ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ*) 2022, Volume 11, Number 3: 1103-1106
P-ISSN.2089-1180, E-ISSN: 2302-2914

Association between metabolic syndrome and knee osteoarthritis

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Received: 2022-06-25
Accepted: 2022-08-05
Published: 2022-09-09

ABSTRACT

Introduction: The inflammatory process underlies either osteoarthritis (OA) or metabolic syndrome. Systemic inflammation that occurs in the metabolic syndrome will result in the production of inflammatory cytokines and activation of macrophages and chondrocytes. This can affect the entire body including joints and the surrounding tissues, causing OA. Type 2 Diabetes Mellitus (DMT2) and hypertension are the first and second most common metabolic syndrome components found in OA patients. This study aimed to determine the relationship between metabolic syndrome and knee OA in DMT2 patients with hypertension.

Methods: By using an analytic observational method and cross-sectional design, this study involved the medical records of patients with DMT2. The sample consisted of 50 medical records selected by using the purposive sampling technique and fulfilling the inclusion and exclusion criteria.

Results: This study involved 25 medical records of patients with and without knee (genu) OA. The characteristics of the sample were as follows: 1 medical record of patient aged 36-45 years, 18 medical records of patients aged 46-55 years, 16 medical records of patients aged 56-65 years, 15 medical records of patients aged > 65 years, 21 medical records of male patients, 29 medical records of female patients, 27 medical records with metabolic syndrome, and 23 medical records without metabolic syndrome. The association between metabolic syndrome and knee (genu) OA was analyzed by using the Chi-Square Test using the SPSS application, where the results showed a significance value of $p < 0.05$ ($p = 0.001$).

Conclusion: This study shows that there is a significant association between metabolic syndrome and knee (genu) OA.

Keywords: knee (genu) osteoarthritis, type 2 diabetes mellitus, hypertension, metabolic syndrome.
Cite This Article: Savitri, A.D., Veterini, L., Widyaswari, M.S., Abdillah, D.S. 2022. Association between metabolic syndrome and knee osteoarthritis. *Bali Medical Journal* 11(3): 1103-1106. DOI: 10.15562/bmj.v11i3.3454

INTRODUCTION

Osteoarthritis (OA) is a degenerative disease that attacks the joints and surrounding components, which include cartilages, joint lining, ligaments, and bones, causing pain, stiffness, and swelling in joints.[1,2] Based on its pathogenesis, OA is divided into two groups, namely primary and secondary OA.[3] The cause of primary OA is unknown, whereas secondary OA is associated with joint overuse, strenuous exercise, history of injury, systemic diseases, or inflammation.[4]

Osteoarthritis occurs because chondrocytes are unable to synthesize a quality matrix. There is chondrocytes failure to maintain homeostasis between degradation and synthesis of extracellular matrix components. It includes excessive production of collagen type I, III, VI, and X and short proteoglycan synthesis. The failure of chondrocytes results in changes in the diameter and orientation of the collagen fibers causing changes in cartilage biomechanics and loss of unique cartilage compressibility.[5] Apart from chondrocytes, synoviocytes also play a role in the pathogenesis of OA. Inflamed synoviocytes will produce matrix metalloproteinases (MMPs) and various cytokines which are released into the joint cavity and damage the cartilage matrix of the joints and activate chondrocytes. In the end, the subchondral bone will also play a role, in which osteoblasts will be stimulated and produce proteolytic enzymes.[5,6]

Metabolic syndrome is a group of symptoms consisting of central obesity, high blood pressure (pre-hypertension or hypertension), dyslipidemia (increased levels of cholesterol, especially LDL, triglycerides and low HDL levels), disorders of insulin resistance and diabetes mellitus (DM), as well as microalbuminuria (urea albumin excretion rate of more than 20 mg/min or an albumin/creatinine ratio of more than 30 mg/g).[7] According to the WHO criteria (1999), the metabolic syndrome diagnosis emphasize impaired glucose tolerance or DM, and/or insulin resistance accompanied by at least two other risk factors, such as hypertension, dyslipidemia, central obesity and microalbuminuria.[8]

Several studies have shown an independent association between OA and several component of the metabolic syndrome.[9] This is indicated by the large number of hypertensive and type 2 DM patients who experience OA in the knee (genu). The association between OA and type 2 DM has also been extensively studied. OA and type 2 diabetes are said to have associated with risk factors; one of which is obesity. It is confirmed by

Purnomo's research conducted at Dr. Kariadi Hospital, Semarang which proved that the most musculoskeletal disorders in DM patients were knee (genu) OA, namely 53.3%.[10] A research conducted by Riska Juliana proved that the highest proportion of other diseases that can be found in OA sufferers was hypertension (29.2%). However, the association between OA and hypertension still generated conflicting results.[11]

Systemic inflammation that occurs in metabolic syndrome is thought to play a role in the occurrence of knee (genu) OA through polarization of macrophages and changes in chondrocytes. This study aimed to determine the relationship between metabolic syndrome and knee OA in DMT2 patients with hypertension.

METHODS

Study Design dan Data Collection

This is an observational analysis study with a cross sectional approach aimed at identifying the association between metabolic syndrome and knee (genu) osteoarthritis. The study was conducted at the Medical Record Unit of RSI Jemursari Surabaya (Jemursari Islamic Surabaya Hospital) by involving a population of type 2 diabetes mellitus patients' with hypertension medical records. The inclusion criteria were the medical records of DMT2 patients who were treated at the Department of Internal Medicine, RSI Jemursari Surabaya in 2019 aged 36-70 years. On the other hand, the exclusion criteria consisted of the medical records of patients with a history of knee trauma, or a history of knee joint arthroplasty.

Data Analysis

The independent variable was metabolic syndrome, whereas the dependent variable was knee (genu) osteoarthritis. Diagnosis of knee (genu) OA, type 2 diabetes mellitus and hypertension were based on the patient's diagnosis stated in the medical records. Whilst, the metabolic syndrome was based on the concurrent diagnosis of type 2 diabetes mellitus and hypertension in one patient's medical record. The association between metabolic syndrome and knee (genu) OA was analyzed using the Chi-Square test.

RESULTS

This study involved 25 medical records with knee (genu) OA and 25 medical records without knee (genu) OA. The results obtained 21 males' medical records (42%) and 29 females' medical records (58%). Based on age, the results obtained 1 medical record of a patient aged 36-45 years (2%), 18 medical records of patients aged 46-55 years (36%), 16 medical records of patients aged 56-65 years (32%), and 15 medical records of patients aged more than 65 years (30%).

From the 50 medical records, there were 27 records with metabolic syndrome (54%) and 23 medical records without metabolic syndrome (46%). The distribution of metabolic syndrome based on sex showed that 13 medical records were males (48.1%) and 14 medical records were females (51.9%) as shown in table 1.

From the 50 medical records, there were 25 medical records with knee (genu) OA (50%) and 25 medical records without knee (genu) OA (50%). The distribution of knee (genu) OA based on sex resulted in 9 medical records of males with knee (genu) OA (36%) and 16 medical records with knee (genu) OA in females (64%) as shown in table 2.

Based on the age group, metabolic syndrome was most found in the age group of 56 - 65 years old, namely 10 medical records (37%). The distribution of the metabolic syndrome by age group is shown in Figure 1 below.

Based on the age group, most cases of knee (genu) OA were found in the age group of 56 - 65 years old, namely 10 medical records (40%). The distribution of knee (genu) OA was shown in Figure 2 below.

The association between knee (genu) OA and metabolic syndrome was tested using the Chi-Square test. Using the SPSS statistics, the result showed a significance value of p 0.001 (<0.05), illustrating that there was a significant association between metabolic syndrome and knee (genu) OA, as seen in table 3 below.

DISCUSSION

Osteoarthritis (OA) is a degenerative joint disease associated with joint cartilage damage. It is a major cause of pain and disability in society globally. According to a study conducted by the Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) in Asia, the prevalence of OA is found to increase following the age and more prevalent in women.[12] Therefore, OA generally occurs in the elderly.

Based on its location, OA generally affects the weight-bearing joints, especially the knee, coxae, lumbar and cervical joints. The knee is the main predilection joint in OA. Based on the data from the World Health Organization (WHO), 40% of the population aged over 70 have knee OA.[13] The data from Arthritis Research Campaign in 2000 showed that knee OA is the reason for 2 million patients to seek treatment at general practitioners or hospitals.[14]

Obesity, hypertension, dyslipidemia, and insulin resistance or type 2 diabetes are

Table 1. The distribution of metabolic syndrome based on sex.

Sex	With Metabolic Syndrome	%	Without Metabolic Syndrome	%	Total
Males	13	48,1	8	34,8	21
Females	14	51,9	15	65,2	29
Total	27	100	23	100	50

Table 2. The distribution of OA based on sex.

Sex	With OA	%	Without OA	%	Total	%
Males	9	36	12	48	21	42
Females	16	64	13	52	29	58
Total	25	100	25	100	50	100

components of the metabolic syndrome. In this study, only 2 components were used to diagnose the metabolic syndrome, namely hypertension and type 2 diabetes. Both are the first and second most common metabolic syndrome components found in OA patients. A large number of hypertensive and type 2 DM patients experience OA in the knee (genu). Moreover, OA, hypertension, and type 2 diabetes have related risk factors and similar pathogenesis processes, which included inflammation process, oxidative stress, and endothelial dysfunction.[15]

Hyperglycemia is able to induce pro-inflammatory state resulting in the deposition of glycation end products in the joints (advanced glycation end products; AGE) in DM patients. Through the activation of macrophages and pro-inflammatory cytokines production, changes occur in chondrocytes and stimulate the synovial fibrosis process, which is the most important step in the pathomechanism of OA.[16,17]

On the other hand, hypertension causes occlusion and stasis of blood flow in the subchondral vessels.[13] These results subchondral ischemia and degradative changes in cartilages which are potential initiators of cartilage changes in OA.[18]

Finding patients with metabolic syndrome involving the two components mentioned above will increase the risk of knee (genu) OA. It is seen in the results of this study where there was a significant association between metabolic syndrome and knee (genu) OA with a significance value of p 0.001.

Local inflammation has been proven to result in cartilage degradation and activation of synovial cells. This will result in physiological and anatomical changes in the knee.[15] Similar with local inflammation, systemic process is thought having the same effect to knee. Pro-inflammatory mediators produced by adipose tissue can reach the joints via subchondral blood vessels which then will initiate the occurrence of knee (genu) OA in patient.[19]

The research conducted by Wang, et al. in 2016 proved that metabolic syndrome not only increased the risk of knee (genu) OA, but also disease progression and prognosis.[18] Yoshimura, et al. also stated that the accumulation of metabolic syndrome components in a patient was related to the incidence and progression of knee (genu) OA.[20]

This study had several weaknesses, including the use of secondary data from medical records, so that the data obtained were not optimal. On the other hand, the sample used in this study was too small and the use of purposive sampling technique, resulting in less variation in the data. Further studies are expected to use primary data with a larger sample size so as to provide more informative and varied data. The association between accumulation of metabolic syndrome components with the incidence and progression of knee (genu) OA has been proven in this study, but it is also advisable to carry out further studies involving other components of the metabolic syndrome to strengthen and increase the evidences of the association between metabolic syndrome and knee (genu) OA.

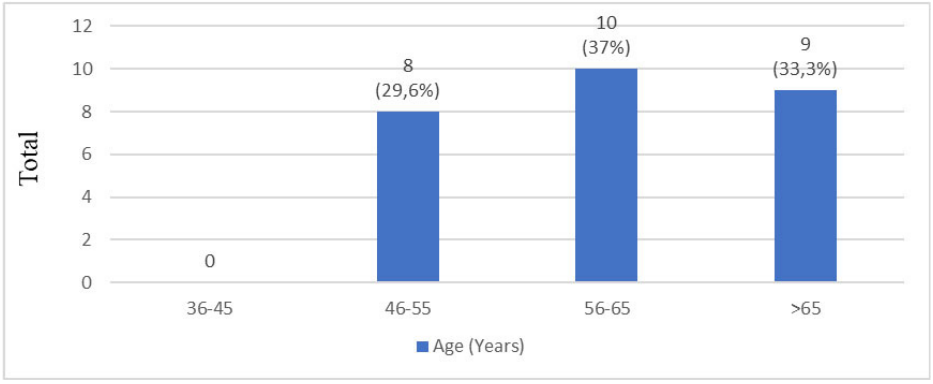

Figure 1. The distribution of metabolic syndrome by age group.

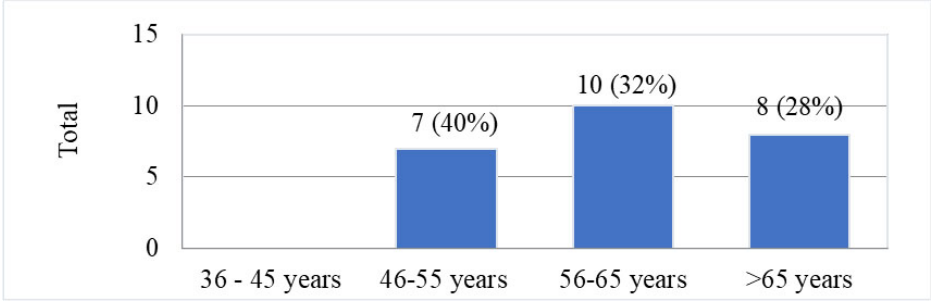

Figure 2. The distribution of knee (*genu*) OA based on age group.

Table 3. The association between knee (genu) OA and metabolic syndrome.

Knee OA	Metabolic Syndrome				Total		P (significance)
	Yes		No				
	N	%	N	%	N	%	
Yes	20	80	5	20	25	100	0,001 (<0,05)
No	7	28	18	72	25	100	
Total	27	54	23	46	50	100	

CONCLUSION

In this study, a significant association was obtained between metabolic syndrome and knee (genu) OA in type 2 DM patients with hypertension at RSI Jemursari Surabaya, in which the significance value of p <0.05 (p = 0.001) is obtained. Further studies need to be conducted to determine the association between knee (genu) OA and other components of the metabolic syndrome by using primary data, so that other risk factors for knee (genu) OA can be identified in patients.

FUNDING

The authors are responsible for all of the study funding without a grant or any external funding source.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTION

All authors similarly contribute to the think about from the investigate concepts, information acquisitions, information investigation, factual investigations, changing the paper, until detailing the consider comes about through publication.

ETHICAL CONSIDERATION

The investigators agreed to conduct this study in full agreement with the principles of the Declaration of Helsinki' and its subsequent related amendments. This study was approved by the Ethics Committee of the Surabaya Islamic Hospital. Letter of exemption Ref. No. 1213/EC.KEPK/UMS/2020.

ACKNOWLEDGMENTS

We would like to extend our simcere gratitude and appreciation to RSI Jemursari Teaching Hospital which has permitted and supported this research. All authors take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published.

REFERENCES

1. CDC (Centers of Desease Control and Prevention). Osteoarthritis (OA) [Internet]. 2019. Available from: https://www.cdc.gov/arthritis/basics/osteoarthritis.htm
2. Tjokroprawiro, A., Setiawan, P. B., Effendi, C., & Santoso D. Buku Ajar Ilmu Penyakit Dalam. In A. Tjokroprawiro, P. B. Setiawan, C. Effendi, & D. Santoso (Eds.). 2nd ed. Airlangga University Press.; 2015.
3. Felix Bronner and Mary C. Farach-Carson. Bone and Osteoarthritis. Bone and Osteoarthritis. London : Springer,; 2007.
4. Davey P. At a Glance Medicine - Google Books [Internet]. Erlangga; 2012. 383 p. Available from: https://www.google.co.id/books/edition/At_a_Glance_Medicine/wzIGJflmD4gC?hl=id&gbpv=1&dq=osteomielitis+adalah&pg=PA383&printsec=frontcover
5. Basaran S, Guzel R, Seydaoglu G, Guler-Uysal F. Validity, reliability, and comparison of the WOMAC osteoarthritis index and Lequesne algofunctional index in Turkish patients with hip or knee osteoarthritis. Clin Rheumatol. 2010 Jul;29(7):749–56.
6. Yanuarty M, Suntoko B. Hubungan Antara Faktor Risiko Osteoartritis Lutut Dengan Nyeri, Disabilitas, Dan Berat Ringannya Osteoartritis. J Kedokt Diponegoro. 2014;3(1):111411.
7. Wulandari, M. Y., & Isfandiar MA. Kaitan sindroma metabolik dan gaya hidup dengan gejala komplikasi mikrovaskuler. J Berk Epidemiol. 2013;1:224–33.
8. Rini. Sindrom Metabolik. J Major [Internet]. 2015;4(4):88–93. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Sindrom+Metabolik#1
9. Courties A, Sellam J, Berenbaum F. Metabolic syndrome-associated osteoarthritis. Curr Opin Rheumatol. 2017 Mar;29(2):214–22.
10. Purnomo, Hery Djagat (Program Pendidikan Dokte Spesialis-1 BIPDFUD. Gangguan Musculoskeletal pada Penderita Diabetes Melitus di RSUP Dr. Kariadi Semarang. 2002.
11. Juliana R. Karakteristik Penderita Osteoartritis Rawat Jalan Di Rsud Dr.Pirngadi Medan Tahun 2015. Unversitas Sumatra Utara. 2015;
12. Haq SA, Davatchi F. Osteoarthritis of the knees in the COPCORD world. Int J Rheum Dis. 2011;14(2):122–9.
13. Baumbach L, Roos EM, Lykkegaard J, Thomsen KS, Kristensen PL, Christensen AI, et al. Patients with osteoarthritis are least likely to receive lifestyle advice compared with patients with diabetes and hypertension: A national health survey study from Denmark. Osteoarthr Cartil Open [Internet]. 2020;2(3):100067. Available from: https://doi.org/10.1016/j.ocarto.2020.100067
14. Prawati. Faktor-faktor Risiko Osteoartritis Lutut. Tesis [Internet]. 2017; Available from: http://eprints.undip.ac.id/17308/1/Eka_Pratiwi_Maharani.pdf
15. Abdillah DS, Savitri AD, . E. Correlation of Metabolic Syndrome With Genu Osteoarthritis in Type 2 Diabetes Mellitus Patients. Curr Intern Med Res Pract Surabaya J. 2022;3(1):1.
16. Santoso A. Hubungan Kendali Glukosa Darah dengan Osteoartritis Lutut pada Pasien DM di RSD Dr. Soebandi (The Relationship between Blood Glucose Control and Knee Osteoarthritis in DM Patients at Dr. Soebandi Hospital). In 2014.
17. Rahman MM, Cibere J, Anis AH, Goldsmith CH, Kopec JA. Risk of Type 2 Diabetes among Osteoarthritis Patients in a Prospective Longitudinal Study. Int J Rheumatol. 2014;2014:620920.
18. Wang H, Cheng Y, Shao D, Chen J, Sang Y, Gui T, et al. Metabolic Syndrome Increases the Risk for Knee Osteoarthritis: A Meta-Analysis. Evid Based Complement Alternat Med. 2016;2016:7242478.
19. Dickson BM, Roelofs AJ, Rochford JJ, Wilson HM, De Bari C. The burden of metabolic syndrome on osteoarthritic joints. Arthritis Res Ther. 2019 Dec;21(1):289.
20. Yoshimura N, Muraki S, Oka H, Tanaka S, Kawaguchi H, Nakamura K, et al. 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. Osteoarthr Cartil. 2012 Nov;20(11):1217–26.