Osteoarthritis Screening Based on Womac Index in Diabetes Mellitus Patients Aged ≤ 45 Years

Nur Lina [1], Siti Novianti [2], Yuldan Faturahman[3], Nur Hidayanti[4]

[1]Universitas Negeri Semarang, Central Java, Indonesia

[2,3,4]Universitas Siliwangi, Indonesia

Corresponding author: nurlina@unsil.ac.id

Abstract: Osteoarthritis (OA) is a chronic and systemic disease and involves joint damage including degradation of hyaline articular cartilage, ligaments, menisci in the knee. Diabetes Mellitus (DM) causes various changes in bone structure, which will increase the risk of OA. The purpose of this study was to conduct OA Screening in DM patients and provide information on OA risk factors in DM patients, especially aimed at preventing OA and DM, preventing further complications, and improving the quality of life of DM patients with OA. This study used a Cross-sectional design. The study population was DM patients aged ≤ 45 years who were recorded at the Kedungreja Health Center totaling 86 people and the Cipari Health Center totaling 67 people who were limited to the age of ≤ 45 years. The sample of this study was the entire population of 153 patients. The WOMAC Index was used to conduct OA screening in DM patients. The average pain score based on the WOMAC Index was 7.23. The average stiffness score based on the Womac Index was 3.65, and the average physical function impairment was 17.5 with an average total score based on the Womac index of 28.03. The results of the Spearman Rank Correlation Statistical Test showed that Age, BMI were related to the Pain Degree Score in DM patients aged ≥ 45 years. Dietary modification to prevent obesity, and intensive glycemic control should be performed and encouraged to delay the onset and severity of pain in OA.

Keywords: Diabetes; Osteoartritis, Womac; IMT; Indeks

INTRODUCTION

Diabetes mellitus (DM) and osteoarthritis (OA) are chronic non-communicable diseases that affect millions of people worldwide. Since the 1980s, it has been observed that those diagnosed with OA also have a diagnosis of DM, and vice versa. Because the two often coexist, OA and DM have a major impact on the health burden both on individuals and society at large. OA and DM are associated with chronic pain and disability. DM is associated with greater levels of osteoarthritis pain(Alenazi et al., 2023).

Osteoarthritis (OA) is the most common progressive musculoskeletal condition that can affect the joints, but it primarily affects the hips and knees as weight-bearing joints the dominant

one. Knee osteoarthritis is characterized by structural modifications mainly in the articular cartilage and subchondral bone, but also the synovial fat pad, ligaments and muscles, leading to overall joint disease. The global prevalence of knee OA is 16.0% in individuals aged 15 years and older and 22.9% in individuals aged 40 years and older(Cui et al., 2020).

OA is a chronic and systemic disease with slow progression and involves damage to the entire joint which mainly includes degradation of hyaline articular cartilage, ligaments, menisci in the knee, hypertrophic changes. Pain in OA is one of the most commonly reported symptoms with varying degrees of severity. Those with poorer glycemic control report increased pain severity compared to those with better glycemic control in controlling HbA1C levels reflecting blood sugar levels over two or three months. months. Patients diagnosed with both DM and OA reported significantly increased severity and frequency of pain attacks, increased incidence of bilateral synovitis, and increased likelihood of requiring knee arthroplasty compared to patients with OA alone. Diabetic OA patients also experienced more severe local inflammation in the affected joint. affected by OA with severe synovitis and higher concentrations of the proinflammatory cytokine IL-6 in synovial fluid compared to non-diabetic OA patients(Eitner et al., 2021).

Blood glucose levels in DM patients play a role in the pathogenesis of OA from the anatomical level to the metabolic level. DM affects the musculoskeletal system, especially bones, tendons, ligaments, and joint cartilage which are most often affected by OA. DM interferes with the mechanisms and mediators involved in joint destruction(Chowdhury et al., 2022).

The prevalence of OA among 5788 DM patients was 29.5% and the prevalence of DM in 645,089 DM OA patients was 14.4%. DM is an independent risk factor for narrowing of the knee joint space, for 3 years, compared to patients without DM(Kim et al., 2020). Osteoarthritis can occur either due to damage to joint cartilage or due to reactivation of joint cartilage growth. Patients with DM and knee OA have lower grip strength and balance compared to those with only knee OA (Primorac et al., 2020).

Microcellular review of DM patients shows accelerated joint destruction and increased inflammation in every aspect of joint anatomy including bone, tendon, ligament, cartilage, and synovium. In addition, the biomechanical and biochemical properties of these tissues are also affected more severely in patients with DM and OA compared to patients without DM, indicating that DM plays an important role in the pathogenesis of OA (Chowdhury et al., 2022).

DM OA through 2 pathways, namely: 1) Chronic hyperglycemia, which induces oxidative stress, excess production of proinflammatory cytokines and AGEs; and 2) insulin resistance, which

can play a role locally but also through low-grade systemic inflammation. Leptin, the main adipokine secreted by adipose tissue, is able to induce chondrocyte apoptosis and also increases the production of cytokines and rheumatoid arthritis MMPs by chondrocytes. Insulin resistance and obesity are also associated with increased free fatty acids (FFAs), which can modulate the development of OA (Abramoff & Caldera, 2020).

In metabolic syndrome, the mechanics of obesity can affect joints and can easily increase the risk of OA in the lower extremities (Brognara et al., 2021). Other components of metabolic syndrome including dyslipidemia, Diabetes Mellitus, blood pressure, hyperglycemia, and atherogenic dyslipidemia can together or independently participate in the pathophysiology of OA (Veronese et al., 2019). Hyperglycemia and metabolic disorders associated with diabetes can cause conditions such as non-enzymatic protein glycosylation resulting in the formation of AGEs, resulting in hardening of connective tissue, nerve damage (neuropathy), blood vessel damage, hyperuricemia, decreased bone density, mild to chronic inflammation, abnormalities. Diabetes, cartilage/bone chondrocytes, insulin resistance, and Diabetes are consequences of visceral obesity, which originates from high levels of pro-inflammatory cytokines, causing chronic metabolic inflammation that can cause structural damage to joints(Allen et al., 2022).

Diabetes and OA are global epidemic problems that if not immediately addressed seriously will result in a significant increase in economic losses, especially for developing countries in Asia and Africa. National Health Insurance (JKN) data also shows an increase in the number of cases and financing of Diabetes services in Indonesia from 135,322 cases with financing of IDR 700.29 billion in 2014 to 322,820 cases with financing of IDR 1.877 trillion in 2017 (Steinmetz et al., 2023).

Radiological examinations are performed for diagnostic classification or to refer to orthopedics in OA patients, but radiological examinations require large costs. Osteoarthritis Monitoring Based on the WOMAC Index can be used to screen for Osteoarthritis in DM patients. The WOMAC Arthritis Index instrument has been declared Valid and reliable with the results of the Validity and Reliability tests of the WOMAC subscales (pain, stiffness, and physical function) being internally consistent with Cronbach's alpha coefficients of 0.91, 0.81, and 0.84, respectively. Screening and analysis of OA risk factors in DM patients are important to identify individuals with OA and DM so that prevention efforts can be carried out, early detection that allows for treatment opportunities, reducing morbidity. Screening and Osteoarthritis in Diabetes Mellitus patients can also be used to provide direction on OA and DM risk factors and are primarily aimed at preventing

OA and DM, preventing further complications, and improving the quality of life of OA and DM patients(Kim et al., 2020).

The prevalence of diabetes is increasing worldwide. The National Diabetes Federation (IDF) estimates that 536.6 million people are living with diabetes (diagnosed or undiagnosed) in 2021, and this number is expected to increase by 46%, reaching 783.2 million in 2045 (51.3%) (Katrine, 2021). Basic Health Research (Riskesdas) shows a significant increase in the prevalence of Diabetes, from 6.9% in 2013 to 8.5% in 2018. Central Java Province is ranked 9th in DM prevalence in Riskerdas 2013-2018 (Kemenkes RI, 2018). The prevalence of diabetes mellitus cases in Central Java province in 2018 was 20.57%, an increase compared to cases in 2017, which was 19.22%, exceeding the National Diabetes Mellitus prevalence rate in 2018, which was 8.5% (Ministry of Health, 2019).

Based on the Cilacap Regency Health Profile, in 2021, cases of Diabetes Mellitus in Cilacap Regency were 29,804 people, then increased in 2022 to 34,502 cases. Diabetes Mellitus is a disease that is included in the top five health problems in the Health Centers in Cilacap Regency, where in 2023 cases of Diabetes Mellitus in Cilacap Regency were mostly found in the Kedungreja Health Center work area. The prevalence of Diabetes Mellitus at the Kedungreja Health Center in 2021 was 1,375 people. Diabetes Mellitus is also one of the top 5 highest diseases at the Cipari Health Center with a prevalence of Diabetes Mellitus in 2021 of 906 people (Dinkes, 2021). Based on data from the Kedungreja Health Center in 2023, the number of DM sufferers in the Kedungreja Health Center work area reached 1,497 people (Dinkes, 2021). A similar thing also happened at the Cipari Health Center, where DM cases at the Cipari Health Center increased from year to year. Based on data from the UPTD Cipari Health Center in 2023, the number of DM sufferers was 1,206 people (P2PTM Cipari Health Center). Given the increasing evidence showing the relationship between DM and OA, it is very important to gain broader insights, to review and evaluate the presence of OA in DM status and vice versa and to evaluate evidence of risk factors for Osteoarthritis in DM sufferers.

METHOD

This study used a Cross-sectional design. The population of the study was patients with Diabetes Mellitus aged ≤ 45 years registered at the Kedungreja Health Center totaling 86 people and the Cipari Health Center totaling 67 people limited to the age of ≤ 45 years. The sample of this study was the entire population

of 153 patients with Diabetes Mellitus aged ≤ 45 years registered at the Kedungreja Health Center and Cipari Health Center (Cilacap Health Office). This study was conducted on DM patients aged ≤ 45 years in order to detect pain, stiffness and impaired function of the knee joints earlier in DM patients. The Womac Index is used to screen for Osteoarthritis in DM patients. The WOMAC Arthritis Index instrument has been declared Valid and reliable with the results of the Validity and Reliability test of the WOMAC subscale (pain, stiffness, and physical function). The Womac Index is a self-reported lower extremity-specific questionnaire containing 24 questions: 17 on physical function, 5 on pain, and 2 on stiffness. Each question has five response options ranging from 0 (no, no difficulty or no symptoms), Mild (1), Moderate (2), Severe (3), and up to 4 (unable to perform activity or extreme symptoms). Subtotal scores for pain, stiffness, and function range from 0 to 20, 0 to 8, and 0 to 68. Higher WOMAC scores indicate worse pain, stiffness, and functional limitations. The total WOMAC score is defined as the unweighted sum of all 24 items and ranges from 0 to 96(S et al., 2020).

RESULTS

Kedungrejo Health Center is located on Jalan Raya Kedungrejo No. 21, Kedungrejo District. The area of Kedungrejo Health Center is 82.01 km2 with a population of 91,489 people in 2023. The boundaries of Kedungrejo Health Center are as follows: to the north is Sidareja District, to the south is Patimuan District, to the east is Gandrungmangu District and to the west is Padaherang District. Cipari Health Center is located on Jalan Jenderal Ahmad Yani Number 2, Cipari District with an area of 107.53 km2 with a population of 68,843 people. The boundaries of Cipari Health Center to the north are Majenang District, to the east is Sidareja District, to the west is Wanereja District and to the south is Kedungreja District.

Table 1. Statistical Data on Characteristics of DM Patients in Cilacap in 2024

Variabel	Min	Max	Mean	SD
Umur	18	45	39,23	5,46
BMI	15,42	42,22	24,28	5,16
Pain	1	15	7,23	3,79
Stiffness	0	8	3,65	2,47
Physical Function	3	39	17,5	9,87
Total Score Womac	5	60	28,03	15,42

Most of the respondents were female (69.3%), with an average age of 39 years. Body Mass Index ranged from 15 to 42. The average pain score based on the WOMAC Index was 7.23. The average stiffness score based on the Womac Index was 3.65, and the average physical dysfunction was 17.5 with a total score based on the Womac Index of 28.03.

Table 2. Knee Pain Degree Score Based on Womac Index in DM Patients in Cilacap in 2024

Pain	None n(%)	Slight n(%)	Moderate n(%)	Very n(%)	Extremely n(%)
Walking	54(35,3)	39(25,5)	52 (34)	8 (5,2)	0 (0)
Stair Climbing	1(0,7)	18(11,8)	56 (36,6)	36(23,5)	42(27,5)
Nocturnal	68(44,4)	48 (31,4)	34 (22,2)	3 (2,0)	0 (0)
Rest	108(70,6)	42 (27,5)	3 (2,0)	0 (0)	0 (0)
Weight bearing	5 (3,3)	20 (13,1)	65 (42,5)	42(27,5)	21(13,7)

Most respondents did not feel pain when walking, at night and at rest but most respondents felt moderate pain when climbing stairs (36.6%) and carrying loads (42.5%). Respondents felt very severe pain when climbing stairs (27.5%) and carrying loads (13.7%).

Table 3. Stiffness Score Based on Womac Index in DM Patients in Cilacap in 2024

Stiffness	None n (%)	Slight n(%)	Moderate n(%)	Very n(%)	Extremely n(%)
Morning stiffness	29(19,0)	31(20,3)	38(24,8)	38(24,8)	17(11,1)
Stiffness occurring later in the day	29(19,0)	36(23,5)	41(26,8)	37(24,2)	10(6,5)

Most respondents felt moderate (24.8%) and severe (24.8%) stiffness in the morning and felt moderate stiffness (26.8%) that occurred the next day. There were respondents who felt very severe stiffness in the morning (11.1%) and the next day (6.5%).

Table 4. Physical Function Index Based on the Womac Index in DM Patients in Cilacap Regency

Physical Function	None n (%)	Slight n(%)	Moderate n(%)	Very n(%)	Extremely n(%)
Descending stairs	1 (0,7)	18 (11,8)	57(37,5)	37(24,5)	40(26,1)
Ascending stairs	1 (0,7)	18(11,8)	56(36,6)	37(24,2)	41(26,8)
Rising from sitting	92(60,1)	46(30,1)	14 (9,2)	1 (0,7)	0 (0)
Standing	108(70,6)	36 23,5)	9 (5,9)	0 (0)	0 (0)
Bending to floor	49 (32)	45(29,4)	29(19,0)	24(15,7)	6 (3,9)
Walking on flat surface	47(30,7)	44(28,8)	54(35,3)	8 (5,2)	0 (0)
Getting in / out of car	127(83,0)	23(15%)	3 (2%)	0 (0)	0 (0)

Going shopping	48 (31,4)	55 (35,9)	49 (32,0)	1 (0,7)	0 (0)
Putting on socks	121 (79,1)	21 (13,7)	11 (7,2)	0 (0)	0 (0)
Lying in bed	128 (83,7)	25 (16,3)	0 (0)	0 (0)	0 (0)
Taking off socks	121 (79,1)	21 (13,7)	11 (7,2)	0 (0)	0 (0)
Rising from bed	100 (65,4)	43 (28,1)	10 (6,5)	0 (0)	0 (0)
Getting in/out of bath	122 (79,7)	30 (19,6)	1 (0,7)	0 (0)	0 (0)
Sitting	87 (56,9)	36 (23,5)	29 (19,0)	1 (0,7)	0 (0)
Getting on/off toilet	58 (37,9)	58 (37,9)	22 (14,4)	15 (9,8)	0 (0)
Heavy domestic duties	0 (0)	0 (0)	44 (28,8)	83 (54,2)	26 (17,0)
Light domestic duties	10 (6,5)	53 (34,6)	89 (58,2)	1 (0,7)	0 (0)

Most respondents experienced moderate physical dysfunction when going down stairs (37.5%), climbing stairs (36.6%), walking on a flat surface (35.5%), and doing light household tasks (58.2%). Most respondents did not experience physical dysfunction when getting up from sitting, standing, bending, getting in/out of a car, putting on socks, lying in bed, taking off socks, getting out of bed, sitting. Respondents experienced extreme physical dysfunction when going down stairs (26.1), climbing stairs (26.8), bending on the floor (3.9) and doing heavy household tasks (17.0). The results of the Kolmogorov Smirnov Test showed that the variables of age, womac score, BMI of respondents had non-normal data distribution so that the statistical test carried out to analyze the relationship between age, womac score, BMI was the Spearman Rank Correlation test.

Table 5. Results of Spearman Correlation Statistical Test on DM Patients Aged ≤45 in Cilacap Regency

Variabel	Mean	SD	Correlation Coefficient	p-value
Age	39.23	5.459	0.62**	0.00
BMI	24.28	5.16	0.29**	0.00

* Spearman's rho test (significant if p-value<0.05)

The results of the Spearman Rank Correlation Statistical Test show that Age is related to the score of the degree of knee pain based on the womac index with a correlation coefficient value of 0.62, which means it is very strongly related with a positive relationship direction, meaning that the higher the age, the higher the degree of knee pain in DM patients aged ≤ 45 years. BMI, Systolic and Diastolic Blood Pressure are related to the Pain Degree Score in DM patients aged ≥ 45 years with a fairly strong positive relationship direction, meaning that the higher the BMI, systolic and diastolic blood pressure with the score of the degree of knee pain in DM patients aged ≤ 45 years.

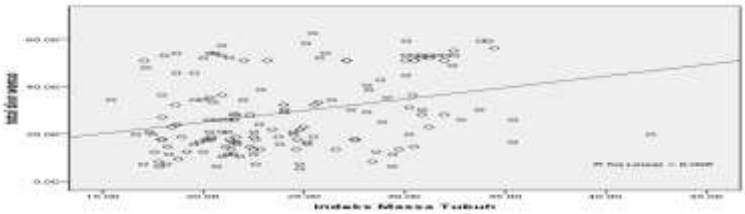
Table 6. Differences in Knee Pain Degree Scores Based on Gender in DM Patients Aged ≤ 45 Years in Cilacap Regency in 2024

Gender	n	%	Mean Rank	Mann Whitney	p-value
Woman	106	69.3	84.93	1650.000	0.001*

Man	47	30.7	59.11

*Mann Whitney test (significant if p-value<0.05)

The results of the Mann Whitney Statistical Test show a p-value <0.05, which means that there is a difference in the degree of pain based on gender, where the degree of knee pain in women has a higher average compared to men.



Graph 1. Relationship between Body Mass Index and Womac Total Score

Based on graph 1, it can be concluded that there is a linear relationship with a positive relationship direction between Body Mass Index and Total Womac Score. The higher the BMI, the higher the total Womac score.

DISCUSSION

The results of this study obtained an average pain score of respondents based on the WOMAC Index of 7.23. The average stiffness score based on the Womac Index was 3.65, and the average physical function disorder was 17.5 with an average total score based on the Womac index of 28.03. The results of this study indicate that most respondents did not feel pain when walking, at night and at rest, but most respondents felt moderate pain when climbing stairs and carrying loads. Respondents felt extreme pain when climbing stairs (27.5%) and carrying loads (13.7%).

Pain in OA is one of the most commonly reported symptoms and its severity varies widely. Those with poorer glycemic control report increased pain severity compared to those with DM with controlled HbA1C levels. Bone and articular cartilage metabolism can be affected by hyperglycemia, which can prove detrimental. The integrity of articular cartilage and extracellular matrix can be compromised in a proinflammatory environment; diabetic patients are more susceptible to inflammatory changes in the cellular environment. This suggests that DM may further complicate the pathology of osteoarthritic joints(Kim et al., 2020).

Hyperglycemia leads to increased levels of AGEs which adversely affect the integrity of the collagen chemical structure resulting in increased microtears. AGEs have an inhibitory effect on tendon-derived stem/progenitor cells (TSPCs), which may reduce their ability to maintain tendon homeostasis and reduce the risk of tendinopathy development. Using the WOMAC Index, one study revealed that patients diagnosed with DM and OA reported significantly increased pain

severity and frequency, increased incidence of bilateral synovitis, and increased likelihood of requiring knee arthroplasty compared to those with OA alone(Samaan & Taha, 2022).

The results of this study indicate that Age, BMI and Systolic and Diastolic Blood Pressure are associated with Pain Degree Scores in DM patients aged ≥ 45 years based on the Results of the Spearman Rank Correlation Statistical Test. Knee osteoarthritis is not fully indicated by the presence or absence of radiographic signs. Although there are many factors that influence symptomatic knee osteoarthritis, muscle weakness is associated with symptom complaints. Quadriceps muscle weakness is an important cause of complaints, and knee extensor muscle strength is a modifiable factor in knee arthritis. Low knee extensor strength has been associated with symptoms in patients with knee osteoarthritis. Low quadriceps muscle strength is associated with the development of radiological knee osteoarthritis(Dell'Isola et al., 2019).

When assessing knee arthritis function, muscle evaluation is also required. In particular, peak knee extension torque and peak knee extension torque. Knee extensor muscle weakness is an important risk factor for knee osteoarthritis and needs to be confirmed because muscle strength is a potential modifiable risk factor. Muscle strength is associated with knee pain and disability. In the definition of sarcopenia, low muscle function is usually assessed by slow walking speed or low handgrip strength. Both features are associated with increased morbidity and mortality in older adults (Kim et al., 2020). The effects of DM on joints are complex, insulin deficiency impairs osteoblastic bone formation and inhibits bone mass during growth in addition, AGEs can, directly and indirectly, alter matrix properties. A constellation of factors such as hyperglycemia, inflammatory cytokines and adipokines, oxidative and osmotic stress, and AGEs collectively inhibit osteocyte function, alter bone turnover, and decrease collagen properties(Tchetina et al., 2020).

The significant synovitis that occurs in OA may be exacerbated by the increased levels of inflammatory cytokines, adipokines, and prostaglandins seen in DM tissue. Signaling through innate immune pathways, such as toll-like receptors, may also contribute to inflammation in DM and OA. The hyperglycemic environment increases the production of reactive oxygen species and oxidants and promotes matrix catabolism. In this environment, cellular glucose transport becomes critical, which if altered as in DM, contributes to excess oxidative stress and tissue damage and accelerates OA. The effects of high glucose may be associated with impaired function of ATP-

sensitive K+ channels, which link GLUT channels to intracellular ATP/ADP levels and membrane potential(Chowdhury et al., 2022).

Aging is a known risk factor for Type 2 Diabetes Mellitus and OA. Radiographically defined knee OA increases dramatically with age, affecting 14% of adults over 25 years of age and 37% of those over 60 years of age. The prevalence of the disease increases sharply with age, with >10% of the population aged 65 years having OA. Prolonged hyperglycemia, both in the fasting and postprandial states, leads to advanced glycosylation end products (AGEs), oxidative stress and low-grade inflammation, and results in damage to blood vessels, especially in the heart, kidneys, eyes, nerves, but also other tissues(Przezak et al., 2022).

Nearly half of patients with type 2 DM have some form of arthritis. OA is a heterogeneous disorder affecting the joints of the hands, hips, and knees. In addition to the various localizations, various phenotypes of OA have been proposed including age-related, metabolic syndrome (closely related to abdominal adiposity), genetic, and post-traumatic OA. In metabolic syndrome-related OA, the mechanical impact of excess weight/obesity on the joints can easily explain lower limb OA. Other components of MetS, including dysglycemia (which can be considered equivalent to prediabetes), high blood pressure, and atherogenic dyslipidemia may jointly or independently participate in the pathophysiology of OA (Brognara et al., 2021). Type 2 DM is a very common complex disease with a genetic background and environmental risk factor interventions, especially poor lifestyle habits that cause overweight and obesity (Veronese et al., 2019).

CONCLUSION

The average pain score of respondents based on the WOMAC Index was 7.23. The average stiffness score based on the Womac Index was 3.65, and the average physical function impairment was 17.5 with an average total score based on the Womac index of 28.03. Early lifestyle changes, dietary modifications, and intensive glycemic control should be done and encouraged to delay the onset and severity of pain in OA.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgment

The author would like to thank the Institute for Research and Community Service of Siliwangi University for providing a grant for Capacity Development Research (PPKAP) to Toddler Mothers in Cisayong District, Tasikmalaya Regency. Students of the Public Health Study Program who are willing to provide assistance in this research.

REFERENCES

Abramoff, B., & Caldera, F. E. (2020). Osteoarthritis: Pathology, Diagnosis, and Treatment Options. In *Medical Clinics of North America* (Vol. 104, Issue 2, pp. 293–311). W.B. Saunders. https://doi.org/10.1016/j.mcna.2019.10.007

Alenazi, A. M., Alhowimel, A. S., Alshehri, M. M., Alqahtani, B. A., Alhwoaimel, N. A., Segal, N. A., & Kluding, P. M. (2023). Osteoarthritis and Diabetes: Where Are We and Where Should We Go? In *Diagnostics* (Vol. 13, Issue 8). Multidisciplinary Digital Publishing Institute (MDPI). https://doi.org/10.3390/diagnostics13081386

Allen, K. D., Thoma, L. M., & Golightly, Y. M. (2022). Epidemiology of osteoarthritis. *Osteoarthritis and Cartilage*, *30*(2), 184–195. https://doi.org/10.1016/j.joca.2021.04.020

Brognara, L., Mazzotti, A., Di Martino, A., Faldini, C., & Cauli, O. (2021). Wearable sensor for assessing gait and postural alterations in patients with diabetes: A scoping review. In *Medicina (Lithuania)* (Vol. 57, Issue 11). MDPI. https://doi.org/10.3390/medicina57111145

Chowdhury, T., Bellamkonda, A., Gousy, N., & Deb Roy, P. (2022). The Association Between Diabetes Mellitus and Osteoarthritis: Does Diabetes Mellitus Play a Role in the Severity of Pain in Osteoarthritis? *Cureus*. https://doi.org/10.7759/cureus.21449

Cui, A., Li, H., Wang, D., Zhong, J., Chen, Y., & Lu, H. (2020). Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine*, *29–30*. https://doi.org/10.1016/j.eclinm.2020.100587

Dell'Isola, A., Vinblad, J., Lohmander, S., Svensson, A. M., Turkiewicz, A., Franzén, S., Nauclér, E., W-Dahl, A., Abbott, A., Dahlberg, L., Rolfson, O., & Englund, M. (2019). Understanding the role of diabetes in the osteoarthritis disease and treatment process: A study protocol for the Swedish Osteoarthritis and Diabetes (SOAD) cohort. *BMJ Open*, *9*(12), 1–9. https://doi.org/10.1136/bmjopen-2019-032923

Dinkes. (2021). *Buku Profil Kabupaten Cilacap tahun 2021*.

Eitner, A., Wildemann, B., & Eitner, A. (2021). Follow us @BoneJointRes BJR Diabetes-osteoarthritis and joint pain. *Bone Joint Res*, *10*(5), 307–309. https://doi.org/10.1302/2046-3758.105.BJR

Kemenkes RI, K. K. (2018). *Laporan Riset Kesehatan Dasar 2018*. http://repository.bkpk.kemkes.go.id/3514/1/Laporan Riskesdas 2018 Nasional.pdf

Kim, M. J., Kang, B. H., Park, S. H., Kim, B., Lee, G. Y., Seo, Y. M., Park, K. S., & Yoo, J. Il. (2020). Association of the western ontario and mcmaster universities osteoarthritis index (WOMAC) with muscle strength in community-dwelling elderly with knee osteoarthritis. *International Journal of Environmental Research and Public Health*, *17*(7), 1–11. https://doi.org/10.3390/ijerph17072260

Primorac, D., Molnar, V., Rod, E., Jeleč, Ž., Čukelj, F., Matišić, V., Vrdoljak, T., Hudetz, D., Hajsok, H., & Borić, I. (2020). Knee osteoarthritis: A review of pathogenesis and state-of-the-art non-operative therapeutic considerations. *Genes*, *11*(8), 1–35. https://doi.org/10.3390/genes11080854

Przezak, A., Bielka, W., & Pawlik, A. (2022). Hypertension and Type 2 Diabetes—The Novel

Treatment Possibilities. *International Journal of Molecular Sciences*, *23*(12). https://doi.org/10.3390/ijms23126500

S, A. R., P, N., MA, S., & AA, S. (2020). Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index as an Assessment Tool to Indicate Total Knee Arthroplasty in Patients with Primary Knee Osteoarthritis. *IIUM Medical Journal Malaysia*, *19*(3), 47–53. https://doi.org/10.31436/IMJM.V19I3.1664

Samaan, S. F., & Taha, S. I. (2022). The Impact of Metabolic Syndrome on Quality of Life Among Individuals With Knee Osteoarthritis Living in Egypt. *Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders*, *15*. https://doi.org/10.1177/11795441221097361

Steinmetz, J. D., Culbreth, G. T., Haile, L. M., Rafferty, Q., Lo, J., Fukutaki, K. G., Cruz, J. A., Smith, A. E., Vollset, S. E., Brooks, P. M., Cross, M., Woolf, A. D., Hagins, H., Abbasi-Kangevari, M., Abedi, A., Ackerman, I. N., Amu, H., Antony, B., Arabloo, J., … Kopec, J. A. (2023). Global, regional, and national burden of osteoarthritis, 1990–2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet Rheumatology*, *5*(9), e508–e522. https://doi.org/10.1016/S2665-9913(23)00163-7

Tchetina, E. V., Markova, G. A., & Sharapova, E. P. (2020). Insulin Resistance in Osteoarthritis: Similar Mechanisms to Type 2 Diabetes Mellitus. In *Journal of Nutrition and Metabolism* (Vol. 2020). Hindawi Limited. https://doi.org/10.1155/2020/4143802

Veronese, N., Cooper, C., Reginster, J. Y., Hochberg, M., Branco, J., Bruyère, O., Chapurlat, R., Al-Daghri, N., Dennison, E., Herrero-Beaumont, G., Kaux, J. F., Maheu, E., Rizzoli, R., Roth, R., Rovati, L. C., Uebelhart, D., Vlaskovska, M., & Scheen, A. (2019). Type 2 diabetes mellitus and osteoarthritis. In *Seminars in Arthritis and Rheumatism* (Vol. 49, Issue 1, pp. 9–19). W.B. Saunders. https://doi.org/10.1016/j.semarthrit.2019.01.005