Symptomatic Knee Osteoarthritis and Dyslipidemia. A study from Kurdistan of Iraq

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Abstract

Background: As a complex multifactorial condition, knee osteoarthritis has been considered as a leading cause of disabilities. Dyslipidemia is a metabolic component that can probably play a role in knee osteoarthritis development and comorbidities; however, this relationship is still debated. The present study was carried out in order to figure out the prevalence of dyslipidemia among knee osteoarthritis patients and to compare their abnormal serum lipid components with non-exposed individuals.

Patients and methods: A total of 60 patients with knee osteoarthritis and 60 non-exposed (without knee osteoarthritis) individuals were studied in a prospective cohort study that was conducted from March 2018 to May 2019. The patients were chosen from those who referred to the Rheumatology Division in Sulaymaniyah, the Kurdistan Region of Iraq. EULAR and ACR diagnostic and classification criteria and radiographic confirmation for definite osteophyte were utilized to diagnose the primary knee osteoarthritis. Required data were collected using a questionnaire, taking blood samples and by conducting several laboratory tests.

Results: The mean age of the patients with knee osteoarthritis was 51.8 years. Female-to-male ratio was 2.1:1. It was seen that dyslipidemia increased two folds among patients with knee osteoarthritis than the non-exposed subjects. Patients and non-exposed subjects were significantly different in terms of dyslipidemia prevalence (p<0.013). Furthermore, all the lipid components were significantly abnormal in those with knee osteoarthritis.

Conclusion: Dyslipidemia is prevalent among knee osteoarthritis patients, and there is a significant association between knee osteoarthritis and high-density lipoprotein, total cholesterol, low-density lipoprotein, and triglyceride. Dyslipidemia prevention may reduce the development of knee osteoarthritis and cardiovascular comorbidities.

Key words: knee osteoarthritis, dyslipidemia, serum lipid components, radiography

Introduction

As the most common chronic, heterogeneous, and debilitating arthritic disorder, osteoarthritis (OA) mainly impacts diarthrodial joints [1-5]. Quality of life can be negatively affected by osteoarthritis, which in turn raises the healthcare and social costs [6]. The prevalence of OA ranges from 3.8-70% depending on different regions of the world [7], and it has been reported to affect 1 million people in Iraq, Yemen, Saudi Arabia, and Syria [8]. In addition, it has been indicated that OA was more prevalent among men than women. However, studies demonstrated that beyond 50 women are more likely to have OA than same age men [9].

The most common type of OA is knee osteoarthritis (KOA) [10]. The prevalence of KOA has been reported to be 12% in those over the age of 55 years [11].

OA is associated with pain and functional limitations [12] and is typically believed to be the result of obesity and aging [13]. In addition to age and obesity, metabolic syndrome (MetS) has been referred to as a major risk factor for OA development [14]. Association between OA and MetS is referred to as metabolic OA, indicating the association between OA and obesity, dyslipidemia, and hypertension [15].

Due to the high prevalence of knee osteoarthritis (KOA) particularly in the middle-aged individuals, the debilitating effect of osteoarthritis and consequently has a negative impact on quality of life. Moreover, due to the reported association between OA and dyslipidemia, the present investigation was carried out in order to study the prevalence of dyslipidemia among individuals with symptomatic KOA.

Materials and Methods

Study design and sample: The present investigation was a prospective cohort study which was carried out in the Rheumatology Division in Sulaymaniyah, Iraqi Kurdistan from March 2018 to May 2019. For this purpose, 60 patients with symptomatic KOA (41 females and 19 males) were chosen as the exposed for the study. Following both ACR classification of OA of the knee [27] and EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis [28], 60 non-exposed (no symptomatic KOA) with the same age range were selected in order to be compared to the exposed.

Selection of the target sample was based on some inclusion and exclusion criteria. The inclusion criteria involved patient consent, age, duration of knee pain not exceeding 2 years, presence of definite osteophyte in at least one joint, and normal body mass index (BMI). Patients with possible secondary causes of dyslipidemia were excluded.

Data collection: The exposed and non-exposed individuals randomly visited the Rheumatology Division, and the required data were collected by conducting face-to-face interviews using a researcher-designed questionnaire.

Statistical analysis: In order to analyze the collected data, Statistical Package for Social Sciences version 25 was used. The descriptive results were expressed as mean ± standard deviation (SD). Normality of the data was verified using Kolmogorov Smirnov test. The categorical variables were analyzed through Chi-square test, and Fisher's exact test was used when more than 20% of the cells were less than five. Pearson's and Spearman's tests were used for the correlation between the variables. Level of significance probability value (p-value) was set at ≤0.05.

Results

A total of 60 patients with KOA were studied. Analyzing the collected data revealed that their mean age was 51.8 (±3.745) years. Regarding their sex, there were 41 (68.3%) females and 19 (31.7%) males, and the female-to-male ratio was 2.1:1 (See Table 1).

The results obtained from analyzing the data collected from the 60 non-exposed subjects indicated that their mean age was 50.95 (±5.077) years. In terms of their sex distribution, 41 (68.3%) females and 19 (31.7%) males were in the control group, with a female-to-male ratio of 2.1:1.

The study demonstrated that 34 cases (56.7%) had bilateral KOA and 26 (43.3%) unilateral KOA. Out of the unilateral cases, 14 had right-side while 12 had left-side KOA, respectively (See Table 2).

The results showed that KOA pain duration ranged from 3 to 18 months, with 47 cases (78.3%) having a disease span of less than 12 months, and 13 (21.7%) more than 12 months (See Figure 1).

Comparing the cases and controls through t-test, revealed that levels of serum lipid had a significant increase in the KOA patients compared to the controls. There was a significant difference between the two groups in terms of all lipid variables including high-density lipoprotein (HDL) at a p-value of 0.001, total cholesterol (TC) at a p-value of 0.001, low-density lipoprotein (LDL) at a p-value of 0.019, and triglyceride (TG) at a p-value of 0.002 (See Table 3).

According to the results obtained from the Chi-square test, the cases had significantly higher levels of abnormal TC, TG, LDL, and HDL compared to the control. Based on these results, it was concluded that KOA had a significant relationship with elevated level of TC (p-value=0.024), TG (p-value=0.016), LDL (p-value=0.018), and HDL (p-value=0.032) (See Table 4).

Compared to the 15 controls (12.5%), 28 cases with KOA (23.3%) had different types of dyslipidemia, and this difference was significant, showing a significant relationship between KOA and dyslipidemia at a p-value of 0.013 (See Figure 2).

Table 1. Demographic characteristics of KOA cases

Variable	Frequency (N)	Percentage (%)
Sex		
Male	19	31.7
Female	41	68.3
Total	60	100.0
Age mean ± SD (51.8 ± 3.745)		
42-44 years	7	11.7
45-49 years	16	26.7
50-54 years	19	31.7
55-59 years	18	30.0
Total	60	100.0

Table 2. Type and site of KOA pattern distribution

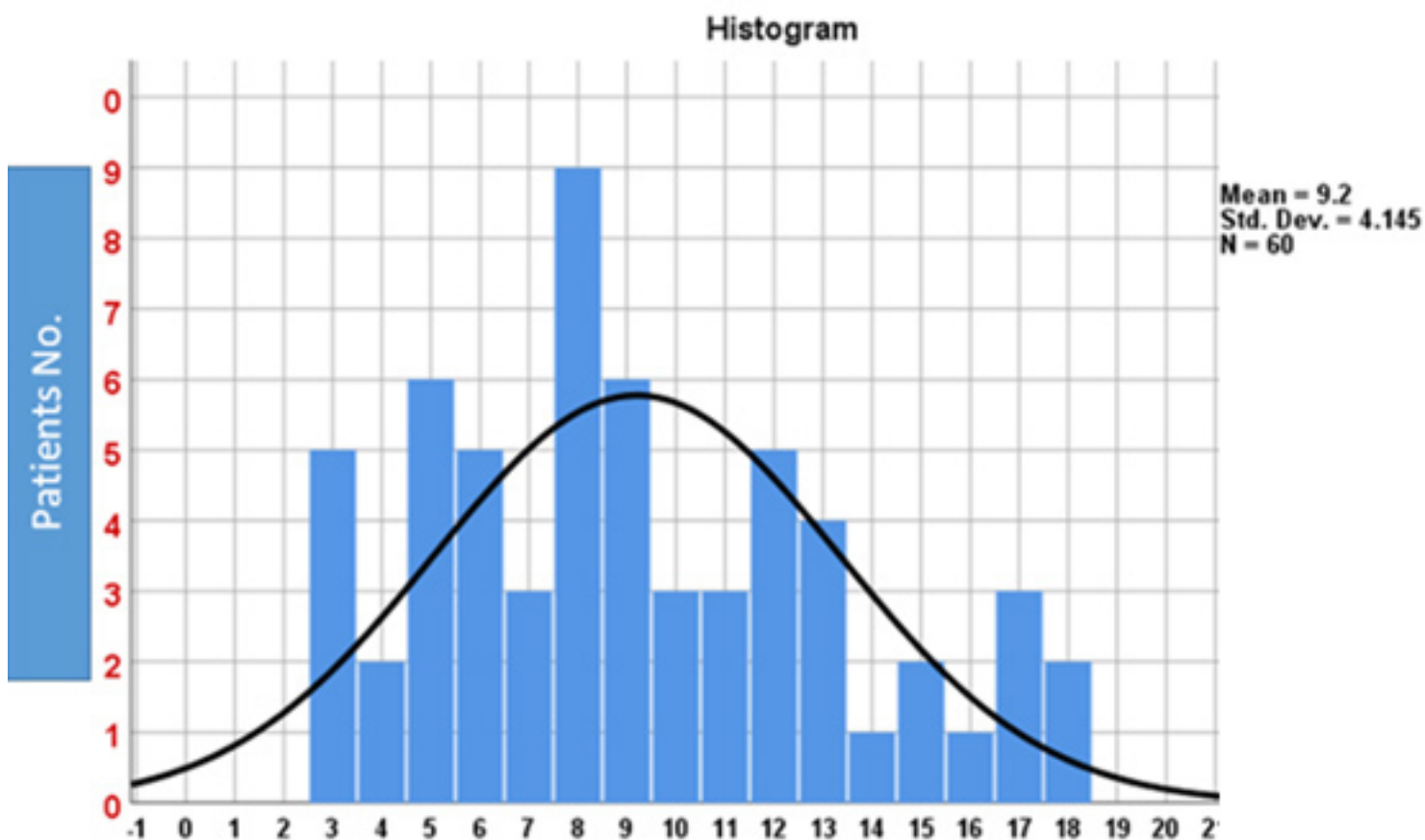| Knee involvement pattern	Frequency (N)	Percentage (%)
Bilateral	34	56.7
Unilateral	26	43.3
Right	14	23.3
Left	12	20.0
Total	60	100.0

Figure 1: Duration of KOA pain (months)

Histogram

Mean = 9.2
Std. Dev. = 4.145
N = 60

Table 3. Analyzing and comparing means with Independent sample T-test

Lipid variable	Type	Mean	SD	P-Value
TC	KOA exposed	189.70	40.305	0.001
	Non-exposed	168.18	28.759	
TG	KOA exposed	166.40	104.694	0.002
	Non-exposed	120.43	40.820	
LDL	KOA exposed	121.47	26.347	0.019
	Non-exposed	110.23	25.550	
HDL	KOA exposed	45.85	9.293	0.001
	Non-exposed	51.18	7.405	

P- Value {Sig (2-Tailed)}is significant whenever it is less than or equal to .05

Table 4. Significant ratio of normal and abnormal percentage and distribution of lipids among exposed and non-exposed

Lipid type	Value	KOA cases	Non-exposed	Odds Ratio	95% confidence interval	Σ^2	P-value
TC	Abnormal	14 (23.3%)	5 (8.3%)	3.3	1.1 - 9.9	5.065[a]	0.024
	Normal	46 (76.7%)	55 (91.7%)				
TG	Abnormal	19 (31.7%)	8 (13.3%)	3.01	1.1 - 7.5	5.783[a]	0.016
	Normal	41 (68.3%)	52 86.7%)				
LDL	Abnormal	13 (21.7%)	4 (6.7%)	3.8	1.1 - 12.6	5.551[a]	0.018
	Normal	47 (78.3%)	56 (93.3%)				
HDL	Abnormal	20 (33.3%)	9 (15.0%)	2.8	1.1 - 6.8	5.502[a]	0.032
	Normal	40 (66.7%)	51 (85.0%)				

Figure 2: Dyslipidemia among KOA exposed and non-exposed
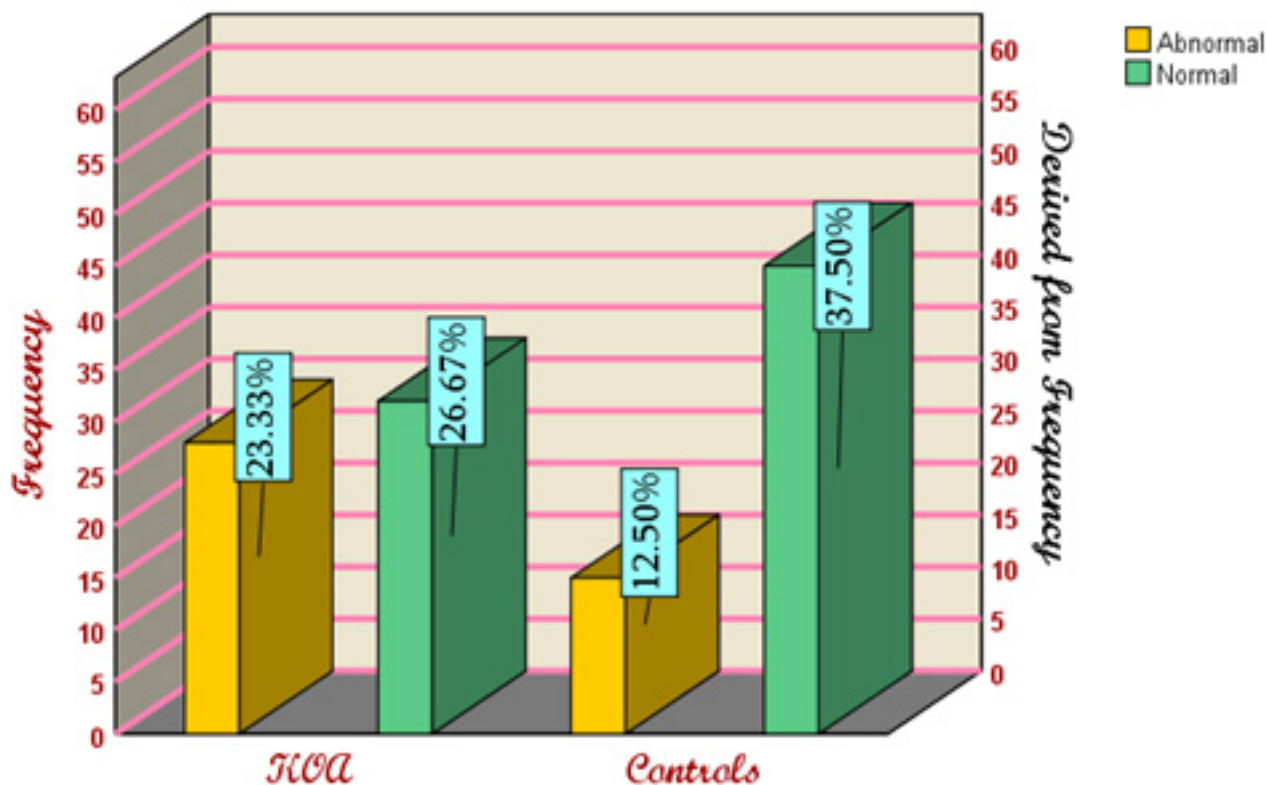
Table 5. Correlation of dyslipidemia with gender and age

Lipid	Gender		P-value	Age		P-value
	Male	Female		4th decade	5th decade	
Normal	10 (16.7%)	22 (36.7%)		15 (25.0%)	14 (36.8%)	
Abnormal	9 (15%)	19 (31.7%)	0.580	8 (13.3%)	13 (34.2%)	0.151
TOTAL	19 (31.7%)	41 (68.3%)		23 (38.3%)	27 (71%)	

Table 6. Correlation of dyslipidemia with duration and joint pattern

Lipid	Duration/months		P-value	KOA joint pattern		P-value
	3-9/m	10-18/m		Bilateral	Unilateral	
Normal	27 (45.0%)	5 (8.3%)		12(20%)	20(33.3%)	
Abnormal	9 (15.0%)	19 (31.7%)	<0.0001	22(36.7%)	6(10.0%)	0.001
TOTAL	36 (60.0%)	24 (40.0%)		34(56.7%)	26(43.3%)	

Table 7. Correlation between joint pain pattern with duration of pain

Duration	Pattern		P-value
	Unilateral KOA	Bilateral KOA	
3-9 months	21 (35.0%)	15 (25.0%)	
10-18 months	5 (8.3%)	19 (31.7%)	0.004
TOTAL	26 (43.3%)	34 (56.7%)	

The results revealed that there was no statistically significant association between sex and age in patients with KAA in terms of dyslipidemia (See Table 5).

The study revealed, that there was a significant relationship between dyslipidemia and pain duration in KOA patients (p<0.0001). Dyslipidemia was more common among patients with knee pain of more than 10 months. Also, dyslipidemia was significantly correlated with bilateral knee joint involvement at a p-value of 0.001 (See Table 6).

Finally, there was a significant connection between pain duration of either ≤ 9 or ≥ 10 months and the site of knee joint involvement (p=0.004). The study revealed that bilateral involvement was more prevalent in patients with knee pain duration of ≥ 10 months (See Table 7).

Discussion

Knee osteoarthritis (KOA) has been defined by the European League against Rheumatism as a condition in which the patients experience functional limitation and/or usage-related pain in their knee(s).[17].Studies has shown that KOA is quite common among middle-aged adults particularly those who are over the age of 55 [11]. In line with this report, the results of the present analysis revealed that the patients' mean age was 51.8 years, with most patients (61.7%) belonging to the age groups 50-54 and 55-59 years. Similarly, Silverwood et al. (2015) reported age of over 50 years to be a risk factor for knee pain/OA [18].

Furthermore, the current results highlighted that most of the patients with KOA (68.3%) were females. In the same way, results from a study carried out by Corti and Rigon (2003) pointed out that women are more likely to develop KOA [9]. According to the current study, more than half of the KOA cases (56.7%) were bilateral, compared to 43.3% unilateral. Similarly, Fathi (2018) studied unilateral versus bilateral primary knee osteoarthritis in Egyptian patients and reported that 65% of the patients had bilateral KOA and 35% unilateral [19].

Comparing patients with KOA and the non-exposed subjects in terms of their serum lipid variables (i.e. high-density lipoprotein, total cholesterol, low-density lipoprotein, and triglyceride) they were significantly higher in the KOA patients (p<0.05). Likewise, Garcia-Gil et al. (2017) who studied serum lipid levels and risk of hand osteoarthritis (HOA) concluded that the patients with HOA had a significantly higher level of total cholesterol (TC) and triglyceride (TG), but not high-density lipoprotein (HDL) and low-density lipoprotein (LDL) [20].

The analysis of this study revealed that abnormal lipid levels, were significantly higher in the cases than the controls, leading to the conclusion that KOA is significantly correlated with increased levels of TC, TG, LDL, and HDL (p<0.05). Correspondingly, Gandhi et al. (2010) noticed a significant relationship between etiopathogenesis of osteoarthritis and hyperlipidemia [21], highlighting the significance of keeping lipid levels within the normal limit. In the same way, Velasques et al. (2010) demonstrated that OA initiation and progression are significantly affected by various interrelated

lipids, metabolic and humoral mediators; therefore, they reported a strong relationship between OA and metabolic factors including dyslipidemia [22].

This study unveiled that dyslipidemia prevalence was found in 23.3% of the KOA patients. This finding agrees with the outcome of a meta-analysis carried out by Baudart et al. (2017) who reported that 30% of the studied KOA patients had dyslipidemia [23]. Moreover, Farnaghi (2014) reported an association between high serum TC and OA. In justifying this association, it was stated that mitochondrial DNA oxidative damage is caused by, and cell dysfunction happens as, a result of high cholesterol-challenged articular cartilage, leading to further apoptosis and overproduction of reactive oxygen species, which in turn leads to development of abnormalities similar to characteristic features associated with OA [24].

Moreover, our study has revealed that serum lipid levels, and KOA duration were significantly correlated (p<0.0001). This finding was not established in any previous research. Additionally, we found a significant relationship between bilateral knee involvement and dyslipidemia with p-value of 0.001. Similarly, Irshad et al (2014) and Al-arfaj (2003) reported a significant relationship between hypercholesterolemia and involvement of both right and left joints in KOA patients [40, 43].

Conclusion

Knee osteoarthritis was found to be more prevalent among middle-aged patients and women. Compared to non-exposed individuals, patients with KOA have a higher mean level of serum lipids including total cholesterol, triglyceride, low-density lipoprotein, and high-density lipoprotein. Dyslipidemia is two-fold higher in patients with knee osteoarthritis than non-exposed individuals. Development and progression of KOA might be restricted and controlled by preventing and controlling dyslipidemia.

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