



Relationship between Osteoarthritis and Endocrine Disease in KSA: A Cross-Sectional Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Osteoarthritis (OA), the most common kind of arthritis, affects millions of people throughout the world. This problem occurs when the protective cartilage that cushions the ends of the bones wears away over time. The goal of this study was to draw attention to the link between osteoarthritis and a number of endocrine illnesses in the Saudi population.

Methods: This was a cross-sectional research with the goal of shedding light on the link between osteoarthritis and endocrine problems. The research was conducted in Saudi Arabia at colleges,

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hospitals, and shopping centers. During the months of June to November 2021, data was collected from patients and the general public.

Results: The study included 743 participants. Among them, there were, 519 females (69.9%) and 224 males (30.1%). The most prevalent age group was 20-30 years (n= 354, 47.6%). Majority of study participants were Saudi (n= 713, 96%) and the rest were non-Saudi. The mean body mass index (BMI) among study participants was 29.47 ± 7.53 with median BMI of 30 kg/m^2 . It was found that 85 participants took anti-inflammatory drugs for more than twice per week during the last three months (11.4%). It is noticed that the prevalence of autoimmune disease among study participants is low. However, female participants were higher in hypothyroid ($P=0.001$).

Conclusion: Finally, it appears that weight, rather than IR, explains the relationship between endocrine disease and knee OA. Individuals with arthritic knee pain may benefit from endocrine disease therapy since the accumulation of endocrine disease components is connected to a higher degree of knee discomfort, independent of age, sex, or weight.

Keywords: Osteoarthritis; endocrine disease; arthritis.

1. INTRODUCTION

Millions of individuals across the world suffer with osteoarthritis (OA), the most prevalent kind of arthritis. The protective cartilage that cushions the ends of the bones wears away over time, causing this condition. Although osteoarthritis may affect any joint, it is most commonly found in the hands, knees, hips, and spine. Although joint degradation cannot be reversed, osteoarthritis symptoms may typically be controlled. Maintaining a healthy lifestyle, eating a well-balanced diet, and undergoing specific therapies can all help delay the course of illness and improve pain and joint function.

Because these factors are required by an energy-consuming immune system in a situation with little or no food/water intake, precisely regulated release of energy-rich substrates (glucose, free fatty acids, and amino acids) and auxiliary elements such as calcium/phosphorus from storage sites (fat tissue, muscle, liver, and bone) is critical during acute systemic infectious disease (sickness behavior).

Chronic inflammatory diseases are also treated with this positive selection method. It was created to cure illnesses that lasted only for a short-term. This article examines the relationship between hormones and inflammation, with a focus on energy storage and expenditure, as well as volume management. Insulin (muscle and bone growth), insulin-like growth factor-1 (IGF-1), androgens (muscle and bone growth), vitamin D (bone growth), and osteocalcin (bone growth) are all energy storage hormones (bone growth, support of insulin, and testosterone).

Noradrenaline/adrenaline (gluconeogenesis and breakdown of liver glycogen/adipose tissue triglycerides/muscle protein; water retention), growth hormone (glucogenic, lipolytic; also has growth-related aspects; water retention), thyroid gland hormones (increase metabolic effects of adrenaline; water retention), cortisol (gluconeogenesis and breakdown of liver glycogen/adipose tissue triglycerides/muscle (induce insulin resistance and retain water). The majority of energy expenditure pathways are activated in chronic inflammatory diseases, resulting in typical hormonal changes such as insulin/IGF-1 resistance, hypoandrogenemia, hypovitaminosis D, mild hypercortisolemia, and increased sympathetic nervous system and renin-angiotensin-aldosterone system activity.

Even if these long-term changes are crucial for acute inflammation in the event of systemic infection or trauma, they contribute to greater mortality in chronic inflammatory illnesses.

The endocrine system's connection with inflammation poses two questions: (a) What is the impact of inflammation on the endocrine system, and how does it affect disease? (a) What function do hormones play in inflammation and immune cell regulation? In recent decades, these issues have gotten a lot of attention (see, for example, [1–3]). Both of these questions were commonly posed separately. A theory that unifies both concerns has recently been established in the context of persistent inflammation in rheumatic illnesses.

This theory, which explains neuroendocrine changes in chronic inflammatory diseases

(CIDs), is based on these pillars: Increased water retention system activity is connected to energy allocation to the immune system, and evolutionary medicine explains that these inflammation-driven energy expenditure

programs were favorably selected for acute but not chronic systemic inflammation. The theory is based on the reality that the brain, muscles, and immune system all require the same quantity of energy-rich substances [4-7].

2. LITERATURE REVIEW

Table 1. Literature Review

Arthritis	The most common kind of arthritis, osteoarthritis (OA), causes joint discomfort and dysfunction. New evidence suggests that metabolic mediators have a role in the onset and advancement of the disease process, in addition to aging and mechanical stress, which are all known to play a role in the development of OA. This has given rise to the idea of metabolic OA. [8-10]
Metabolic syndrome and arthritis	As a result, OA has been labeled as a new component of the metabolic syndrome (MetS) [1–3], a condition marked by a cluster of metabolic risk factors including insulin resistance (IR), central obesity, dyslipidemia, and hypertension [11]. The discovery that a number of variables implicated in MetS pathophysiology may potentially play a role in the development and progression of OA [1, 2] lends credence to this theory. Several studies have looked at the link between MetS or its components and knee OA based on this theory [12-14]. When looking for a weight-independent link between MetS and knee OA, however, the majority of them failed to account for weight or BMI (BMI). Furthermore, no studies have been conducted to investigate if MetS affects the immune system.
Diabetes mellitus and arthritis	Moreover, the deleterious effects of excessive hyperglycemia on AGE formation, oxidative stress, and systemic inflammation may suggest the relationship between the two diseases [15-17]. In the rat model of streptozotocin-induced diabetes, spontaneous cartilage damage demonstrates this condition [18]. Others, on the other hand, have questioned whether DM and OA are linked [19]. Osteoarthritis (OA) and Type 2 Diabetes Mellitus (T2DM) are two common chronic diseases in the United States. OA affects 14% of persons aged 25 and up, and 34% of people aged 65 and up [20]. Around 40% of patients with OA experience arthritis-related limits in everyday activities, and 30% report difficulty completing work-related duties [20]. Diabetes affects 12% of those aged 20 and above, as well as 26% of those aged 65 and beyond [21]. Diabetes is linked to death and significant consequences such as heart disease and stroke, renal failure, and amputation of the lower limbs [21]. Coexistence of OA and T2DM is common in the elderly, and it can result in greater disability and financial burden [22-23]. Patients with T2DM have a higher risk of developing OA [17-18]. A recent study of people aged 18 to 64 found that 52 percent of those with T2DM had arthritis, compared to 27 percent of those without T2DM [22]. It's unknown why T2DM individuals have such a high frequency of arthritis. Obesity and advanced age are substantial risk factors for both OA and T2DM, which may explain why diabetics have a higher chance of developing OA [24].
Cushing syndrome and arthritis	Recent research has linked OA to systemic metabolic abnormalities, which are frequent in T2DM patients, showing that diabetes in persons with OA is a genuine condition. The existence of Cushing's syndrome has no bearing on the development of arthritis. In fact, cortisone's anti-inflammatory qualities

Addison's disease and arthritis	<p>help many persons with arthritis who acquire Cushing's syndrome on their own [25].</p> <p>Endocrine myopathies include myxedema, hyperthyroidism, acromegaly, and hyperparathyroidism [26]. Excessive corticosteroids, whether exogenous or endogenous, can cause myalgia, as well as muscle weakness and fatigue. 1 Patients with hypoadrenalism, whether primary or secondary, experience tiredness, weakness, gastrointestinal issues, and weight loss. Musculoskeletal symptoms afflict 6–13 percent of persons with adrenocortical insufficiency [27,15], and a range of rheumatic symptoms, including myalgia, arthralgia, joint stiffness, muscular spasms, low back pain, and flexion contracture, have been recorded in the literature [16–17].</p>
Thyroid disease and arthritis	<p>Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease that produces inflammatory polyarthritis, joint deterioration, limited mobility, and disability [1]. The frequency of RA in the general population is around 1%, and it has been linked to a number of co-morbidities [2–4]. Both genetic and environmental factors have a role in the development of RA, which is yet unknown and has to be researched [5]. Despite the clinical consequences of the illness, RA patients are more likely to develop co-morbidities such as cardiovascular disease (CVD) [6,7]. Although the mechanism underlying the higher risk of co-morbidities in RA patients is unknown, experts prefer to blame it on their inflammatory state [8, 9].</p> <p>Hyperthyroidism and hypothyroidism are the two most common kinds of thyroid malfunction. Overt and subclinical phases of hyperthyroidism and hypothyroidism can be distinguished [10–12]. Graves' illness is the most common cause of hyperthyroidism, which is defined as an excess of thyroid hormones (GD). The most prevalent cause of hypothyroidism is Hashimoto's thyroiditis, which is characterized by a shortage of thyroid hormones (HT). Both hyperthyroidism and hypothyroidism are bad for your health and can increase your risk of heart disease and death. Thyroid dysfunction is common in RA patients, according to previous research [13,14], with rates ranging from 6 to 34 percent. Thyroid function should be examined in people who exhibit symptoms including cold intolerance, weight loss, high metabolism, or thyroid goiter [10,20].</p> <p>Furthermore, because people with type 1 diabetes or Addison's disease are more likely to have thyroid problems, some guidelines indicate that thyroid-related tests be conducted on them [21]. A conventional thyroid function test, on the other hand, is not recommended in RA patients. Thyroid dysfunction is a worry in RA patients that has yet to be clearly proved.</p>

3. METHODS

3.1 Study Design

This was a cross-sectional research with the goal of shedding light on the link between osteoarthritis and endocrine problems. This is an appropriate strategy for this study because the goal was to shed light on the association between osteoarthritis and endocrine problems.

3.2 Study Setting

The research was conducted in Saudi Arabia at colleges, hospitals, and shopping centers. During

the months of June to November 2021, data was collected from patients and the general public.

3.3 Sampling and Sample

Participants were recruited using a basic random selection procedure based on likelihood. The participants were chosen from the general public. A total of 500 people were included in the final sample size. However, 743 people took part in the study.

Patients and the general public are both included in the study.

Osteoarthritis: Osteoarthritis is a joint condition characterized by cartilage deterioration and underlying bone expansion, as well as bony enlargement.

There are no excluding criteria.

Instruments: The data collecting tool was created by the researcher and is based on the most recent literature. It included the following details: (1) basic participant information and (2) disease-related information. For both Saudi and non-Saudi participants, the instrument was available in Arabic and English.

3.4 Statistical Analysis

The information gathered from the questionnaire was input and analyzed using the SPSS program version 23. Descriptive statistics such as means, medians, percentages, and standard deviation are used to present sociodemographic data. To demonstrate statistical significance between patient features and tool scores, the independent T test and one-way Anova are utilized. To demonstrate a link between categorical variables, the Chi square test is utilized. To explore the relationship between parent gender, education level, and knowledge and prevention of tooth decay, univariate and multivariate

analysis will be used. A P value of 0.05 or less is considered statistically significant.

4. RESULTS

The study included 743 participants. Among them, there were, 519 females (69.9%) and 224 males (30.1%). The most prevalent age group was 20-30 years (n= 354, 47.6%). Age distribution among study participants is presented in Fig. 1. Majority of study participants were Saudi (n= 713, 96%) and the rest were non-Saudi. The mean body mass index (BMI) among study participants was 29.47 + 7.53 with median BMI of 30 kg/m². This reflects that most of study participants are overweight or obese.

Participants were asked to describe having pain in any joint in the body. Participants answers varied and some of them had pain in more than one joint at once. Participants responses to these answers are presented in Table 2.

Table 2. Joint pain among study participants

Joint pain	Frequency	Percentage
Neck	92	12.4
Hand	113	15.2
Low back	180	24.2
Hip	89	12
knee	152	20.5

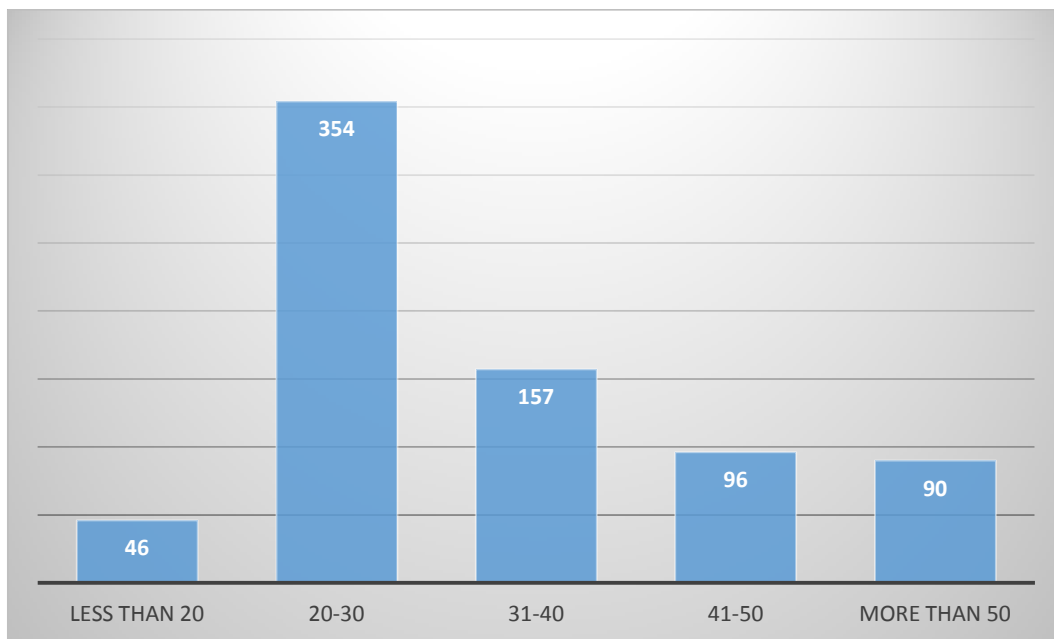


Fig. 1. Age distribution among study participants

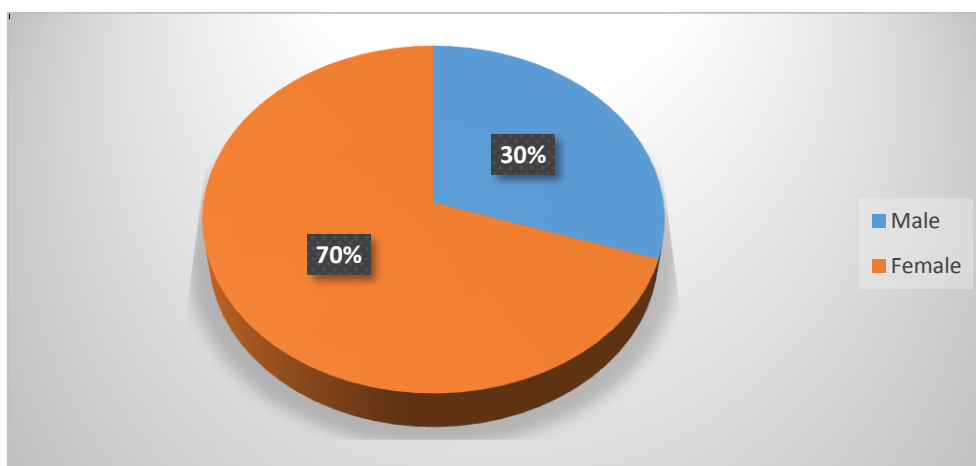


Fig. 2. Gender distribution

Participants were also asked if they took any anti-inflammatory drugs during the last three months. It was found that 85 participants took anti-inflammatory drugs for more than twice per week during the last three months (11.4%). The female to male ratio in the use of anti-inflammatory was 2.5:1. The joint pain was severe enough to wake the participants from sleep at night among 109 patients (14.7%).

Participants were also asked if they had any autoimmune disease along with the joint pain. They were asked about diabetes mellitus, Cushing, Addison and thyroid disease. Their responses are presented in Table 3.

Table 3. Prevalence of autoimmune diseases among study participants

Autoimmune disease	Frequency	Percentage
Diabetes mellitus	70	9.4
Addison's disease	1	0.1
Cushing syndrome	5	0.7
Hypothyroidism	135	18.2
Hyperthyroidism	21	2.8

It is noticed that the prevalence of autoimmune disease among study participants is low. However, female participants were higher in hypothyroid (P= 0.001).

About the comorbid state, participants were asked to answer if they had any comorbid conditions other than autoimmunity. There were 562 of participants had no comorbid conditions (75.6%). On the other hand, there were 18 participants (2.4%) had cubital or carpal tunnel syndrome, 33 participants (4.4%) had knee ligaments injury and 26 participants (3.5%) suffered from osteoporosis.

Site of joint pain was correlated with the autoimmune condition. Results and statistically significant values are presented in Table 4.

It is noticed that most of autoimmune conditions are associated with the joint pain in statistically significant relationship as presented in Table 4.

Patients with osteoarthritis were diagnosed using spine and hand x-ray imaging (Fig. 3).

Table 4. Relationship between joint pain and autoimmune conditions

Autoimmune condition	Site of joint pain Frequency (P value)				
	Neck	Hand	Low back	Hip	Knee
Diabetes mellitus	12	25 (0.000)	33 (0.000)	16 (0.005)	32 (0.000)
Addison disease	1	1	1	1	1
Cushing Syndrome	2	2	3	2	2
Hypothyroid	28 (0.002)	34 (0.001)	55 (0.000)	28 (0.001)	43 (0.000)
Hyperthyroid	12 (0.000)	9 (0.002)	12 (0.001)	5	8 (0.046)

* P value is written where significant only, i.e. less than 0.05

* Some patients with autoimmune condition had more than one site of joint pain

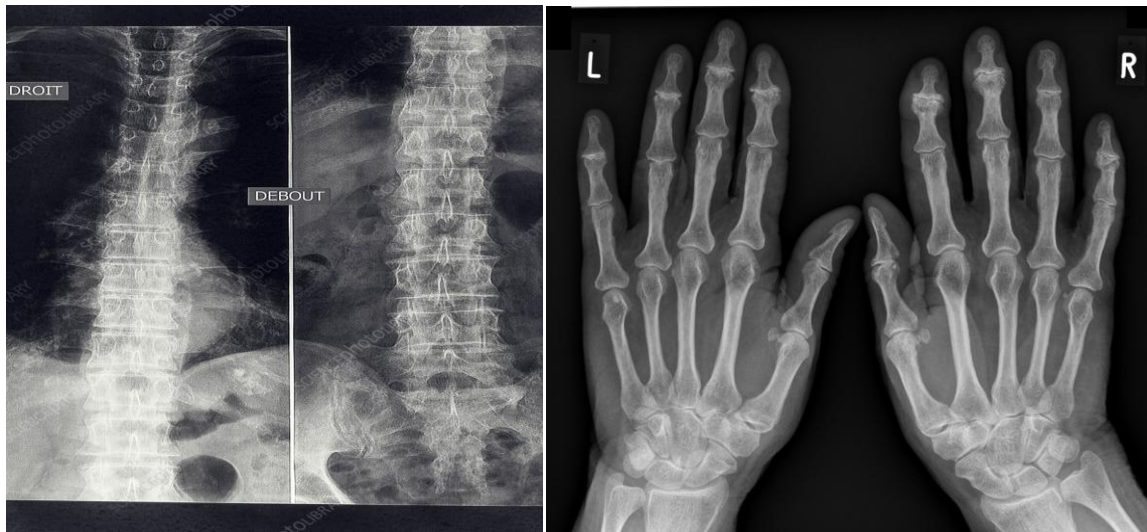


Fig. 3. Osteoarthritis of back and hand

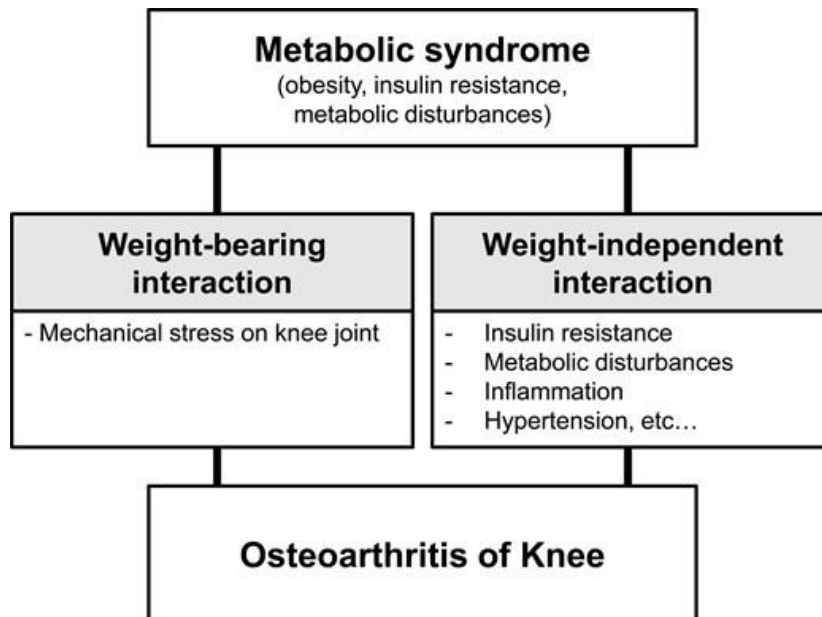


Fig. 4. Basic concept of the association between MetS and OA

5. DISCUSSION

After controlling for a variety of demographic and behavioral factors, many favorable connections between radiographic knee OA and MetS or its components, particularly abdominal obesity and high blood pressure, were discovered. Weight, but not IR, a critical pathophysiology of MetS, was revealed to be a significant predictor of these correlations [4].

The basic notion of the link between MetS and knee OA is depicted in Fig. 2. Obesity is both a

critical component of MetS [4] and a substantial risk factor for knee OA due to increased mechanical stress on knee joints [21], suggesting a weight-bearing interaction between MetS and knee OA. However, there might be a weight-independent link between MetS and knee OA, which has recently gotten a lot of attention because to a new concept called metabolic OA. Until recently, only a few epidemiological studies [5–9] examined the link between MetS and knee OA, but their techniques were unreliable, and the results were inconsistent.

Furthermore, because the majority of these studies did not adjust for weight or BMI, they were unable to investigate the weight-independent link between MetS and knee OA. Only one Swedish cohort research looked at it, and no evidence of a substantial weight-independent connection was discovered [8]. Rather, they discovered that the beneficial link between MetS and knee OA was mostly mediated by MetS patients' greater weight [8]. These findings were consistent with our own. However, because the Swedish study's diagnosis of knee OA was based on surgical treatment [8], it's possible that the percentage of healthy persons who were eligible for surgery was skewed. In contrast, our research is unique in the following ways: 1) We used the radiological definition of a knee.

In this investigation, abdominal obesity and high blood pressure were found to be linked to radiographic knee OA among the MetS components. The favorable linkages between those components and knee OA may simply be explained by weight bearing on knee joints in persons with abdominal obesity or hypertension. Obesity or hypertension, on the other hand, may have weight-independent effects on knee OA. Increased metabolic agents produced by adipocytes in obese persons [22–24], as well as subchondral bone ischemia induced by atheromatous vascular alterations in hypertension patients [3,25], can all impact knee OA. In the current study, however, after adjusting for weight and BMI, the relationship between abdominal obesity or high blood pressure and knee OA was no longer significant. As a result, the potential weight-independent contributions of these components.

I postulated that IR, a primary pathophysiology of MetS [4], might partially explain the relationship between MetS or its components and knee OA, in addition to the obesity-related mechanical stress. The results did not change significantly after controlling for HOMA-IR, indicating that IR did not mediate these correlations.

We discovered that, regardless of age, sex, or weight, the degree of arthritic knee pain, as measured by a self-reported 11-point NRS, increased as the number of MetS components rose (or BMI). As far as we know, this is the first study to look at the relationship between MetS component accumulation and self-reported knee pain severity. This finding was consistent with a recent research that demonstrated a substantial

association between MetS and the incidence of total knee joint replacement after controlling for BMI [26].

Although the mechanism behind the link between MetS and knee pain severity is unknown, it might be explained by MetS patients' systemic inflammation. Inflammatory indicators have been shown to improve pain sensitivity in patients by causing hypersensitive perceptions and structural changes in the knee joints [27,15,16]. After controlling for numerous covariates, including BMI, blood levels of inflammatory markers such as C-reactive protein, IL-6, and TNF- were found to be positively connected with worsening of knee pain in a recent prospective research [16]. In addition, people who had more MetS components had greater levels of inflammatory markers than people who had less components [17, 18].

When these data are considered together, it appears that those with more MetS components, regardless of weight, have more severe arthritic knee pain as a result of the negative impact of higher inflammatory markers on knee pain. As a result, in addition to weight loss, adequate MetS therapy should become a critical component of arthritic knee pain management.

This research has a number of issues. First, because this was a cross-sectional research, I was unable to establish a clear cause-and-effect relationship between MetS and knee OA. As a result, further study is required to back up these claims. Second, using a single 11-point NRS, I was unable to measure various aspects of acute and chronic pain, including functional impairment. Nonetheless, it is a basic, widely used pain intensity measure that has been shown to be accurate and trustworthy [19,28]. Despite these flaws, the study was significant because 1) it was the first to attempt to conceptualize and verify both the weight-bearing and weight-independent interactions between MetS and radiographic knee OA in a large population, and 2) it was the first to attempt to conceptualize and verify both the weight-bearing and weight-independent interactions between MetS and radiographic knee OA in a large population.

6. CONCLUSION

Finally, it appears that weight, rather than IR, explains the relationship between endocrine disease and knee OA. Individuals with arthritic

knee pain may benefit from endocrine disease therapy since the accumulation of endocrine disease components is connected to a higher degree of knee discomfort, independent of age, sex, or weight.

CONSENT AND ETHICAL CONSIDERATIONS

The unit of biomedical ethical research committee will be consulted for administrative permission. The ethics committee of the faculty of medicine of King Abdul-Aziz University was consulted for permission. The participants were asked to give their informed consent.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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