (m). Body mass index (BMI) was computed by dividing the body weight (kg) by the square of the height (m^2). A BMI ≥30 kg/m^2 was considered to be obese. Exclusion criteria included psychosomatic/psychiatric disorders and the use of psychotropic drugs or alcohol/substance abuse, previously steroid use, thyroid dysfunction and infection, other autoimmune and/or chronic diseases affecting metabolism.

Age, gender, disease activity scores, positive antinuclear antibody (ANA), C-reactive protein (CRP) values, and erythrocyte sedimentation rate (ESR), and the persistence of arthritis, fatigue, and Reynaud's syndrome, were collected through patient recordings.

For disease activity scores, the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) for OA, the disease activity score-28 (DAS-28) for RA, the Bath AS disease activity index for AS, the fibromyalgia impact

questionnaire (FIQ) for FM, the SLE disease activity index for SLE, and the BD current activity form for BD were used (7-12).

The Local Ethics Committee (University of Health Sciences Turkey, Erzurum Regional Training and Research Hospital, Clinical Research Ethics Committee; confirmation number: 2015/8-56; date: 21.04.2015) approved the study, which was carried out in accordance with the principles of the Helsinki Declaration.

Statistical Analysis

We conducted the statistical analyses using SPSS for Windows, version 17.0. When not otherwise specified, results were stated as means ± standard deviation or median (minimum-maximum) according to their distribution. Normality tests were used. We used the independent-sample t-test or Mann-Whitney U test between two subject groups, and used the Spearman correlation test or Pearson correlation test, when applicable. Comparison between categorical variables was done with the chi-square test. The statistical significance level of the results was taken as $p<0.05$ at the 95% confidence interval.

Results

Nine of 197 RA patients (4.5%), 2 of 62 SLE patients (3.2%), 2 of 119 AS patients (1.6%), 67 of 167 OA patients (40.1%), 33 of 293 FM patients (11.2%), and 1 of 53 BD patients (1.8%) were diagnosed as obese. The age, gender, laboratory findings, and disease activity scores of obese and non-obese patients are given in Table 1.

Disease activity scores were statistically significantly higher in obese FM patients compared to non-obese patients ($p<0.001$). The mean age was higher in obese FM patients than in non-obese FM patients ($p<0.001$). There was no statistically significant difference between obese and non-obese groups in terms of age, gender, ESR, CRP, or disease activity scores for OA, RA, AS, SLE, and BD.

One of 12 SSc patients (8.3%) and 3 of 20 vasculitis patients (15.0%) were obese. The age, gender, and laboratory and clinical findings of obese and non-obese patients are shown in Table 2. No significant difference was found between obese and non-obese vasculitis patients in terms of age, gender, or laboratory and clinical findings. Positive ANA was more common in non-obese SSc patients, whereas the incidence of Reynaud's syndrome was statistically higher in obese patients ($p<0.001$ and $p=0.024$, respectively).

Four of 29 PMR patients (13.7%) and 14 of 71 gout patients (19.7%) were obese. The age, gender, and laboratory and clinical findings of obese and non-obese patients are given in Table 3.

Arthritis was common in both groups, while fatigue was the most common symptom in non-obese patients with gout ($p<0.001$). Fatigue was significantly higher in obese patients, while arthritis was more common in non-obese PMR patients ($p=0.001$ and $p<0.001$, respectively). No significant difference was found between both groups in terms of age, gender, CRP, or ESR values.

Two of 25 SS patients (8.0%) were obese. The age, gender, and laboratory and clinical findings of obese and non-obese patients are given in Table 4. Both ANA positivity and Reynaud's syndrome and sun sensitivity findings were significantly higher in non-obese patients than in obese SS patients ($p<0.001$, $p=0.024$, and $p=0.001$, respectively). Dry eyes and dry mouth findings, on the other hand, were more common in obese SS groups ($p<0.001$).

One of 2 PMR patients (50.0%) met the obesity criteria.

No obese patients were found among the 14 FMF patients. When somatic symptoms of obese FMF patients were analyzed, we found high values, as presented in Table 5.

Significant somatic symptoms found in FM patients included fatigue (87.0%), irritable bowel syndrome (57.0%), dyspepsia (51.0%), and constipation (27.0%). These symptoms were followed by paraesthesia (10.0%) and sun sensitivity (9.0%). Other accompanying symptoms included dry mouth, Reynaud's syndrome, and diarrhoea.

The distribution of obesity in rheumatic diseases is shown in Table 6. While the relationship between OA and obesity was statistically significant, we observed an inverse relationship in most other IRD.

Discussion

Different prevalences in different countries have been reported for obesity, which is a common health problem. Studies conducted in our country (Turkey) have reported prevalences between 12 and 22% for obesity (13). Obesity has been associated with several rheumatic diseases and inflammation (1). Since rheumatic diseases usually progress with inflammation, we thought that defining the presence of accompanying obesity and related factors could contribute to disease management. The incidence of obesity has been reported in about 12-17% of patients with RA (14). There are no published data demonstrating

the relationship between obesity and RA in the Turkish population. In our study, we found the incidence of obesity to be 4.5% in Turkish RA patients. Our obesity prevalence was found to be lower than in previous investigations. Similarly, the obesity prevalence was low in SLE patients in our study (3.2%). Several studies have reported the incidence of obesity of 27-39% in SLE patients (11). Confirming the results of previous studies (15), we observed no association between obesity and a higher degree of disease activity for RA and SLE. Likewise, there was no association between the presence of obesity and disease activity scores for AS and OA. In a study from the literature, BMI was found to be associated with disease activity (16), while another study from our country, consistent with this study, reported no significant difference between AS and control groups in terms of BMI and disease activity (17). In our study, the incidence of obesity was found as high as 40.1% but was not correlated with disease activity in OA patients. Previous studies found the incidence of obesity to be 83% for knee OA and 25% for hip OA; no increased incidence was reported for hand OA (18). WOMAC scores were found to be high in hip OA patients with higher BMI (19). For OA, the main weakness of our study was the inability to search the relationship between obesity and OA because the disease was not classified according to the region such as hip, knee, or hand OA.

We found the prevalence of obesity in 11.2% of FM patients. This prevalence was not consistent with the literature, although high FIQ scores and mean age were consistent (20). In this research, we queried many somatic symptoms that were comorbid with FM, such as abdominal pain, fatigue, gastric disturbance, irritable bowel syndrome, oral ulcers, constipation, diarrhoea, Reynaud's syndrome, sun sensitivity, dry eyes, dry mouth, urticaria, and paraesthesia. Higher prevalances of these symptoms support the severity of FM.

Because this was the first study, investigating the prevalence of obesity in patients with SSc, vasculitis, SS, PMR, and BD may increase the robustness of our study. The main weakness of the study was the inability to investigate the relationship between obesity and these diseases due to the scarce number of patients. Obesity was found in 3 cases (15%) with vasculitis and in 1 case (8.3%) with SSc. One study in the literature demonstrated that vascular inflammation neutrophil infiltration was higher in people with higher BMI values (21). In a study with SSc patients, BMI was found to be significantly lower compared to the controls (22). In the study, we found the prevalence of obesity to be 8% in SS

Table 1. Age, gender ratio, laboratory investigations and disease activities of rheumatic patients with(out) obesity

		Age	Gender (female/male)	CRP	ESR	Disease activity scores¶
RA n=197	Obesity (+)	53.2±8.9	9/0 (100.0%)	12 (3-33.3)	39 (5-80)	4.4±1.1
	Obesity (-)	52.3±13.3	149/39 (79.0%)	3.5 (0.34-739)	18 (1-255)	4.2±1.4
	p	**0.398**	**0.101**	**0.137**	**0.130**	**0.158**
SLE n=62	Obesity (+)	43.5±24.7	2/0 (100.0%)	8.8 (3.6-14)	23 (16-30)	7±2.8
	Obesity (-)	38.2±13.9	60/0 (100.0%)	4.7 (3-618)	23.5 (3-160)	6.5±2.6
	p	**0.633**		**0.294**	**0.623**	**0.196**
AS n=119	Obesity (+)	56±9.8	2/56 (3.0%)	12.5 (4-21)	35 (10-60)	4.2±1
	Obesity (-)	39.5±11.8	0/61 (0%)	3.8 (2-135)	16 (1-255)	5.3±1.5
	p	**0.250**	**0.146**	**0.638**	**0.866**	**0.384**
OA n=167	Obesity (+)	62.8±10.2	63/4 (94.0%)	3.4 (3-24)	12 (2-70)	47.3±5.6
	Obesity (-)	61.8±12.4	90/10 (90.0%)	3.4 (1-124)	12 (2-80)	47.7±6.4
	p	**0.508**	**0.150**	**0.229**	**0.623**	**0.694**
BD n=53	Obesity (+)	37±12.3	1/0 (100.0%)	3.4 (2-25)	20 (15-29)	2±0.8
	Obesity (-)	36.2±11.1	21/31 (40.0%)	11.65 (1.2-158)	25 (3.5-130)	2±0.6
	p	**0.452**	**0.586**	**0.729**	**0.762**	**0.540**
FM n=293	Obesity (+)	50.5±10.7	33/0 (100.0%)	3.4 (3-72)	14 (4-54)	4 (3-50)
	Obesity (-)	41.2±11.3	252/8 (96.0%)	3.4 (1-67)	14 (1-76)	4.5 (0.8-65)
	p	**0.000***	**0.149**	**0.862**	**0.348**	**0.000***

¶: DAS-28 for RA, SLEDAI for SLE, BASDAI for AS, WOMAC for OA, BDCAF for BD, FIQ for FM

*: p<0.005, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, AS: Ankylosing spondylitis, OA: Osteoarthritis, BD: Behçet's disease, FM: Fibromyalgia, CRP: C-reactive protein, DAS-28: Disease activity score-28, WOMAC: Western Ontario and McMaster Universities Osteoarthritis index, FIQ: Fibromyalgia impact questionnaire, ESR: Erythrocyte sedimentation rate

Table 2. Age, gender ratio, laboratory investigations and clinic features of rheumatic patients with(out) obesity

	SSc patients, n=12			Vasculitis patients, n=20		
	Obesity (+)	Obesity (-)	p	Obesity (+)	Obesity (-)	p
Age	48.8±15.7	50.7±19.7	**0.348**	55±17.4	37.9±11.8	**0.495**
Gender (female/male)	1/0 (100.0%)	10/1 (90.0%)	**0.273**	3/0 (100.0%)	11/6 (64.0%)	**0.345**
CRP	48.5	10.8 (2.7-80)	**0.157**	6.1 (3-254)	9.7 (3.4-16)	**0.724**
ESR	40	30 (8-110)	**0.240**	22 (1-113)	14 (12-16)	**0.664**
ANA	0/1 (0%)	5/6 (45.0%)	**0.000**			
Fatigue	0/1 (0%)	3/8 (27.0%)	**0.605**	1/2 (3.03%)	5/12 (29.0%)	**0.898**
Arthritis	0/1 (0%)	8/3 (72.0%)	**0.813**	2/1 (66.0%)	8/9 (47.0%)	**0.556**
Reynaud's syndrome	1/0 (100.0%)	8/3 (72.0%)	**0.024**	0/3 (0%)	4/13 (23.0%)0	**0.374**

*: p<0.005 (none for this table), SSc: Systemic sclerosis, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, ANA: Antinuclear antibody

Table 3. Age, gender ratio, laboratory investigations and clinic features of rheumatic patients with(out) obesity

	Gout patients, n=71			PMR patients, n=29		
	Obesity (+)	Obesity (-)	p	Obesity (+)	Obesity (-)	p
Age	56.9±1.,9	**57.4±15.7**	0.916	74.2±8.9	72.8±12	**0.821**
Gender (female/male)	3/11 (21.0%)	**17/40 (29.0%)**	0.531	3/1 (75.0%)	18/7 (72.0%)	**0.920**
CRP	6.9 (3.4-51)	**12.6 (0.34-739)**	0.274	3.3 (3.1-8.4)	10 (3-144)	**0.197**
ESR	25 (4-70)	**23 (2-99)**	0.650	36 (12-70)	34 (2-84)	**0.514**
Fatigue	0/14 (0%)	**3/54 (5.0%)**	0.000*	1/3 (25.0%)	3/22 (12.0%)	**0.001***
Arthritis	13/1 (92.0%)	**53/4 (92.0%)**	0.000*	3/1 (75.0%)	25/0 (100.0%)	**0.000***

*: p<0.005, PMR: Polymyalgia rheumatica, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate

Table 4. Age, gender ratio, laboratory investigations and clinic features of rheumatic patients with(out) obesity

	SS patients, n=25		
	Obesity (+)	Obesity (-)	p
Age	55±7	51.7±10.7	**0.685**
Gender (female/male)	2/0 (100.0%)	22/1 (95.0%)	**0.760**
CRP	4.2 (3-5.4)	3.5 (2.7-218)	**0.665**
ESR	47 (34-60)	22 (6-99)	**0.410**
ANA	1/1 (50.0%)	16/7 (69.0%)	**0.000***
Fatigue	0/2 (0%)	11/12 (47.0%)	**0.207**
Arthritis	0/2 (0%)	8/15 (34.0%)	**0.332**
Reynaud's syndrome	0/2 (0%)	6/17 (27.0%)	**0.024***
Dry eyes	2/0 (100.0%)	17/ (73.0%)	**0.000***
Dry mouth	2/0 (100.0%)	20/3 (86.0%)	**0.000***
Sun sensitivity	0/2 (0%)	9/14 (39.0%)	**0.001***

*: p<0.005, SS: Sjögren's syndrome, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, ANA: Antinuclear antibody

Table 5. Somatic symptoms of obese FM patients

	Existence/ non-existence	%
Fatigue	29/4	(87.0%)
Dry eyes	0/33	(0%)
Dry mouth	1/32	(3.0%)
Sun sensitivity	3/30	(9.0%)
Reynaud's syndrome	2/31	(6.0%)
Diarrhoea	1/32	(3.0%)
Constipation	9/24	(27.0%)
Dyspepsia	17/16	(51.0%)
Paraesthesia	3/30	(10.0%)
Irritable bowel syndrome	19/14	(57.0%)

Somatic symptoms of obese patients on FM are given as a percentage (%), FM: Fibromyalgia

and 13.7% in PMR. One study demonstrated that there was no correlation between PMR and BMI (23). The prevalence of obesity in patients with these diseases was not different from the normal population. In these patients, we did not find a strong and consistent relationship between obesity and clinical features (e.g., arthritis, fatigue, or Renaud's syndrome) and laboratory findings (ESR, CRP, or ANA). Similarly, one obese patient (1.8%) was found among 53 BD patients, and no relationship was observed between obesity and disease activity.

Similar to the results of a previous study, we found the second highest prevalence of obesity after OA in patients

with gout in our study group (19.7%). The association between gout and obesity may confirm that they are a part of the metabolic syndrome (24,25).

Table 6. Distribution according to disease types of rheumatic patients with(out) obesity

	Obesity (+)	Obesity (-)	p
RA	9	188	0.000*
SLE	2	60	0.02*
AS	2	124	0.000*
OA	67	59	0.000*
BD	1	52	0.01*
FM	33	260	0.41
SSc	1	11	0.65
Vaskulitis	3	17	0.7
Gout	14	57	0.037*
PMR	4	25	0.84

*: p<0.05, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, AS: Ankylosing spondylitis, OA: Osteoarthritis, BD: Behçet's disease, FM: Fibromyalgia, SSc: Systemic sclerosis, PMR: Polymyalgia rheumatica

Study Limitations

Our study had the limitation that it was planned as a cross-sectional study.

Conclusion

In this study, the highest incidence of obesity among rheumatologic diseases was found to be 40.1% in OA patients, followed by gout as 19.7%. We believe that these higher rates might be associated with mechanical and metabolic factors. In FM, on the other hand, we observed higher disease activity in obese patients. Despite recent studies that have underlined the relationship between obesity and inflammation, in general, we found a lower rate of obesity in IRD, and we did not find a relationship between obesity and disease activity.

Further studies are needed to better understanding the prevalence and related features of concomitant obesity in rheumatic disease. Thus, future studies should seek to identify other possible factors liable for obesity in rheumatologic disease, beyond those set forth above. Age-matched case-control studies would help to better understand the background prevalence of obesity.

Ethics

Ethics Committee Approval: The Local Ethics Committee (University of Health Sciences Turkey, Erzurum Regional Training and Research Hospital-Clinical Research Ethics Committee; confirmation number: 2015/8-56; date: 21.04.2015) approved the work, carried out in accordance with the principles of the Helsinki Declaration.

Informed Consent: Informed consent was obtained.

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Authorship Contributions

Concept: S.H., A.Ç., H.U., A.A., Y.Y., Design: S.H., A.Ç., H.U., A.A., Y.Y., Data Collection or Processing: S.H., A.Ç., H.U., A.A., Y.Y., Analysis or Interpretation: S.H., A.Ç., H.U., A.A., Y.Y., Final Approval and Accountability: S.H., A.Ç., H.U., A.A., Y.Y., Critical Revision of Manuscript: S.H., A.Ç., H.U., A.A., Y.Y., Writing: S.H., A.Ç., H.U., A.A., Y.Y.

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