Factors Associated with the Occurrence of Osteoarthritis: A Path Analysis Evidence from Surakarta, Central Java

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ABSTRACT

Background: Musculoskeletal conditions are an important public health problem. The population burden from arthritis is considerable. The implications of this burden are poor quality of life, restrictions in daily activities, and disability. This study aimed to analyze factors associated with the occurrence of osteoarthritis in Surakarta, Central Java, using a path analysis model.

Subjects and Method: This was a cross-sectional study conducted at Dr. Moewardi Hospital, Surakarta, Central Java, in June 2018. A sample of 200 patients was selected by fixed disease sampling, consisting of 50 knee OA patients and 150 patients without knee OA. The dependent variable was knee OA. The dependent variables were age, gender, body mass index (BMI), diabetes mellitus, history of injury, and physical activity. Data on knee OA, BMI, and diabetes mellitus status were obtained from medical record. The other variables were measured by questionnaire. The data were analyzed by path analysis.

Results: The risk of OA increased with diabetes mellitus (b=1.04; 95% CI= 0.17 to 1.92; p=0.020), older age (b= 4.03; 95% CI= 1.97 to 6.09; p<0.001), and BMI \geq 25 (b= 1.28; 95% CI= 0.39 to 2.17; p= 0.005). The risk of OA decreased with history of knee injury (b= -0.90; 95% CI= 0.57 to 1.74; p= 0.003) and female (b= -1.19; 95% CI= -2.06 to -0.31; p=0.008). The risk of OA was indirectly affected by physical activity, female gender, and BMI.

Conclusion: The risk of OA increases with diabetes mellitus, older age, and BMI \geq 25, but decreases with history of knee injury and female gender. The risk of OA is indirectly affected by physical activity, female gender, and BMI.

Keywords: knee osteoarthritis, sociodemographic factor, diabetes mellitus, path analysis

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BACKGROUND

Osteoarthritis (OA) is one of the health problems experienced by the human body and has the potential to reduce the degree of physical and spiritual health. 400 out of 1000 world population over the age of 70 years suffer from OA and 800/1000 OA suffer from mild to severe degrees of motion which leads to the decrease of life quality of patients (WHO, 2016).

OA is a degenerative disease in the joints that is the damage of joint cartilage and the formation of new bone on the joint surface that can cause muscle weakness and tendon, so it limitsthe motion and causes pain. OAs that attack the knee joint cause the knee to become an abnormal knee joint function. Knee is a joint that sustains the body, so that when experiencing OA, it will result in disruption of patient's activity (Hochberg, 2013).

OA often attacks the weight bearing joints such as the hip joint, knees, vertebrae, but it may also affect the shoulders, joints of the fingers, and ankles (Sudoyo, 2009).

OA of the knee causes an impairment at the level of impairment, functional limitation and disability. At the level of impairment, the thing that occurs is pain, weakness of knee joint muscles, and limited knee motion scope (LGS) knee. At the level of functional limitation, the things that occur are basic functional disorders such as squatting to standing, walking, up and down stairs and functional activity that burdens the knee. At the level of disability, the thing that occurs is the inability to carry out certain activities related to work or socializing activities with the community.

Several risk factors of OA include age, gender, ethnicity, genetics, obesity, metabolic diseases, history of joint injury, occupation, exercise, growth abnormalities and other lifestyle factors that may also increase the risk of OA Knee (Dullu et al ., 2016).

One of the risk factors of knee OA in the form of metabolic disease is Diabetes Mellitus (DM). Musculoskeletal disorders that occur in patients of DM include: (1) complications of soft tissue, in the form of frozen shoulder, flexor tenosynovitis, carpal tunnel syndrome, duplictred contractions, limited scope of joint motion, (2) joint complications, OA, gout arthritis, osteolysis, and neuro-arthropathy, (3) bone complications: osteopenia, hyperostosis (Piva et al., 2015). DM type 2 is a factor affecting the severity of OA. Schett et al. (2013) conducted a 20-year study (1990-2010) in 927 subjects aged 40-80 years to evaluate changes in the severity of knee OA in the subjects group with DM type 2 or not. Research of Luoati et al. (2015), also supported the results by taking the source of 49 studies selected from 299 studies in the form of 28 cross sectional studies, 11 cohort studies, and 10 studies with casecontrol designs which show that DM patients were at higher risk of suffering from knee OA than those who did not suffer DM.

Age is the most dominant risk factor in OA because the prevalence of OA will increase along with the age (Solomon). OA can occur due to the decrease of collagen and proteoglycan elasticity of joint cartilage that can occur due to degenerative factors (Anderson et al., 2011). Age is a factor that significantly affects degeneration of the cartilage structure. Research by Ding et al. (2015) proves that any additional age aggravating OA has been demonstrated by research, in which each increase in age affects the severity change of cartilage cartilage thinning, damage, and the increase of bone size, and changes in the volume of cartilage (OR = 1.05-1.10).

Gender is also an irreversible risk factor for knee OA, in which women are more commonly exposed to OA than men in postmenopausal women especially because the function of the estrogen hormone is to help synthesize chondrocytes in the bone matrix that has decreased, increasing the risk exposed to knee OA (Hame et al., 2013). According to research by Silverwood et al. (2015) women are more affected by knee OA than men (OR = 1.68). In addition to that, waist-hip-ratio and BMI are significantly associated with knee OA risk factors and are more common in women compared to men (Gandhi et al., 2010).

BMI is considered as a very strong knee OA risk factor. The loading of the knee and pelvis can cause cartilage damage, ligament failure and other structural support. Each additional weight + ¹/₂ kg, total pressure on one knee increased by 1-1 ¹/₂ kg. Each addition of 1 kg increases the risk of OA by 10%. For obese people, any weight loss even if it is only 5 kg will reduce the risk factor of OA in the future by 50% (Solomon, 2010). Any increase in BMI increases the risk of OA occurring in the knee. Study by Zheng et al. (2015) proves that from 14 studies analyzed show that overweight and obesity significantly 2.45 times greater potential for knee OA occurrence. Of the 12 studies analyzed with the aim of identifying the association of BMI with the occurrence of knee OA show that the risk of knee OA increased with increasing BMI so controlling body weight was the prevention of knee OA (Zhou et al., 2015).

Knee injury is a predisposing factor for the occurrence of knee OA. Imperfect muscle and joint coordination in injured knees result in a knee injury having a 5 to 6 fold higher risk of developing OA (Lin et al., 2017). This is supported by the Blagojevic (2010) study which states that knee injuries increase the risk of knee OA by 3.86 times greater than those without knee injury.

Occupation that requiresgreat power will provide a large mechanical load on the joints. For heavy lifting work, it will cause musculoskeletal disorders. Occupation which requires kneeling positions becomes a risk factor with knee osteoarthritis occurrences in both women and men. The greatest risk is found in the group working with the activity of squatting or kneeling more than 30 minutes a day (Palmer et al., 2012). The prevalence of OA is found in heavy physical workers, especially those that use a lot of support on knee joints. The higher prevalence of knee OA is found in porters, farmers and miners than in workers who do not use knee strength as administrative workers (Muraki et al., 2015).

Based on the background, the researchersare interested in conducting research entitled "The Relationship of Diabetes Mellitus and Sociodemographic Factors with Knee Osteoarthritis at Dr. Moewardi Hospital, Surakarta ".

SUBJECTS AND METHOD

1. Study Design

This was an analytic observational study with a cross sectional design. The study was conducted at Dr. Moewardi hospital, Surakarta, Central Java, in June 2018.

2. Population and Samples

The source population in this study were outpatients with knee OA at the physiotherapy clinic, Dr. Moewardi, Surakarta. A sample of 200 patients was selected for this study by fixed disease sampling, comprising were 50 patients with knee OA and 150 patients without knee OA.

3. Study Variables

The dependent variable was knee OA. The independent variables were history of knee injury, age, gender, DM, BMI, and physical activity.

4. Operational Definition of Variables Knee OA was defined as a degenerative disease characterized by the joint cartilage damage in the knee joint. The data were taken from medical record. The measurement scale was categorical, coded o for no and 1 for yes.

The history of knee injury was defined as a history of trauma or knee injury that has been experienced by the patients. The data were taken from medical record. The measurement scale was categorical, coded o for no and 1 for yes.

Age was defined as how old the subjects when being interviewed. The data were collected by questionnaire. The measurement scale was continuous.

Gender was defined as the identity of subjects according to biological or physical condition. The data were were collected by questionnaire. The measurement scale was categorical, coded 0 for female and 1 for male.

Diabetes mellitus was defined as excess blood sugar levels in the body resulting in the increase of blood sugar levels due

to lack of insulin. The data were taken from medical record. The measurement scale was categorical, coded 0 for no and 1 for yes.

BMI was is a simple assessment to monitor the nutritional status of adults, especially those related to lack and excess body weight which is calculated as weight in kilograms divided by the square of height in meter (kgBB/m²). The measurement scale was continuous, coded o for BMI <25 and 1 for BMI \geq 25.

Physical activity was defined as an activity carried out daily by study subjects other than sports that can burden the knee. The data were collected by questionnaire. The measurement scale was continuous.

5. Data Analysis

The data analysis was conducted using path analysis with program Stata 13 to know the influence of determinant influence, either directly or indirectly. The steps of path analysis including model specification, model identification, model suitability, parameter estimation, and model re-specification.

6. Research Ethics

The research ethics includes informed consent, anonymity, confidentiality and ethical clearance. The ethical clearance in this study was conducted at Dr. Moewardi hospital, Surakarta.

HASIL

1. Study Subjects Characteristics

The history variable of knee injury showed that most of the subjects in the non-knee OA group had no knee injury (73%) and in the knee OA group had knee injury (62%). The age variable showed that most of the subjects in the non-OA group were <40 years old (52.7%) and in the knee OA group is >40 years (98%) .The gender variables indicated that most of the subjects in the non-knee OA group were female (67.3%) and in the male knee OA group is (52%). The DM variable showed that most subjects in the non-knee OA group did not have DM (73.3%) and in the knee OA group had DM (64%).

	Knee C	Total		
Independent variables	No	Yes	n=200 Frequency (%)	
independent variables	n= 150	n= 50		
	Frequency (%)	Frequency (%)		
History of Knee Injury				
No	110 (73.3%)	19 (38%)	129 (64.5%)	
Yes	40 (26.7%)	31 (62%)	71 (35.5%)	
Age				
< 40 years old	79 (52.7%)	1 (2%)	80 (40%)	
\geq 40 years old	71 (47.3%)	49 (98%)	120 (60%)	
Gender				
Male	49 (32.7%)	26 (52%)	75 (37.5%)	
Female	101 (67.3%)	24 (48%)	125 (62.5%)	
DM				
No	110 (73.3%)	18 (36%)	128 (64%)	
Yes	40 (26.7%)	32 (64%)	72 (36%)	
BMI				
$< 25 \text{ kgBB/m}^2$	93 (62%)	13 (26%)	106 (53%)	
\geq 25 kgBB /m ²	57 (38%)	37 (74%)	94 (47%)	
Physical Activity				
Mild Activity	95 (63.3%)	19 (38%)	114 (57%)	
Heavy Activity	55 (36.7%)	31 (62%)	86 (43%)	

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Most of the study subjects in the control group the non knee OA group had a BMI <25 (62%) and in the knee OA group had BMI >25 (74%). Physical activity variables showed that most subjects in the group not knee OA performed mild activity (63.3%) and in knee OA group performed heavy activity (62%).

2. Path Analysis

Data processing was using Stata 13 program. Path analysis steps were model specification, model identification, parameter estimation, and model re-spesification. The number of measured variables were 7, endogenous variables were 3, and exogenous variables were 4. So, the score of degree of freedom (df): 14. Then, it was concluded that "df= over identified" which mean path analysis can be done. The model in this study was in accordance with the sample data shown by the saturation model.

Structural model of path analysis with estimation was shown in Figure 1, and the results of the path analysis were shown in Table 2.

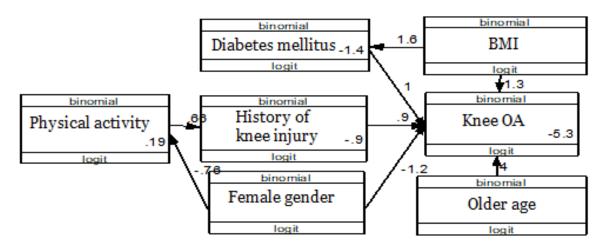


Figure 1. Structural Model of Path Analysis with Estimation

		Indonandant		95% CI		
Dependent Variable		Independent variable	b	Lower Limit	Upper Limit	р
Direct Effect						
Knee OA	←	History of knee injury	0.90	0.57	1.74	0.003
Knee OA	←	Age	4.03	1.97	6.09	<0.001
Knee OA	←	Female Gender	-1.19	-2.06	-0.31	0.008
Knee OA	←	DM	1.04	0.17	1.92	0.020
Knee OA	←	BMI	1.28	0.39	2.17	0.005
Indirect Effect						
History of knee injury	←	Physical activity	0.66	0.77	1.25	0.027
Physical activity	←	Female Gender	-0.76	-1.34	-0.18	0.010
DM	←	BMI	1.57	0.94	2.19	<0.001
Observation Score =200						
Log Likelihood=-445.59						

Table 2. Path analysis results of the relationship between DM and socio-
demographic factors on knee OA

Table 2 showed that there was a positive relationship between history of knee injury and knee OA and it was statistically significant. OA patients with history of knee injury increased the risk of knee OA (b= 0.90; 95% CI= 0.57 to 1.74; p= 0.003).

There was a positive relationship between age and the risk of knee OA and it was statistically significant. Patients with age \geq 40 years increased the risk of knee OA (b= 4.03; 95% CI= 1.97 to 6.09; p<0.001).

There was a negative relationship between gender and knee OA. Male gender reduced the risk of knee OA (b= -1.19; 95% CI= -2.06 to -0.31; p<0.001).

There was a positive relationship between DM and the risk of knee OA. DM increased the risk of knee OA (b= 1.04; 95% CI= 0.17 to 1.92; p=0.020).

There was a positive relationship between BMI and the risk of knee OA. BMI \geq 25 increased the risk of knee OA (b= 1.28; 95% CI= 0.39 to 2.17; p=0.005).

There was a positive relationship between physical activity and the risk of knee. Heavy physical activity increased the risk of knee OA (b= 0.66; 95% CI= 0.76 to 1.25; p=0.027).

There was a positive relationship between female gender and physical activity. Female gender reduced physical activity (b= -0.76; 95% CI= -1.34 to -1.18; p= 0.010).

There was a positive relationship between BMI and DM status. BMI \geq 25 increased the risk of DM (b= 1.56; 95% CI= 0.94 to 2.19; p<0,001).

DISCUSSIONS

1. The relationship between history of knee injury and knee OA

The results of this study showed that history of knee injury increased the risk of knee OA. Patients with history of knee injury were more likely to have knee OA. The result of this study is consistent with a study by Silverwood *et al.* (2015), which stated that previous knee trauma increased the risk of knee OA (OR=2.83). History of knee injury is conditions that have been traumatized due to incomplete coordination of muscles and joints resulting in wrong movements and resulting injury. History of knee injury increased the risk of knee OA 5-6 times (Lin *et al.*, 2017). Similar study also conducted by Blagojevic *et al.* (2010), which stated that knee trauma/injury increased the risk of knee OA with OR=3.86.

Knee osteoarthritis can also occur in 80 - 90% of patients who have done surgery which was an operation in the knee joint area which mainly was a menisectomy surgery (surgery on the meniscus). Meniscus tissue loss due to meniscectomy lead to greater pressure on joint cartilage, which became a factor of the occurence of knee OA. After meniscectomy, patients experienced meniscal degeneration and rips which might become wider and changes in joint cartilage would be greater than those who did not do meniscectomy. (Muthuri *et al.*, 2011).

2. The relationship between age and knee OA

The results of this study showed that older age increased the risk of knee OA. The result of this study is consistent with a study by Fernández-Cuadros *et al.* (2017), which stated that age affected the occurrence of knee OA which would continue to undergo total knee arthroplasty.

Age was a factor that significantly affected the degeneration of cartilage structures with OR= 1.05-1.10 and it worsen the OA for each year. Increased age affected the changes in severity from cartilage damage, cartilage thinning, and increased bone size and also volume changes from cartilage (Ding *et al.*, 2015). Age was the most dominant risk factor in OA because the prevalence of OA would increase with age. The enhancement of OA occurred at the age of more than 65 years old with an average age in men of 59.7 years old and the average age in women of 65.3 years old. Knee OA almost never occurred in children, it rarely occurred under the age of 40 years old and often occured at the age of over 60 years old (Loeser, 2011).

3. The relationship between gender and knee OA

The results of this study showed that female gender reduced the risk of knee OA. Female gender also had a negative relationship with physical activity. The results of this study showed that male gender had higher physical activity than female. If someone worked in the office, then the person tend to sit for a long time, but if he was a construction worker, then the person tend to walked for a long time, lifted heavy loads, and etc. The use of joints in heavy activity that lasted for a long time was a risk factor for knee OA disease. The work of lifting heavy objects such as porters, climbers, and other work which commonly done by men could lead to the increased risk of knee OA (Palmer *et al.*, 2012.

4. The relationship between DM and knee OA

The results of this study showed that there was a positive and direct relationship between DM and the risk of knee OA. DM increased the risk of knee OA. The result of this study is consistent with a study by Nieves-Plaza et al. (2013), which stated that DM patients were more affected by knee OA than non-DM patients with OR= 2.18. DM would increase the incidence of OA due to disruption of blood sugar metabolism which would cause musculoskeletal disorders including: (1) complications in soft tissue (flexor tenosynovitis, carpal tunnel syndrome, limitation of joint motion); (2) joint complication (OA, gout arthritis, osteolysis, and neuroartropathy); (3) bone complications (osteopenia and hyperostosis).

5. The relationship between BMI and knee OA

The results of this study showed that BMI ≥ 25 increased the risk of knee OA. BMI also had a positive relationship with DM. BMI ≥ 25 was the greater of possibility to suffer from knee OA and DM. The result of this study is consistent with a study by Zhou *et al.* (2014), which stated that the risk of knee OA increased with higher BMI. It was suggested to control BMI as knee OA prevention.

The result is in line with a study by Zheng *et al.* (2015), which stated that overweight and obesity were 2.45 times more likely to had knee OA. Excess body weight would increase stress on the body's supporting joints so that it would provide pain. When someone walked, the weight of the body was transferred to the knee joint for 3-6 times of the body weight. So, if the proportion of body weight was more than height (obesity), the joint work would be heavier (Weiss, 2018).

In addition, OA body mass index was also associated with the incidence of DM where there was a significant correlation between obesity and blood glucose levels, in the degree of obesity with a BMI of >25, it could cause an enhancement in blood glucose levels to 200 mg% (Indonesian Endocrinology Association, 2015). Therefore, the increased BMI would also increase blood sugar level which resulted in DM and could increase the incidence of OA.

6. The relationship between physical activity and knee OA

The results of this study showed that there was a and indirect relationship between physical activity and knee OA through knee injury. High physical activity increased the

risk of knee injury, which would lead to the incidence of knee OA.

According to WHO (2015), physical activity was any body movement produced by skeletal muscle that required energy expenditure. Lack of physical activity was an independent risk factor for chronic disease, and overall was thought to be the cause of death globally. Physical activity involved 3 components, namely endurance, flexibility, and strength.

Heavy physical activity such as standing for a long time (2 hours or more each day), walking long distances (2 hours or more daily), lifting heavy items (10 kg - 50 kg for 10 times or more each week), pushing heavy objects (10 kg - 50 kg for 10 times or more each week), up and down the stairs every day were the factors that significantly increased the risk of knee OA (Muraki *et al.*, 2015).

Work that used large power would provide a large mechanical load on the joints. Heavy lifting work would cause musculoskeletal disorders. Work with kneeling positions was a risk factor for the incidence of knee osteoarthritis in both women and men. The greatest risk was found in groups that worked with squatting or kneeling positions for more than 30 minutes a day (Palmer *et al.*, 2012).

REFERENCES

- AbulhasanJF, Grey MJ (2017). Anatomy and Physiology of Knee Stability. Journal of Functional Morphology and Kinesioloy. 2 (34).
- ADA (American Diabetes Association) (2017). Classification and Diagnosis of Diabetes. Diabetes Care. 40 (1):S11– S24.
- Alfieri FM, Silva NC, de OV, Battistella LR (2017). Study of the relation between body weight and functional limitations and pain in patients with knee

osteoarthritis. Einstein (São Paulo), 15(3), 307–312.

- Anderson AS, Loeser RF (2011). Why is Osteoarthritis an Age-Related Disease. NIH Public Access, 24(1):15. 1–18.
- ARC (2010). Osteoarthritis and Obesity. United Kingdom: Arthritis Research Campaign.
- ArdenNK, Leyland KM (2013). Osteoarthritis year 2013 in review: clinical. Osteoarthritis and Cartilage, Osteoarthritis Research Society International, 21(10), 1409–1413.
- Baynes HW (2015). Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. J Diabetes Metab, 6(651).
- Blagojevic M, Jinks C, Jeffery A, Jordan KP (2010). Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and metaanalysis. Osteoarthritis Research Society International, 18(1), 24–33.
- Connor MIO (2007). Sex and Gender Differences in Hip and Knee Osteoarthritis. Touch Briefings Journal. 71–72.
- Deshpande BR, Katz JN, Solomon DH, Yelin EH, Hunter DJ, Messier SP, Suter LG, Losina E (2016). Number of Persons With Symptomatic Knee Osteoarthritis in the US: Impact of Race and Ethnicity, Age, Sex, and Obesity. Arthritis Care and Research, 68(12), 1743–1750.
- Ding C, Cicuttini F, Scott F, Cooley H, Jones G (2015). Association between age and knee structural change: A cross sectional MRI based study. Annals of the Rheumatic Diseases, 64(4), 549–555.
- Dullu SKA, Gessal J, Marpaung E (2016). Jenis modalitas yang digunakan pada osteoartritis lutut di instalasi rehabilitasi medik RSUP Prof. Dr. R. D.

Kandou Manado. Jurnal Kedokteran Klinik (JKK), 1 (1)

- Eymard F, Parsons C, Edwards MH, Petit-Dop F, Reginster JY, Bruyère O, Richette P, Cooper C, ChevalierX (2015). Diabetes is a risk factor for knee osteoarthritis progression.Osteoarthritis Research Society International, 23(6), 851–859.
- Fernández-Cuadros M (2017). Age and Sex Affect Osteoarthritis and the Outcome on Knee Replacement. MOJ Orthopedics & Rheumatology, 9(4).
- Ferrree MM (2012). Filling the Glass: Gender Perspectives on Families. Journal of Marriage and Family. 7(2): 420– 439.
- Flandry F, Hommel G (2011). Normal Anatomy and Biomechanics of the Knee, Sports Med Arthrosc Rev, 19(2), 82– 92.
- Frey N, Hügle T, Jick SS, Meier CR, Spoendlin J (2016). Type II diabetes mellitus and incident osteoarthritis of the hand: a population-based case-control analysis. Osteoarthritis Research Society International, 24(9), 1535-1540.
- Gandhi R, Dhotar H, Tsvetkov D, Mahomed NN (2010). The relation between body mass index. Canadian Medical Association . Can J Surg, 53(3), 151– 154.
- Hame SL, Alexander RA (2013). Knee osteoarthritis in women, Osteoarthritis Research Society International 182– 187.
- Heidari B (2011). Knee osteoarthritis prevalence, risk factors, pathogenesis and features: Part I. Caspian J Intern Med, 2(2):205-212.
- IDF (International Diabetes Federation). 2015. IDF Diabetes Atlas. The7 Ed. Online version of IDF Diabetes Atlas: www.diabetesatlas.org.

- James EW, Laprade CM, Laprade RF (2015). Anatomy and Biomechanics of the Lateral Side of the Knee and Surgical Implications, Sports Med Arthrosc Rev, 23(1), 2–9
- Kalpana JG, Thirunavukkarasu P, Ramesh C, Shivaranjani I, Srinivasan P (2017). Correlation Between Body Mass Index And Womac Scores Among Population With Osteoarthritis Knee, Stanley Medical Journal, 4 (1) l2–5.
- Kasper D, Fauci A, Braunwald E, Hauser S, Longo D, Jameson L (2018). Osteoarthritis. Dalam; Harrison's Principles of Internal Madicine. 17th ed. New York: McGraw Hill Medical: 2158 – 2165.
- Kementerian Kesehatan RI. 2013. Health Statistics. Jakarta: Kementerian Kesehatan RI.
- Kertia N, Asdie AH, RochmahW, Marsetyawarr(2011). Berbagai Keluhan Fisik yang Dialami Pasien Osteoarthritis Akibat Terapi Natrium Diklofenak Dibandingkan Kurkuminoid Ekstrak Rimpang Kunyit. Jakarta : Bulletin of Helath Research, 9(03): 145-153.
- Kohn MD, Sassoon AA, Fernando ND (2016). Classifications in Brief. Clinical Orthopaedics and Related Research®, 474(8), 1886–1893.
- Kondo K, Ohfuji S, Fukushima W, Takahashi S, Miura H, Takasugi S, Iwamoto Y (2013). Orthopedic & Muscular System Association between Dietary Habits and Knee Osteoarthritis in Japanese Older Adults: A Cross-Sectional Study, Orthop Muscul Sys, t2(120), 1–6.
- Laprade MD, Kennedy MI, Wijdicks CA, Laprade RF (2015). Anatomy and Biomechanics of the Medial Side of the Knee and Their Surgical Implications, Sports Med Arthrosc Rev, 23(2), 63– 70.

- Loeser RF (2010). Age-Related Changes in the Musculoskeletal System and the Development of Osteoarthriti S. NIH Public Access. Clin Geriatr Med, 26(3), 371–386.
- (2011). Aging and Osteoarthritis. NIH Public Access. Curr Opin Rheumatol, 23(5), 492–496.
- Louati K, Vidal C, Berenbaum F, Sellam J (2015). Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. RMD Open, 1(1).
- Mark R (2016). Diabetes and Osteoarthritis Disability: An Important Underrepresented Topic in the Related Literature. Austin Journal of Endocrinology and Diabetes, 3(1): 1039.
- Murti B (2013). Desain dan Ukuran Sampel untuk Penelitian Kuantitatif dan Kualitatif di Bidang Kesehatan. Yogyakarta: Gajah Mada University Press.
 - (2016). Prinsip Dan Metode Riset Epidemiologi. Surakarta: Program Studi Ilmu Kesehatan Masyarakat, Program Pascasarjana, Universitas Sebelas Maret.
- Mutiwara E, Najirman, Afriwardi (2016). Hubungan Indeks Massa Tubuh dengan Derajat Kerusakan Sendi pada Pasien Osteoartritis Lutut di RSUP Dr. M. Djamil Padang. Jurnal Kesehatan Andalas. 5 (2) : 1-5.
- Nieves-Plaza M, Castro-Santana LE, Font YM, Mayor AM, Vila LM (2014). NIH Public Access. J Clin Rheumatol, 19(1), 1–16.
- Nurhaeni IDA (2009).Kebijakan Publik Pro Gender. Surakarta: UPT Penerbitan dan Percetakan UNS (UNS Press).
- Nuttall FQ (2015). Body Mass Index: Obesity, BMI, and Health: A Critical Review. Nutrition Today, 50(3), 117– 128.

- Paulsen F, Waschke (2013). Sobotta: Atlas anatomi manusia, Jakarta : EGC
- PERKENI (Perkumpulan Endokrinologi Indonesia). (2015). Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia 2015. Jakarta: PB PERKENI.
- Piva SR, SuskoAM, Khoja SS, Josbeno SA, Fitzgerald GK, Toledo FGS (2016). Links between Osteoarthritis and Diabetes:Implications for Management from a Physical Activity Perspective. Clin Geriatr Med, 31(1), 67–87.
- Reyes C, Leyland KM, Peat G, Cooper C, Arden NK, Prieto-Alhambra D (2016). Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis: A Population-Based Cohort Study. Arthritis & Rheumatology, 68(8), 1869–1875.
- Schett G, Kleyer A, Perricone C, Sahinbegovic E, Iagnocco A, ZwerinaJ, Lorenzini R, Aschenbrenner F, Berenbaum F, D'Agostino M, Willet J, Kiechl S (2013). Diabetes is an independent predictor for severe osteoarthritis: Results from a longitudinal cohort study. Diabetes Care, 36(2), 403–409.
- Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP (2015). Current evidence on risk factors for knee osteoarthritis in older adults: A systematic review and metaanalysis. Osteoarthritis and Cartilage, 23(4), 507–515.
- Solomon L (2010). Apley's System of Orthopaedics and Fractures, London: Hodder Arnold, hal 85-102.
- Srikanth VK, Fryer JL, Zhai G, Winzenberg, TM, Hosmer D, Jones G (2005). A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. Osteoarthritis Research Society International, 13(9), 769–781.

- Weiss E (2018). Concise report Knee osteoarthritis, body mass index and pain: data from the Osteoarthritis Initiative. British Society for Rheumatology, 2095–2099.
- Wright RW, Ross JR, Haas AK, Huston LJ, Garofoli EA, Harris D, Dunn WR (2014). Osteoarthritis Classification Scales: Interobserver, Reliability and Arthroscopic Correlation. The Journal Of Bone and Joint Surgery 1145–1151.
- WHO 2016. Global Report On Diabetes. Geneva: World Health Organization.
- _____ (2016). Global Report On Musculoskeletal Disorder. Geneva: World Health Organization.

- Yin TZ, Seng YH (2010). Weight Status, Body Image Perception and Physical Activity of Malay Housewives in Kampung Chengkau Ulu, Negeri Sembilan, International Journal For The Advancement Of Science & Arts, 1(1), 35–45.
- Zheng H, Chen C (2015). Body mass index and risk of knee osteoarthritis: Systematic review and meta-analysis of prospective studies. BMJ Open, 5(12).
- Zhou ZY, Liu YK, Chen HL, Liu F (2014). Body mass index and knee osteoarthritis risk: A dose-response metaanalysis. Obesity, 22(10), 2180–2185.