American Journal of Biomedical Research, 2020, Vol. 8, No. 1, 19-24
Available online at http://pubs.sciepub.com/ajbr/8/1/4
Published by Science and Education Publishing
DOI:10.12691/ajbr-8-1-4

Dyslipidemia and High Adiposity are Risk Factors for Osteoarthritis in Adults in Nigeria

Razaq Abiodun Ogunbona[1], Bose Etaniamhe Orimadegun[1,*], Samuel Olusegun Ogunlade[2], Adesoji A. Fasanmade[3], Emmanuel Oluyemi Agbedana[1]

[1]Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria
[2]Department of Surgery, College of Medicine, University of Ibadan, Ibadan, Nigeria
[3]Department of Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria
*Corresponding author: orimadegunbose@yahoo.co.uk

Received February 12, 2020; Revised March 18, 2020; Accepted March 27, 2020

Abstract Clinical anecdotal evidence suggests that the risk of cardiovascular disease among adult Nigerians with osteoarthritis (OA) exist, but evidence from analytical research remains scarce in the literature. Therefore, this research was conducted to examine the relationship between OA and certain risk factors for cardiovascular disease in adults in Nigeria. We identified 40 consecutive cases of OA, age- and sex-matched adults who had no symptoms or signs suggestive of OA as controls at the medical outpatient clinics of two tertiary hospitals in Ibadan, Nigeria. Plasma lipids and glucose, as well as serum homocysteine, were determined following standard procedures. Other indices of cardiovascular risk factors included body mass index, waist and hip circumference, and body adiposity index. The associations between OA and the factors were explored using logistic regression analysis at p = 0.05. Participants' ages ranged from 31 to 74 years. There were four males and 36 females in cases and controls, respectively. The odds of low high-density lipoprotein cholesterol (OR=6.71; 95% CI: 4.58, 10.31), high low-density lipoprotein (OR=5.68; 95% CI: 3.74, 11.42), high body adiposity index (OR=1.27; 95% CI: 1.11, 1.46) and high total cholesterol-to-high-density lipoprotein ratio (OR=0.02; 95% CI: 0.01, 0.51) were higher in individuals with OA than controls. Dyslipidaemia and increased adiposity are important risk factors for osteoarthritis in adults in Nigeria. These factors could be useful for routine screening and stratification of cardiovascular risk in susceptible individuals.

Keywords: *dyslipidaemia, excess body fatness, dyslipoproteinemia, hypercholesterolemia, osteoarthritis*

Cite This Article: Razaq Abiodun Ogunbona, Bose Etaniamhe Orimadegun, Samuel Olusegun Ogunlade, Adesoji A. Fasanmade, and Emmanuel Oluyemi Agbedana, "Dyslipidemia and High Adiposity are Risk Factors for Osteoarthritis in Adults in Nigeria." *American Journal of Biomedical Research*, vol. 8, no. 1 (2020): 19-24. doi: 10.12691/ajbr-8-1-4.

1. Introduction

Osteoarthritis (OA), a degenerative joint disorder characterised by pain, tenderness, motion restriction, crepitus, and occasional effusion of the large joints, [1] is the leading chronic joint-related illnesses in adults globally [2,3,4]. An estimated 9.6% of males and 18.0% of females over 60 years of age have symptomatic osteoarthritis [5]. The burden of OA is expected to increase with the ageing population and rising rates of overweight and obesity worldwide. According to the population projection by the United Nations, over 20% of the world's population will be people over 60 years old by 2050 [6] and about 15% of these individuals will have symptomatic OA [7]. This implies that 130 million individuals globally will be suffering from OA by 2050, 40 million of whom will be significantly handicapped by the disease [6].

Recently, increasing attention has been paid to identifying lipid bioactive molecules that could explain the pathophysiology of OA since the discovery of its contribution to enhanced risk and progression. For instance, OA has been associated with many components of metabolic diseases, including dyslipidaemia, obesity, and hypertension [8,9] and some of these are preventable. It is foreseeable that the rapidly rising incidence of OA may lead to an increased negative impact on healthcare and public health systems as well as disabilities. However, the causal link between OA and some of the cardiometabolic risks such as dyslipidaemia is still unclear, but studies have shown that some risk factors are common to both, namely; age, obesity, gender, physical inactivity, impaired fasting glucose, hypertension, and chronic inflammation [10,11].

Though the exact prevalence of OA in Nigeria is unknown, recent studies suggest that more than 16% of patients in medical clinics across the country present with OA-related features and most of them have obesity as well as some metabolic diseases that are rapidly emerging [12,13,14]. It could, therefore, be inferred that Nigeria will have a remarkable burden of OA sooner than imagined.

As the risk factors for cardiometabolic diseases and OA are known, it may be instructive to investigate the interactions between the two chronic conditions. Although studies have reported the link between metabolic diseases and osteoarthritis, the roles of dyslipidaemias and homocysteine remain incompletely understood and controversially discussed in the literature [11,15]. To this end, this study was carried out to examine the association between cardiovascular risk factors and OA among adult Nigerians.

2. Materials and Methods

2.1. Study Design, Site, and Participants

In this case-control study, we identified 40 patients with a first-time recorded diagnosis of OA aged 31 to 74 years at the medical clinics of the University College Hospital, Ibadan and Adeoyo State Hospital, Ibadan Nigeria. These patients were age- and sex-matched with 40 healthy individuals who presented for routine medical examination. We excluded patients with a history of cancer, HIV or drug abuse.

2.2. Study Variables and Co-variables

The following variables were recorded as the characteristics of the participants: age, any current medications such as statins and hormone replacement therapy, menopause, weight, height, body mass index (BMI) and diabetes mellitus diagnosis. The exposure of interest was cardiovascular risk factors. Hypertension was diagnosed if the systolic blood pressure readings were ≥140 mmHg and/or diastolic blood pressure readings ≥90 mmHg on two different days. Other variables were body mass index (BMI), waist circumference (WC), waist-to-hip ratio, plasma lipid, fasting blood glucose and serum homocysteine levels at the time of diagnosis. Dyslipidaemias were defined as elevated LDL cholesterol (≥130 mg/dL), low HDL cholesterol (<40 mg/dL for men and <50 mg/dL for women) and elevated triglycerides (TG) (≥150 mg/dL) [16]. Visceral obesity was defined by the measurement of lipid accumulation product index (LAP). The LAP was calculated using the equations [17]: in men = [(WC-65) × TG], and in women = [(WC-58) × TG]. The equation: (hip circumference)/((height)$^{1.5}$) minus 18 was used to calculate Body Adiposity Index (BAI) as reported by Bergman et al [18]. The BAI greater than 21% and 33% were considered as high for men and women, respectively as did by Gallagher et al [19]. The study cases was characterized as the presence of OA, assessed by qualified clinician and radiological index using the standard Kellgren and Lawrence scale methods, including joint spatial narrowing; osteophyte formation; cyst presence within the subchondral bone; and bone margin sclerosis [20].

2.3. Blood Collection and Biochemical Analysis

Venous blood was aseptically obtained after an overnight fast (between 8-10 hours). The blood samples were centrifuged at 4,000 rpm for five minutes after which the plasma and serum were separated and stored frozen at -20°C until analysed. Total cholesterol, HDL-cholesterol, triglyceride, and glucose were determined by enzymatic methods using appropriate test kits (Dialab, Austria). The LDL-cholesterol was calculated using the Friedewald formula [21]. The serum homocysteine concentration was determined using solid-phase ELISA (Melsin Medical Co., China).

2.4. Data Analysis

We summarised continuous variables as mean and standard deviation and categorical variables as percentages. The t-test or chi-square used to compare cases and controls as needed. Unadjusted odds ratios were reported for the association of OA with each lipid and homocysteine. To further explore the variables for identification of independent factors associated with OA, forward conditional multivariate logistic regression was used, and it resulted in four models. All the variables that showed significant associations with OA at the bivariate analyses were included in generating the models. We used SPSS for Windows software (version 20) for all data analysis, with two-sided tests. P-values < 0.05 were considered statistically significant.

2.5. Ethical Considerations

The UI/UCH Research Ethics Committee reviewed and approved the study protocol (approval number: UI / EC/16/0370). Before enrolment, written informed consent was gotten from the participants. Voluntary participation in the research and their right to refuse was conveyed to the participants.

3. Results

3.1. Characteristics of Study Participants

The study population characteristics were as shown in Table 1. The distribution of study participants in cases and control was similar by sex, menopausal status among women, whether diabetic and hypertensive or not. Similarly, the mean values of age, weight, height, body mass index (BMI), waist and hip circumferences, systolic and diastolic blood pressure did not differ between cases and controls. However, the mean waist-to-hip ratio in cases was significantly higher than controls by 0.07 (95% CI = 0.04, 0.11); p<0.001.

3.2. Mean Values and differences in Plasma Lipids among Cases and Controls

Table 2 shows that the mean total cholesterol level was higher in cases than controls by 1.27 mmol/L (95% CI = 0.10, 1.63); p<0.001. Also, the mean low-density lipoprotein cholesterol (LDL-c) level in cases was significantly higher than controls by 1.25 mmol/L (95% CI = 0.91, 1.58); p = 0.001 (Table 2). Other markers of cardiovascular risk found relatively higher among cases than controls were TC/HDL ratio, LDL/HDL ratio,

TG/HDL ratio, lipid accumulation products (LAP), and body adiposity index (BAI) (Table 2). Conversely, the mean triglyceride, high-density lipoprotein cholesterol (HDL-c), fasting plasma glucose (FPG) and homocysteine values did not differ significantly between cases and controls as shown in Table 2.

Table 1. Characteristics of study population

Characteristics	Cases	Controls	p
Sex			
Male, n (%)	4 (10.0)	4 (10.0)	1.000
Female, n (%)	36 (90.0)	36 (90.0)	
Mean age ±SD	59.2 ±7.6	56.5 ±8.3	0.128
Menopause			
Yes	29 (80.6)	29 (80.6)	1.000
No	7 (19.4)	7 (19.4)	
Diabetes Mellitus			
Yes, n (%)	2 (5.0)	1 (2.5)	0.556
No, n (%)	38 (95.0)	39 (97.5)	
Mean Weight (kg)	65.7 ±13.2	68.4 ±13.4	0.367
Mean Height (cm)	1.57 ±0.7	1.58 ±0.09	0.356
BMI (kg/m^2)	26.9±5.6	27.2±5.1	0.749
Waist circumference (cm)	95.6±11.7	92.5±12.3	0.240
Hip circumference (cm)	100.5±10.6	104.9±11.3	0.074
Waist-to-hip ratio	0.95±0.08	0.88±0.08	<0.001
Mean Systolic BP	128.3 ± 14.1	130.7 ±18.3	0.580
Mean Diastolic BP	82.4 ±9.3	84.1 ±11.4	0.469
Hypertensive			
Yes, n (%)	14 (35.0)	9 (22.5)	0.217
No, n (%)	26 (65.0)	31 (77.5)	

Table 2. Mean values of plasma lipid, glucose and homocysteine

Cardiovascular Risk Factors	Cases (N=40)	Controls (N=40)	Mean diff. (95% CI)	p
TC (mmol/dL)	4.56±0.86	3.30±0.79	1.27 (0.10, 1.63)	0.000
HDL-C (mmol/dL)	1.15±0.40	1.31±0.23	-0.16 (-0.30. -0.02)	0.300
LDL-C (mmol/dL)	2.78±0.72	1.53±0.80	1.25 (0.91, 1.58)	0.001
TG (mmol/dL)	0.98±0.09	0.98±0.11	0.02 (-0.05, 0.04)	0.843
TC-HDL-c ratio	2.05±0.34	1.87±0.13	1.71 (1.23, 2.17)	<0.001
LDL-HDL ratio	4.28±1.30	2.57±0.72	1.44 (1.03, 1.86)	<0.001
TG-HDL-c ratio	2.67±1.14	1.22±0.69	0.18 (0.07, 0.30)	0.002
FPG (mmol/dL)	5.14±0.75	4.97±0.89	0.17 (-0.19, 0.53)	0.357
Homocysteine (µmol/L)	10.80±8.87	9.40±2.25	1.40 (-1.48, 4.28)	0.336
LAP	36.51±13.18	29.34 ±12.70	7.173 (1.41, 12.93)	0.015
Body adiposity index	33.57±7.04	24.94±6.79	8.63 (5.55, 11.71)	<0.001

TC: Total cholesterol, HDL: High-Density Lipoprotein cholesterol, LDL: Low-Density Lipoprotein cholesterol, FPG: Fasting plasma glucose, LAP – Lipid Adiposity Product

Table 3. Biophysical and risk factors among study participants

Cardiovascular Risk factors	Cases	Control	Unadjusted model		
	n (%)	n (%)	OR	95% CI	p
High waist circumference (cm)	36 (90.0)	32 (80.0)	2.25	0.62, 8.18	0.210
High waist-to-hip ratio	37 (92.5)	24 (60.0)	8.22	2.16, 11.27	0.001
Overweight/obese	25 (62.5)	24 (60.0)	1.11	0.45, 2.73	0.818
Hypertensive	14 (35.0)	9 (22.5)	1.86	(0.69, 4.97	0.217
Elevated TC	14 (35.0)	5 (12.5)	3.77	1.21, 11.78	0.018
Elevated LDLc	8 (20.0)	1 (2.5)	9.75	1.16, 32.11	0.013
Low HDL-c	18 (45.0)	2 (5.0)	15.55	3.29, 37.41	<0.001
Elevated Triglyceride	13 (32.5)	6 (15.0)	2.72	0.92, 8.13	0.066
High TC-HDL-c ratio	22 (55.0)	5 (12.5)	8.56	2.78, 26.35	<0.001
High LDL-HDL ratio	7 (17.5)	5 (12.5)	1.49	0.43, 5.14	0.531
High TG-HDLc ratio	16 (40.0)	7 (17.5)	3.14	1.12, 8.82	0.026
BAI >75th percentile	28 (70.0)	10 (25.0)	7.01	2.62, 18.73	<0.001
LAP >75th percentile	15 (37.5)	10 (25.0)	1.80	0.69, 4.70	0.228

TC: Total cholesterol, HDL-c: High-Density Lipoprotein cholesterol, LDL-c: Low-Density Lipoprotein cholesterol, TG: Triglyceride, FPG: Fasting plasma glucose, BAI: Body Adiposity Index, LAP: Lipid Adiposity Product
High waist circumference: WC ≥102 cm for males and ≥88 cm for females
High waist-to-hip ratio: ≥0.90 cm for males and ≥0.85 cm for women.

Table 4. Cardiovascular risk factors as predictors of osteoarthritis

		B	S.E.	Wald	df	p	AOR	95% CI
Model 1	LDL-C (mmol/dL)	1.80	0.37	23.69	1	<0.001	6.03	2.93, 12.43
	Constant	-3.91	0.87	20.28	1	<0.001	0.02	
Model 2	LDL-C (mmol/dL)	1.83	0.43	18.25	1	<0.001	6.21	2.69, 14.36
	BAI	0.20	0.06	11.35	1	<0.001	1.22	1.09, 1.36
	Constant	-9.66	2.23	18.69	1	0.001	0.00	
Model 3	Low HDL-C (mmol/dL)	2.23	1.01	4.85	1	0.028	9.31	1.28, 67.91
	LDL-C (mmol/dL)	1.55	0.42	13.34	1	<0.001	4.69	2.05, 10.76
	BAI	0.18	0.06	10.42	1	0.001	1.20	1.07, 1.34
	Constant	-9.17	2.14	18.40	1	<0.001	0.00	
Model 4	Low HDL-C (mmol/dL)	4.23	1.38	9.37	1	0.002	6.71	4.58, 10.31
	TC-HDL ratio	-3.89	1.64	5.63	1	0.018	0.02	0.01, 0.51
	LDL-C (mmol/dL)	3.03	0.87	12.06	1	0.001	5.68	3.74, 11.42
	BAI	0.24	0.07	11.38	1	0.001	1.27	1.11, 1.46
	Constant	-13.25	3.29	16.19	1	<0.001	0.00	

TC: Total cholesterol
HDL-c: High-Density Lipoprotein cholesterol,
LDL-c: Low-Density Lipoprotein cholesterol
BAI: Body Adiposity Index.

3.3. Association of Cardiovascular Risk and Osteoarthritis

Table 3 shows the proportion of study participants who have elevated cholesterol and increased values of potential cardiovascular risk factors among cases and controls. Notably, the odds of abnormal values were higher in cases than control with respect to high waist-to-hip ratio (OR = 8.22), elevated TC (OR = 3.77), elevated LDL-c (OR = 9.75), low HDL-c (OR = 15.55), high TC-HDL ratio (OR = 8.56), high TG-HDL ratio (OR = 3.14), high BAI (OR = 7.01) and high LAP (OR = 1.80). The conditional forward logistic regression analysis output suggests four models as shown in Table 4. Model 4 suggests that four cardiovascular risk factors were independently associated with osteoarthritis. These were low HDL-c (OR= 6.71; 95% CI = 4.58, 10.31), TC-HDL ratio (OR = 0.02; 95% CI = 0.01, 0.51), LDL-c (OR = 5.68; 95% CI = 3.74, 11.42) and BAI (OR = 1.27; 95% CI = 1.11, 1.46).

4. Discussion

This study demonstrated high waist-to-hip ratio, total cholesterol, LDL-c, TC-HDL-c ratio, LDL-HDL-c ratio, TG-HDL-c ratio, lipid accumulation index and body adiposity index but a lower level of HDL-c in OA patients. Conversely, the observed differences in the levels of TG, homocysteine and FPG were not significant. Overall, our findings suggest that OA patients in Nigeria have increased cardiovascular risk as low HDL-c, high ratio of total cholesterol to HDL, LDL-c and index of body adiposity. These patterns of cardiovascular risk have been demonstrated in some studies conducted in other populations, Caucasians [22]. To our knowledge, information on the links between OA and cardiovascular risks in the Nigeria population as well as sub-Saharan Africa are scarce in the literature.

Our findings suggest that OA and high cholesterols, as well as body adiposity, may share a common predisposition as previously mentioned [22]. Some previous observational studies have shown that OA and many cardiovascular diseases share some risk factors such as hypertension [23,24], diabetes [25], hypercholesterolemia [26], and obesity [27,28]. The finding of hypercholesterolaemia from our data agreed with reports by Raham et al [29] and Singhs et al [30]. However, Raham and colleagues [29] adopted a retrospective study design while Singhs and colleagues [30] used a longitudinal study design. On the other hand, our results disagree with some previous observational studies [31,32,33]. Two of these studies [31,33] were longitudinal while the other one [32] is cross-sectional in design. In particular, the Chingford study reported an association between OA and elevated TC in males but not females [32].

Although many studies have attempted to explain the relationship between OA and cardiovascular risks or diseases, the exact underlying mechanisms remained unclear. Many explanations are possible for this relationship. The presence of OA reduces affected person's physical activities and exercises, thus increasing their chance of developing cardiovascular problems including obesity. While adjustments for body mass index had been made in the present study, it is possible to explain this result by uncertainty attributable to some variables such as body circumferences. A reasonable alternative theory has also been suggested by Sayer and colleagues [34]. In a community-based study, Sayer and colleagues [34] studied the relationships between weight and hand OA. They confirmed that OA is associated with obesity and linked it with poor fetal growth and altered “programming” of the development of tissues.

Another explanation for the link between cardiovascular risk factors and OA is that key pathological features, including arterial thickening, stiffness, and atherosclerosis, which contribute to inadequate tissue perfusion (ischemia), are also responsible for decreasing bone cartilage nutrition and causing multiple bone infarctions. This effect of bone ischemia has been presented as an explanation for the association between OA and cardiovascular disease by many authors [34,35]. Moreover, some others have also assumed OA to be a result of altered lipid metabolism in

stromal-cell differentiation, thereby linking atheromatous vascular diseases with OA [35].

In this study, the body adiposity index, which is a component of metabolic syndrome, was an independent predictor of OA. Like metabolic syndrome, OA is characterized by an inflammatory vascular endothelial cell dysfunction capable of damaging cartilage and subchondral bones [36]. Also, it is known that obesity is associated with excess production of pro-inflammatory cytokine expression that can degrade enzymes and inhibit cartilage matrix synthesis leading to osteoarthritis [36]. A recent review of OA pathophysiology has shown that dietary lipid and the effects of dysfunctional fat producing excess adipokines such as leptin, resistin and visfatin increase OA risk by inducing proinflammatory mediators [37]. The authors also highlighted that other common metabolites like vitamin D interact with inflammatory mediators to impair cartilage and bone development [37].

The strength of our study lies in the fact that the diagnosis of OA was made based on clinical and radiologic features, which reduce the uncertainty of case ascertainment. Also, we matched cases and controls by sex and age. Our results were adjusted for potential confounding variables. However, the results of this study need to be interpreted bearing in mind the possible limitations. Since the study design makes it impossible to establish temporality, that is whether lipids abnormality preceded OA or not, further genetic linkage studies may be worthwhile to confirm if high LDL-c, low HDL-c or high body adiposity were innately present in our study population. Some of the information used to generate our data was self-reported by the research participants. This implies some potential recall bias. Nonetheless, we made a frantic effort to guide against information bias by cross-checking information collected against each patient's medical records. Finally, while our analyses have been adjusted for many confounders, we cannot rule out the influence of the fact that we did not gather evidence such as co-morbidity and the effects of drugs, including anti-inflammatory drugs and anti-hypertensive medicines.

5. Conclusion

This study demonstrated an increased risk of cardiovascular disease among adults with osteoarthritis in Nigeria. Given the increasing prevalence and incidence of osteoarthritis and cardiovascular disease among the population of developing countries, the relationship has clinical and public health significance. Clinicians, public health workers and policymakers must, therefore, emphasize routine cardiovascular risk screening and promote active risk-factors-based investigation during consultations and public health promotion exercises. Also, patients with osteoarthritis need to be encouraged to pay attention to potential cardiovascular risk factors such as indices of adiposity.

Competing Interests

The authors declare no conflict of interest.

Acknowledgements

The authors are grateful to Professor A. E. Orimadegun of the Institute of Child Health for assisting with data analysis and review of the draft of the manuscript.

Authors' Contributions

BEO conceived the study, review of the literature and wrote the first draft of the manuscript, RAO contributed to review of literature, study design and collection of data, SOO and AAF identified the participants and established diagnosis while EOA supervised all activities. All the authors contributed to the writing, edited and approved the final version of the manuscript.

References

[1] Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Organ*. 2003; 81: 646-56.

[2] McDonough CM, Jette AM. The contribution of osteoarthritis to functional limitations and disability. *Clin Geriatr Med*. 2010; 26: 387-99.

[3] Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. *Best Pract Res Clin Rheumatol*. 2014; 28: 5-15.

[4] Allen KD, Golightly YM. Epidemiology of osteoarthritis: state of the evidence. *Curr Opin Rheumatol*. 2015; 27: 276.

[5] WHO. Chronic rheumatic conditions. Chronic diseases and health promotion. Geneva: World Health Organization; 2000.

[6] United Nation. WORLD POPULATION TO 2300 New York: Department of Economic and Social Affairs, Population Division, United Nation; 2004.

[7] Maetzel A, Li LC, Pencharz J, Tomlinson G, Bombardier C, Community H, Arthritis Project Study T. The economic burden associated with osteoarthritis, rheumatoid arthritis, and hypertension: a comparative study. *Ann Rheum Dis*. 2004; 63: 395-401.

[8] Yoshimura N, Muraki S, Oka H, Tanaka S, Kawaguchi H, Nakamura K, Akune T. Accumulation of metabolic risk factors such as overweight, hypertension, dyslipidaemia, and impaired glucose tolerance raises the risk of occurrence and progression of knee osteoarthritis: a 3-year follow-up of the ROAD study. *Osteoarthritis Cartilage*. 2012; 20: 1217-26.

[9] Kluzek S, Newton JL, Arden NK. Is osteoarthritis a metabolic disorder? *British Medical Bulletin*. 2015; 115: 111-21.

[10] Fernandes GS, Valdes AM. Cardiovascular disease and osteoarthritis: common pathways and patient outcomes. *Eur J Clin Invest*. 2015; 45: 405-14.

[11] Gandhi R, Razak F, Tso P, Davey JR, Mahomed NN. Asian ethnicity and the prevalence of metabolic syndrome in the osteoarthritic total knee arthroplasty population. *J Arthroplasty*. 2010; 25: 416-9.

[12] Ogbu V, Enweani U, Madu K, Iyidobi E. Prevalence and pattern of osteoarthritis of the knee at National Orthopaedic Hospital Enugu. *Niger J Med*. 2016; 25: 336-40.

[13] Ibrahim D, Borodo M, Adelowo O. Clinical pattern of knee osteoarthritis in patients seen at rheumatology clinic of Aminu Kano Teaching Hospital, Northwestern Nigeria. *Afr J Rheumatol* 2014; 2: 13-7.

[14] Yerima A, Adelowo O, Mustapha S. Prevalence and pattern of knee osteoarthritis in patients presenting at a rheumatology clinic of a tertiary hospital in north east Nigeria. *Afr J Rheumatol*. 2018; 6: 34-40.

[15] Visser AW, de Mutsert R, le Cessie S, den Heijer M, Rosendaal FR, Kloppenburg M, Group NEOS. The relative contribution of mechanical stress and systemic processes in different types of osteoarthritis: the NEO study. *Ann Rheum Dis*. 2015; 74: 1842-7.

[16] Giles TD, Berk BC, Black HR, Cohn JN, Kostis JB, Izzo Jr. JL, Weber MA. Expanding the Definition and Classification of Hypertension. *The Journal of Clinical Hypertension*. 2005; 7: 505-12.

[17] Onat A, Avci GS, Barlan MM, Uyarel H, Uzunlar B, Sansoy V. Measures of abdominal obesity assessed for visceral adiposity and relation to coronary risk. *Int J Obes Relat Metab Disord*. 2004; 28: 1018-25.

[18] Bergman RN. A better index of body adiposity. *Obesity (Silver Spring)*. 2012; 20: 1135.

[19] Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC, Jr., Spertus JA, Costa F, American Heart A, National Heart L, Blood I. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005; 112: 2735-52.

[20] Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957; 16: 494-502.

[21] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972; 18: 499-502.

[22] Wang H, Bai J, He B, Hu X, Liu D. Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies. *Sci Rep*. 2016; 6: 39672.

[23] Puenpatom RA, Victor TW. Increased prevalence of metabolic syndrome in individuals with osteoarthritis: an analysis of NHANES III data. *Postgrad Med*. 2009; 121: 9-20.

[24] Conaghan PG, Vanharanta H, Dieppe PA. Is progressive osteoarthritis an atheromatous vascular disease? *Annals of the rheumatic diseases*. 2005; 64: 1539-41.

[25] Louati K, Vidal C, Berenbaum F, Sellam J. Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. *RMD open*. 2015; 1: e000077.

[26] Zhang YM, Wang J, Liu XG. Association between hypertension and risk of knee osteoarthritis: A meta-analysis of observational studies. *Medicine (Baltimore)*. 2017; 96: e7584.

[27] Yusuf E, Nelissen RG, Ioan-Facsinay A, Stojanovic-Susulic V, DeGroot J, van Osch G, Middeldorp S, Huizinga TW, Kloppenburg M. Association between weight or body mass index and hand osteoarthritis: a systematic review. *Annals of the rheumatic diseases*. 2010; 69: 761-5.

[28] Jiang L, Tian W, Wang Y, Rong J, Bao C, Liu Y, Zhao Y, Wang C. Body mass index and susceptibility to knee osteoarthritis: a systematic review and meta-analysis. *Joint Bone Spine*. 2012; 79: 291-7.

[29] Rahman MM, Kopec JA, Anis AH, Cibere J, Goldsmith CH. Risk of cardiovascular disease in patients with osteoarthritis: a prospective longitudinal study. *Arthritis Care Res (Hoboken)*. 2013; 65: 1951-8.

[30] Singh G, Miller JD, Lee FH, Pettitt D, Russell MW. Prevalence of cardiovascular disease risk factors among US adults with self-reported osteoarthritis: data from the Third National Health and Nutrition Examination Survey. *Am J Manag Care*. 2002; 8: S383-91.

[31] Martin K, Lethbridge-Cejku M, Muller DC, Elahi D, Andres R, Tobin JD, Hochberg MC. Metabolic correlates of obesity and radiographic features of knee osteoarthritis: data from the Baltimore Longitudinal Study of Aging. *J Rheumatol*. 1997; 24: 702-7.

[32] Hart DJ, Doyle DV, Spector TD. Association between metabolic factors and knee osteoarthritis in women: the Chingford Study. The Journal of rheumatology. 1995; 22: 1118-23.

[33] Ong KL, Wu BJ, Cheung BM, Barter PJ, Rye KA. Arthritis: its prevalence, risk factors, and association with cardiovascular diseases in the United States, 1999 to 2008. Ann Epidemiol. 2013; 23: 80-6.

[34] Sayer AA, Poole J, Cox V, Kuh D, Hardy R, Wadsworth M, et al. Weight from birth to 53 years: a longitudinal study of the influence on clinical hand osteoarthritis. Arthritis Rheum. 2003; 48: 1030-3.

[35] Aspden RM, Scheven BA, Hutchison JD. Osteoarthritis as a systemic disorder including stromal cell differentiation and lipid metabolism. The Lancet. 2001; 357: 1118-20.

[36] Zhuo Q, Yang W, Chen J, Wang Y. Metabolic syndrome meets osteoarthritis. Nat Rev Rheumatol. 2012; 8: 729-37.

[37] Wang X, Hunter D, Xu J, Ding C. Metabolic triggered inflammation in osteoarthritis. Osteoarthritis Cartilage. 2015; 23: 22-30.