



## Cross-sectional Study

# Association between diabetes mellitus, hypertension, and knee osteoarthritis in secondary referral hospitals in Indonesia with retrospective cross-sectional study



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## ABSTRACT

**Introduction:** Osteoarthritis is a disease with degenerative joints. There are some risk factors for osteoarthritis, including age, gender, diabetes mellitus, smoking, and hypertension. The previous study also showed a relationship between osteoarthritis and diabetes mellitus. Besides diabetes mellitus, hypertension may be a risk factor for osteoarthritis. However, research about the relationship between diabetes mellitus and hypertension based on the degree of osteoarthritis is still controversial. This study aims to determine the association between diabetes mellitus and hypertension with the severity of knee osteoarthritis in general and based on gender.

**Methods:** This research used a retrospective cross-sectional research study with a sample size of 35 patients in Orthopaedic and Traumatology in East Java, who suffered from knee osteoarthritis. Data was collected with medical records, the questionnaire, and the Kellgren & Lawrence system to assess the grade of knee osteoarthritis.

**Results:** The Chi-Square test results showed no significant relationship ( $p > 0.05$ ) between diabetes mellitus and hypertension on the severity of osteoarthritis, both in general and by gender.

**Conclusion:** This study concludes that there is no association between diabetes mellitus and hypertension on the severity of knee osteoarthritis between male and female patients.

## 1. Introduction

Osteoarthritis is a disease with degenerative joints related to the cartilage [1]. Patients with osteoarthritis will experience pain, stiffness, and swelling, limiting their ability to do daily activities [2]. Clinically, knee osteoarthritis is one of the most common types of osteoarthritis, followed by hand and hip osteoarthritis. There are around 654.1 million individuals (40 years and older) with knee osteoarthritis in 2020 worldwide. According to 2018 data [3], the prevalence of osteoarthritis in Indonesian females and males reached 8.5% and 6.1%, respectively.

There are some risk factors for osteoarthritis that are categorized as non-modifiable factors and modifiable factors. Non-modifiable factors consist of age, disability or imbalance in the body, and gender. And for

the modifiable factors, such as hypercholesterolemia, diabetes mellitus, body mass index (BMI), smoking, and hypertension [4]. A higher prevalence of osteoarthritis was reported among patients with metabolic syndrome and diabetes mellitus, which was predicted to be an independent predictor of osteoarthritis. Hyperglycemia and osteoarthritis have interactions at both local and systemic levels. As a result of hyperglycemia, low-grade glyceemic inflammation contributes to a toxic internal environment that exacerbates osteoarthritis. Another reason for osteoarthritis and diabetes mellitus was diabetic peripheral neuropathy causes muscle weakness and joint laxity [5].

Hypertension is a common disease among the elderly (those over the age of 60), accounting for 63.5% of all cases [6]. In the survey community, the prevalence of osteoarthritis in females was three times that

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of males, and hypertension was associated with knee osteoarthritis. Based on an analysis of females aged 45–64 years [7], there was a significant association between osteoarthritis and metabolic syndrome, including hyperglycemia and hyperlipidemia. Conventional studies have suggested that another component of metabolic syndromes, such as hypertension, may be an independent risk factor for knee osteoarthritis [8].

Research about the relationship between diabetes mellitus and hypertension based on the severity of osteoarthritis is limited and still controversial. Therefore, the goal of the study is to determine the association between diabetes mellitus and hypertension with the severity of knee osteoarthritis in general and based on gender. The hypothesis in this study is that there was an association between diabetes mellitus and hypertension with the severity of knee osteoarthritis.

## 2. Patients and methods

### 2.1. Patients and study design

This research used a retrospective cross-sectional study from April to May 2020. The population in this research were patients who suffered from knee osteoarthritis in Orthopaedic and Traumatology Secondary Referral Hospital in East Java.

The inclusion criteria were patients who suffer from knee osteoarthritis are confirmed by radiological examination and willing to be interviewed, and the exclusion criteria were patients who suffer from pain in the knees that is caused by another disease, and patients with no or incomplete medical records, and patients who suffer from osteoarthritis degree 0. This study proposal has been reviewed and approved by the ethical committee from the Faculty of Medicine, Universitas Brajijaya, as mentioned in the ethical clearance certificate No 73/EC/KEPK/03/2020.

### 2.2. Methods

Data about age, gender, medical history about diabetes mellitus and hypertension were collected with a questionnaire and medical records. The Kellgren & Lawrence system to assess the grade of knee osteoarthritis. There are several grades in the Kellgren-Lawrence system: grades 0–4 (none, doubtful, minimal, moderate, and severe) [9]. This method has been reported in line with the STROCSS criteria [10].

### 2.3. Statistical analysis

The data in this research was analyzed using the Chi-square correlation test to determine the association between two variables based on the Kallgren-Lawrence system with the  $p < 0.05$ . This research hypothesizes that there would be an association between diabetes mellitus and hypertension to the severity of knee osteoarthritis in general and based on gender.

## 3. Results

Among 35 patients with knee osteoarthritis, 10 (28.6%) were males and 25 (71.4%) were females (Table 1). Three patients (8.6%) were aged <45 years and 32 patients (91.4%) were aged >45 years. Six patients (17.1%) suffered from osteoarthritis grade 1, 12 patients (34.3%) grade 2 and 17 patients (48.7%) grade 3. Sixteen patients (45.7%) suffered from hypertension and 19 patients (54.3%) did not suffer from hypertension. Nine patients (25.7%) with diabetes mellitus and 26 patients (74.3%) did not suffer from diabetes mellitus (Table 1).

Among 16 patients with hypertension, two patients (12.5%) had osteoarthritis grade 1, five patients (31.3%) grade 2, and nine patients (56.3%) grade 3. From 19 patients with no hypertension, four patients (21.1%) had osteoarthritis grade 1, seven patients (36.8%) grade 2, and eight patients (41.1%) grade 3 (Table 2).

**Table 1**  
General osteoarthritis distribution.

Characteristic	n	%	
Age	<45	3	8.6
	>45	32	91.4
	Total	35	100
Gender	Male	10	28.6
	Female	25	71.4
	Total	35	100
Grade of osteoarthritis	Grade 1	6	17.5
	Grade 2	12	34.3
	Grade 3	17	48.6
	Total	35	100
Hypertension	Yes	16	45.7
	No	19	54.3
	Total	35	100
Diabetes mellitus	Yes	9	25.7
	No	26	74.3
	Total	35	100

**Table 2**  
Osteoarthritis distribution to hypertension.

Grade of osteoarthritis	Hypertension		No hypertension	
	n	%	n	%
Grade 1	2	12.5	4	21.1
Grade 2	5	31.3	7	36.8
Grade 3	9	56.3	8	42.1
Total	16	100	19	100

Among nine patients with diabetes mellitus, one patient suffered from knee osteoarthritis grade 1, three patients (33.3%) grade 2, and five patients (56.5%) grade 3. From 26 patients with no diabetes mellitus, five patients (19.2%) with osteoarthritis grade 1, nine patients (34.6%) grade 2, and 12 patients (46.2%) grade 4 (Table 3).

Among seven patients who suffered from diabetes mellitus and hypertension, one patient had osteoarthritis grade 1, and three patients (42.9%) had grade 2 and grade 3, respectively. Two patients who suffered from diabetes mellitus but with no hypertension also suffered from osteoarthritis grade 3. Among nine patients who suffered from hypertension with no diabetes mellitus, one patient had osteoarthritis grade 1, two patients (22.2%) grade 2, and six patients (66.6%) grade 3. From 17 patients with no hypertension and no diabetes mellitus, four (23.5%) suffered from osteoarthritis grade 1, seven patients (41.2%) grade 2, and six patients (35.3%) grade 3 (Table 4). There was no significant relationship between diabetes mellitus in males ( $p = 0.082$ ) and females ( $p = 0.564$ ) (Table 5). And also there was no significant relationship between hypertension in males ( $p = 0.221$ ) and females ( $p = 0.847$ ) (Table 6).

## 4. Discussion

This research uses a retrospective cross-sectional study with 35 respondents. Based on the results of the study, the distribution of respondents by age showed that most of the respondents were elderly people who were more than 45 years old, and there were 32 patients (91.4%). These results are similar to the research of Subroto et al. [11],

**Table 3**  
Osteoarthritis distribution to diabetes mellitus.

Grade of osteoarthritis	Diabetes mellitus		No diabetes mellitus	
	n	%	n	%
Grade 1	1	12.1	5	19.2
Grade 2	3	33.3	9	34.6
Grade 3	5	55.6	12	46.2
Total	9	100	26	100

**Table 4**  
The relationship between diabetes mellitus and hypertension to the degree of osteoarthritis.

Diabetes mellitus	Hypertension	Grade of osteoarthritis						Total	
		Grade 1		Grade 2		Grade 3			
		n	%	n	%	n	%	n	%
Yes	Yes	1	14.3	3	42.9	3	42.9	7	20
	No	0	0	0	0	2	100	2	5.7
No	Yes	1	11.1	2	22.2	6	66.7	9	25.7
	No	4	23.5	7	41.2	6	35.3	17	48.6

**Table 5**  
Chi-square analyze in diabetes mellitus to a degree of osteoarthritis based on gender.

Gender	Diabetes mellitus	Grade of osteoarthritis						Total		P-value
		Grade 1		Grade 2		Grade 3				
		n	%	n	%	n	%	n	%	
Male	Yes	0	0	2	50	2	50	4	100	0.082
	No	3	50	0	0	3	50	6	100	
Female	Yes	1	20	1	20	3	60	5	100	0.564
	No	2	10	9	45	9	45	20	100	
Total	Yes	1	11.1	3	33.3	5	55.6	9	100	0.826
	No	5	19.2	9	34.6	12	46.2	26	100	

**Table 6**  
Chi-square analysis in hypertension to the degree of osteoarthritis based on gender.

Gender	Hypertension	Grade of osteoarthritis						Total		P-value
		Grade 1		Grade 2		Grade 3				
		n	%	n	%	n	%	n	%	
Male	Yes	1	14.3	2	28.6	4	57.1	7	100	0.221
	No	2	66.7	0	0	1	33.3	3	100	
Female	Yes	1	11.1	3	33.3	5	55.6	9	100	0.847
	No	2	12.5	7	43.8	7	43.8	16	100	
Total	Yes	2	12.5	5	31.3	9	56.3	16	100	0.668
	No	4	21.1	7	36.8	8	42.1	19	100	

which states that elderly patients are at high risk for knee osteoarthritis. Supartono et al. [12] stated that someone who is more than 65 years old has a high risk of experiencing calcification of the knee joint. The ageing process results in tissue swelling and the release of substances that are toxic to cartilage, resulting in progressive damage.

The distribution of respondents by gender shows that most of the respondents were females and there were 25 patients (71.4%). These results were similar to the research of Subroto et al. [11], who stated that knee osteoarthritis was more common in females than males. Females are more at risk for knee osteoarthritis, especially after menopause, which is influenced by the role of estrogen [13].

The distribution based on the degree of knee osteoarthritis showed that most of the respondents had knee osteoarthritis grade 3, which was 17 patients (48.6%). Ali's research [14] showed that patients diagnosed with knee osteoarthritis were most commonly found in grades 3 and 4.

The results showed that the majority of patients with knee osteoarthritis were patients without diabetes, 26 patients (74.3%), and without hypertension, 19 patients (54.3%). And the result of the Chi-square test shows that there is no significant relationship between diabetes mellitus and the severity of osteoarthritis. These findings are consistent with meta-analysis studies by Khor et al. [15] that diabetes mellitus is not a risk factor for osteoarthritis. There are two possibilities. First, diabetes mellitus may not be a risk factor for osteoarthritis. Second, if body mass index (BMI) is one of the strong risk factors for osteoarthritis, any weaker risk factor would be masked by the confounding effect of BMI. It is because BMI is a strong risk factor for diabetes mellitus and osteoarthritis, particularly for weight bearing joints. In contrast to Neumann's [16] findings, diabetes mellitus has a significant relationship with

cartilage meniscus abnormality over 4 years when compared to patients without diabetes mellitus. Neumann [17] also said the same thing that diabetes mellitus is associated with an increase in cartilage matrix and then found a faster increase in collagen breakdown on cartilage, which is a sign of increased severity of osteoarthritis. Eymard [18] explains that diabetes mellitus is one factor associated with the severity of osteoarthritis in males but not in females.

Another result of this research is that there is no significant relationship between hypertension and the severity of osteoarthritis. Eymard [18] demonstrates that metabolic factors such as hypertension, dyslipidemia, and obesity have no significant relationship to the severity of knee osteoarthritis. Based on Lee's [19] studies, females with hypertension have a significant relationship with a risk factor for osteoarthritis and the severity of osteoarthritis, but in males, there is a significant relationship with the risk factor for osteoarthritis but not in the severity of osteoarthritis. Research by Liu [20] shows that there is a significant relationship between hypertension in males and females and the risk factor of osteoarthritis, but does not mention the relationship with the severity of osteoarthritis. Some factors can affect this result, such as controlled anti-hypertension medicine. Anti-hypertension medicines such as ACEi and ARB have the function of increasing endothelial that can prevent the remodelling of blood vessels. Besides that, ARB also prevents atherosclerosis by reducing the expression of inflammatory mediators and blocking renin-angiotensin-aldosterone, which will reduce the development and process of vascular diseases such as atherosclerosis in large and small vessels.

There are some limitations in this study such as the number of samples used in this study is still small enough that it does not describe

the population with osteoarthritis. In addition, this study uses a retrospective cross-sectional research study design, so it cannot be known which diseases affect each other. This study also takes only some parts of the metabolic syndrome, such as hypertension and diabetes mellitus, which can not show the relationship between other metabolic factors and osteoarthritis. However, this study can be used as a guideline for the treatment of osteoarthritis in patients who also have hypertension and/or diabetes mellitus or be used as a guide in further research on the factors that cause knee osteoarthritis.

## 5. Conclusion

In conclusion, there were no significant association between diabetes mellitus and hypertension with the severity of osteoarthritis in males and females. This study uses a retrospective cross-sectional research study design, so it cannot be known which diseases affect each other. We suggest further study of other factors such as BMI, age, and physical activity in the research to better understand the factors that affect knee osteoarthritis clearly. In addition, it is also necessary to increase the number of samples so that they are able to represent the population of patients with knee osteoarthritis.

## Ethical approval

This study has been reviewed and approved by the authors' Institutional Review Board.

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## Author contribution

Panji Sananta: conceptualization, writing original draft preparation, supervision, project administrator, validation Vio Tsamratul Zahrah: data collecting, data interpretation, writing original draft preparation, writing the paper and editing, validation Dhelya Widasmara: data collecting, data interpretation, writing original draft preparation, writing the paper and editing, validation Eka Noviya Fuzianingsih: data collecting, data interpretation, writing original draft preparation, writing the paper and editing, validation.

## Registration of research studies

This Case report is not "First in Man" Study.

## Guarantor

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## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Contributorship

Written informed consent was obtained from the patient for publication of this case report.

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## Declaration of competing interest

We declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104155>.

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