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The Impact of Pesticides and Workload on Osteoarthritis Incidence in Farmers: A Narrative Review

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Abstract

Osteoarthritis (OA) is a degenerative joint disease with abnormalities including bone remodeling, cartilage degradation, synovial inflammation, and osteophyte formation. Patients complain of pain, swelling, limitation of motion, and loss of joint function. One of the risk factors for OA is physically demanding jobs, such as agriculture. The World Health Organization (WHO) states that farming for 1-9 years and ≥10 years increases the risk of OA by 4.5 times and 9.3 times, respectively. This study aimed to determine the relationship between pesticides and workload (working period, work attitude/posture, and lifting heavy loads) with OA incidence in farmers. This research is a narrative review of the last ten years' journals. The study results concluded no relationship between pesticides and farmers' OA because there was no difference in pyrethroid, neonicotinoids, organophosphate, and their metabolites in OA patients' serum. The workload is related to the farmer's OA, especially attitude/work posture and working period. Squatting and kneeling pose becomes a risk of knee OA while lifting heavy objects is not associated with OA of farmers. This study concludes that there is no relationship between pesticides and OA, but there is a relationship between attitude/posture and tenure with OA in farmers.

Keywords: farmers, osteoarthritis, pesticides, posture, workload, working period

Review Article

Dampak Pestisida dan Beban Kerja dengan Kejadian Osteoarthritis pada Petani: Tinjauan Naratif

Abstrak

Osteoarthritis (OA) merupakan penyakit degeneratif sendi dengan patologi meliputi *remodelling* tulang, degradasi tulang rawan, peradangan sinovial, dan pembentukan osteofit. Pasien sering mengeluhkan nyeri, bengkak, keterbatasan gerak dan hilangnya fungsi normal sendi. Salah satu faktor risiko terjadinya OA adalah pekerjaan yang membutuhkan kekuatan fisik, contohnya bidang pertanian. *World Health Organization (WHO)* menyebutkan bertani selama 1-9 tahun dan ≥10 tahun meningkatkan risiko OA berturut-turut sebesar 4,5 kali dan 9,3 kali. Tujuan

penelitian ini mengetahui hubungan penggunaan pestisida dan beban kerja (masa kerja, sikap/postur kerja, dan mengangkat beban berat) dengan kejadian OA pada petani. Penelitian ini merupakan tinjauan naratif dari jurnal yang terbit selama 10 tahun terakhir. Hasil penelitian menyimpulkan tidak ada hubungan antara pestisida dengan OA petani, karena tidak ada perbedaan konsentrasi serum piretroid, neonicotinoid, dan organofosfat serta metabolitnya pada penderita OA. Beban kerja berhubungan dengan OA petani, khususnya sikap/postur kerja dan masa kerja. Sikap jongkok dan berlutut berisiko menyebabkan OA lutut, sedangkan mengangkat benda berat tidak berhubungan dengan OA petani. Penelitian ini menyimpulkan tidak ada hubungan pestisida dengan OA, namun terdapat hubungan

sikap/postur dan masa kerja dengan OA pada petani.

Kata Kunci: beban kerja, masa kerja, osteoarthritis, pestisida, petani, postur kerja

INTRODUCTION

According to the American College of Rheumatology, Osteoarthritis is a collection of joint pathologies including cartilage degradation, bone remodeling, osteophyte formation, and synovial inflammation that causes pain, stiffness, swelling, and loss of normal joint function. The appendicular joints that are most commonly affected by osteoarthritis include the knees, hips, and hands (Kolasinski et al., 2020). Osteoarthritis causes pain and disability for sufferers, thus interfering with daily activities and causing severe socioeconomic impacts (Pratiwi, 2015). Eighty percent of people with osteoarthritis have limited mobility, and 25% cannot carry out their main daily activities (WHO, 2020). The increasing prevalence of osteoarthritis is associated with physically demanding jobs or heavy work, such as agriculture (CDC, 2020). WHO states that farming for 1-9 years and ≥ 10 years increases OA risk by 4.5 times and 9.3 times, respectively (WHO, 2020). The Centers for Disease Control and Prevention (CDC) mentions the risk factors for osteoarthritis in farmers related to workload, while the WHO has not clearly stated the risk factors of osteoarthritis in farmers.

The workload is one of the risk factors for osteoarthritis in farmers. The narrative review research by Schram et al. (2020) showed that lower extremity osteoarthritis increased in occupations involving heavy physical workloads such as heavy lifting, squatting, bending the knees, kneeling, and climbing. Reducing workload has been shown to reduce the risk of lower extremity osteoarthritis. Narrative umbrella review research by Schram et al. (2020) discussed occupational risk in general (farmers and other occupations), not only specific to farmers. Therefore, this study is the first narrative review that discusses the risk factors for workload and the incidence of osteoarthritis in farmers. The workload studied was heavy physical activity. Strenuous activities such as prolonged standing long walks, lifting heavy weights, and pushing heavy objects are risk factors for knee osteoarthritis due to the stress on the joint. Excessive and continuous pressure on the cartilage causes meniscus degeneration and

changes in joint cartilage, further risking knee osteoarthritis (Rahmanto and Aisyah, 2019). In addition, the workload is also associated with hip and hand osteoarthritis. Hip osteoarthritis is associated with lifting and prolonged standing, whereas hand osteoarthritis is more common in manual dexterity work (Johnson et al., 2014).

There is a risk factor for farmers' osteoarthritis in addition to the workload, which is the use of pesticides. Spraying pesticides that are not by standards or not wearing personal protective equipment (PPE) causes the entry of pesticides into the body through inhalation (inhalation), digestion, or injured skin (Mahyuni, 2015). Exposure to pesticides affects bone health. Animal studies have shown that Thiram, a commonly used carbamate-type pesticide, adversely affects bone health. Thiram reduces chondrocytes' vascular distribution and cell death in the tibial growth plates (TGPs), which further increases the risk of osteoarthritis (Huang et al., 2019). However, studies are still needed to assess whether pesticide exposure in humans increases the risk of osteoarthritis. This study is the first narrative review to discuss the risk factors of pesticides with the incidence of osteoarthritis in humans.

Therapy to cure osteoarthritis is not yet available. Therapy is more aimed at reducing pain, maintaining mobility, preventing disability, and improving quality of life. Education plays an essential role in managing osteoarthritis (Winangun, 2019) and is strongly supported by knowledge about risk factors for osteoarthritis. Based on this description, this study aims to determine the relationship between pesticides and workload (which includes work attitude/posture, working period, and lifting heavy loads) with the incidence of osteoarthritis in farmers. The benefits of this research can be used as a source of literature/educational reference to prevent and reduce the prevalence of osteoarthritis in farmers.

METHOD

Research Method

This research uses a narrative review method. The literature search was carried out through Pubmed, ScienceDirect, Google Scholar, and Garuda databases using keywords listed in Table 1. The literature search was limited from 2010 to 2020. The selected literature was in English and Indonesian, in the form of human research results (case-control, cross-sectional, or cohort). Journal search results using keywords in the databases are also carried out by citation searching. The literature is then selected through

titles and abstracts, and a quality assessment is carried out using the JBI critical appraisal tool. The literature has good study quality if it answers "Yes" to 80-100% of questions, sufficient quality if it answers "Yes" to 50-79% of questions, and poor quality if it answers "Yes" to <50% of questions based on the JBI critical appraisal tool. The literature is then extracted based on the components needed to answer the research problem. Literature is also synthesized through paraphrasing to produce conclusions. The addition of other articles and textbooks aims to sharpen the discussion of research results.

Table 1. Keywords in each *database*

Database	Kata Kunci
Pubmed	("osteoarthritis" OR "osteoarthritis"[Mesh]) AND ("pesticide" OR "working duration" OR "working position" OR "physical workload" OR "weightlifting" OR "heavy lifting") AND ("agri*" OR "farmer")
Science Direct	"osteoarthritis" AND ("pesticide" OR "working duration" OR "physical workload" OR "working position" OR "weightlifting" OR "heavy lifting") AND ("agricultural worker" OR "farmer")
Google Scholar	"osteoarthritis" AND ("pesticide" OR "working duration" OR "working position" OR "physical workload" OR "weightlifting" OR "heavy lifting") AND ("agri*" OR "farmer") ("osteoarthritis" OR "osteoarthritis") AND ("pestisida" OR "beban kerja fisik" OR "masa kerja" OR "posisi kerja" OR "postur kerja" OR "sikap kerja" OR "durasi kerja" OR "lama kerja" OR "beban berat" OR "angkat beban") AND "petani"
Garuda	risiko osteoarthritis (Title / Abstract) risiko osteoarthritis (Title / Abstract)

The operational definition of *workload* is task demands or efforts to do work (Tarwaka, 2015). The workloads studied included work attitudes/postures, years of service, and lifting heavy loads. Meanwhile, a farmer in this study is defined as someone who works to fulfill his needs from agricultural business activities, whether in the form of agricultural businesses in horticulture, food crops, plantations, animal husbandry, and fisheries (Koto, 2014).

Literature Search Result

A search using keywords yielded a total of 786 works of literature with details of Pubmed (n=7), ScienceDirect (n=24), Google Scholar (n=594 for English keywords, n=114 for Indonesian keywords), and GARUDA (n=47). After going through the selection process and adding citation searching, the researchers determined the number of 8 literature that met the inclusion criteria. Seven works of literature have good quality, and one work of literature has sufficient quality based on the JBI critical appraisal tool (Table 2).

Table 2. Literature Search

Author and Year of Publication	Study type	Research Subject	Results associated with the Research Problem	Quality of study
(Webber <i>et al</i> , 2020)	Cross-sectional	299 participants consist of breeders and farmers	There is no relationship between years of work in agriculture (agriculture and animal husbandry) with joint health, particularly the diagnosis of osteoarthritis ($p=0.28$) in age-adjusted results and BMI as a coefficient	Good (100% or 8/8)
(Andersen <i>et al</i> , 2012)	Cohort	2,117,298 participants (217,055 farmers, 487,156 construction workers, 4381 bricklayers, 496,478 health care assistants, 912,228 office workers)	Male farmers had an increased risk of hip osteoarthritis after 1-5 years working as a farmer (HR 1.63) and a threefold increased risk (HR 3.00) after 10 years. Female farmers had a risk of hip osteoarthritis at 6-10 years (HR 1.59) and more than 10 years of service (1.62). Furthermore, there is a dose-response relationship between cumulative years of farming and hip osteoarthritis (HR 4.20) in male farmers who have worked for more than 20 years.	Good (90% atau 10/11)
(Do <i>et al</i> , 2020)	Cross-sectional	264 female farmers	Cumulative squatting working time (CSWT) is positively correlated with the femoral bowing angle (FBA), meaning that prolonged squatting positions can increase FBA. On the other hand, cumulative heavy lifting working time (CLWT) decreases FBA, meaning that the longer it takes to lift heavy loads, the FBA decreases.	Good (100% atau 8/8)
(Hong <i>et al</i> , 2020)	Cross-sectional	486 participants are farmers, 238 of them are men and 248 are women	Cumulative squatting working time (CSWT) is associated with a meniscus tear, meaning that a prolonged squatting position is associated with a meniscus tear. On the other hand, cumulative heavy lifting working time (CLWT) is not significantly associated with meniscus tear	Good (100% or 8/8)
(Rachmi <i>et al</i> , 2018)	Cross-sectional	117 participants work as dairy farmers	Squatting position, working period 5 years, and lifting weights (grass feed and concentrate) were associated with knee pain ($p<0.05$). Working period of more than 6 years is associated with knee pain.	Good (100% or 8/8)
(Franklin <i>et al</i> , 2010)	Case-control	1,408 participants (576 men and 832 women) were assigned to the case group. In addition, 490 male participants and 592 female first-degree relatives from the case group served as the control group.	Farmers' jobs, especially men, increase the likelihood of undergoing TKR (total knee replacement) and THR (total hip replacement) due to osteoarthritis. Farmer work is inherited in families, so inherited osteoarthritis-related genes interact with workload risk. Heavy physical workload (in men) is associated with TKR and THR due to osteoarthritis.	Good (100% or 10/10)
(Muraki <i>et al</i> , 2011)	Cross-sectional	1,402 participants (512 males and 890 females)	Agricultural, forestry, and fishing workers had the highest rates for kneeling, crouching, walking, and lifting weights. For women, agricultural, forestry, and fisheries workers have significantly lower mJSW values compared to other occupations. Furthermore, <u>work activities such as kneeling and squatting were</u>	Good (100% or 8/8)

(Li et al, 2020)	Cross-sectional	25 people with osteoarthritis	significantly associated with lower mJSW and higher OPA, whereas walking and lifting weights were significantly associated with lower mJSW, but not with OPA. In patients with osteoarthritis, there is no difference in serum pesticide concentrations based on a history of arthritis	Moderate (75% or 6/8)
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DISCUSSION

The Relationship of Pesticide with Osteoarthritis in Farmers

Recent research on pesticides associated with osteoarthritis in humans was conducted by Li et al. (2020). This research is based on the WHO statement, which states that farming activities increase the risk of osteoarthritis. This research is also based on the research background of Huang et al. (2019) on experimental animals that the pesticide Thiram affects bone health. Li et al. (2020) studied pesticide serum in osteoarthritis sufferers, although it is not clear whether the population came from agricultural workers or not. A total of 25 patients with osteoarthritis were taken venous blood to analyze serum pesticides using the ultraperformance liquid chromatography-tandem mass spectrometry method. This study concluded that there was no difference in the concentration of pesticides in the serum of patients with osteoarthritis. However, it is not explained further about the pathomechanism. The conclusion of the research of Li et al. (2020) should be interpreted with caution concerning the small sample size (n=25), the population from which the sample was derived, and the analysis of a single serum to represent pesticide exposure over time is debatable.

The research results of Li et al. (2020) are different from previous research by Lee et al. (2007) about the relationship between serum concentrations of persistent organic pollutants (POPs) and arthritis status in 1,721 participants. POPs are highly toxic organic chemical compounds that persist in the environment, accumulate biologically in the fatty tissues of living organisms, travel long distances, and flow naturally to colder climates. The POPs studied included polychlorinated biphenyl and organochlorine pesticides. Li et al. study concluded that Rheumatoid Arthritis (RA) was strongly associated with serum POPs concentrations, and osteoarthritis was weakly associated with serum

POPs concentrations. Although the strength of the association with osteoarthritis was weaker than RA, osteoarthritis was still associated with POPs in a sample of women. POPs may be involved in the pathogenesis of osteoarthritis because they are deposited in adipose tissue, causing metabolic disturbances, including excess leptin secretion. Leptin secretion is associated with the onset and development of osteoarthritis because it is a metabolic factor associated with obesity (Lee et al., 2007). Obesity causes the pathogenesis of osteoarthritis in two ways, namely increasing joint load and mechanical wear of joints and increasing local and systemic inflammation (Xie and Chen, 2019).

Differences in the research results by Li et al. (2020) with Lee et al. (2007) were caused by differences in the types of pesticides studied. Li et al. (2020) investigated the serum of organophosphate, pyrethroid, and neonicotinoid pesticides and their metabolites. In comparison, Lee et al. (2007) examined the serum of organochlorine pesticides. The nature of organochlorines as a persistent pollutant in the environment also influenced the study results. In addition, it may also be influenced by the number of samples that differ significantly. Li et al. (2020) mention that research results must be interpreted with caution about small sample sizes. Research by Li et al. (2020) has sufficient quality and does not meet all the JBI critical appraisal tool criteria. Research by Li et al. (2020) has not included a strategy to deal with confounding factors.

The Relationship of Work Attitude/ Posture with Osteoarthritis in Farmers

The results of Do et al. (2020) on female farmers in Korea showed that cumulative squatting working time (CSWT) was positively correlated with the femoral bowing angle (FBA), meaning that the prolonged squatting position increased the femoral bowing angle (FBA). The squatting position of female farmers in Korea is in the form of the Asian squat, which is a deep

squatting posture by widening the distance between the knees and making contact between the thighs and calves. This study took the femoral bowing angle (FBA) as a variable because of its association with knee osteoarthritis, namely increasing the load on the mechanical axis. The femoral bowing angle (FBA) is an acute angle formed by the intersection of 2 lines. The first line (red line) extends from the center of the femur below the level of the lesser trochanter (point A) past a point 5 cm distal to point A (point B). The second line (blue line) extends from the center of the distal femoral condyle through the center of the femur in a 5 cm proximal direction (point C) and a point located 5 cm proximal to point C (point D) (Figure 1).

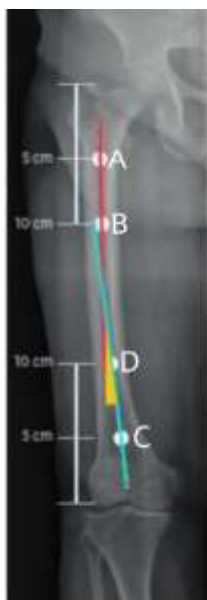


Figure 1. Femoral Bowing Angle/FBA (yellow shaded area) (Source: Do et al, 2020)

Similar research was conducted by Hong et al. (2020) on farmers in Korea. This research shows that the cumulative squatting working time (CSWT) or the cumulative squatting time at work is significantly related to meniscus tears. Meniscus tears were assessed using magnetic resonance imaging (MRI), then the tear pattern was classified based on the MRI Osteoarthritis Knee Score. Meniscus tears were studied because they are a major risk factor for the progression of knee osteoarthritis. Research by Do et al. (2020) and Hong et al. (2020) is research that takes data from the Korean farmers' knee cohort of Jeonnam Center for Farmers' Safety and Health (KFKC). This KFKC agency was established to identify work-related factors associated with knee osteoarthritis among farmers. Furthermore, from the JBI critical

appraisal tool results, these two studies meet all of the criteria, and it can be concluded that the studies are of good quality.

Research by Rachmi et al. (2018) in Indonesia also reported that a squatting position is associated with knee pain, as measured by the Knee Injury and Osteoarthritis Outcome Score (KOOS) according to bivariate analysis. This study took the subject of dairy farmers (dairy cattle farmers). Then, Muraki et al. (2011) reported that agriculture, forestry, and fisheries workers have the highest kneeling, squatting, walking, and lifting weights. Agricultural, forestry, and fishery workers, especially women, have significantly lower minimum joint space width (mJSW) values compared to other occupations. The minimum joint space width (mJSW) is the minimum vertical joint space distance (Figure 2). Work activities such as kneeling and squatting had a significant relationship with lower mJSW values and higher osteophyte area (OPA). The osteophyte area (OPA) or osteophyte area was defined as the area protruding medially from the extension of the tibial border (Fig. 3). This study focuses on the value of mJSW and OPA because these variables can be measured with continuous values and differ from previous studies that used categorical variables such as Kellgren-Lawrence grading and knee arthroplasty surgery status. Kneeling and squatting activities have a significant relationship with lower mJSW values and higher OPA, which indicates that these activities have a strong relationship with knee osteoarthritis because they have a relationship with two variables at once. Research by Rachmi et al. (2018) and Muraki et al. (2011) has met all the criteria in the JBI critical appraisal tool, and it can be concluded that the quality of the study is good.

Many studies identify squatting and kneeling activities as major risk factors for knee osteoarthritis (Verbeek et al., 2017). Studies in cadavers show that the pressure increases dramatically when the knee is flexed between angles of 90° and 120°. This pressure is caused by the contact pressure when the knee is deeply flexed. Too much pressure (> 25 MPa) triggers cartilage damage and may initiate the development of degenerative joint disease (Thambyah, Goh, and Das De, 2005).



Figure 2. Minimum Joint Space Width / mJSW (red line) (Source: Muraki et al, 2011)



Figure 3. Osteophyte Area/OPA (red area) (Source: Muraki et al, 2011)

The Relationship of Working Period with Osteoarthritis in Farmers

The research results by Webber et al. (2020) showed that there was no relationship between years of service in agriculture (agriculture and livestock communities) and osteoarthritis after adjusting for age and BMI as a coefficient. This result was beyond the researcher's expectations and explained by the highly collinear relationship between age and years of service, resulting in a type 2 error. Research by Rachmi et al. (2018) in Indonesia stated that five years of dairy farmers are associated with knee pain as measured by the Knee Injury and Osteoarthritis Outcome Score (KOOS) in a bivariate analysis, as well as tenure of more than six years associated with knee pain in a multivariate analysis. Research by Andersen et al. (2012) with a larger sample and cohort study design reported that male farmers have an increased risk of hip osteoarthritis after 1-5 years of employment (HR 1.63) and a threefold increased risk (HR 3.00) after ten years. Meanwhile, female farmers risk developing hip osteoarthritis at 6-10 years (HR 1.59) and more than ten years of service (1.62). In addition, it was found that there was a relationship between the length of work and hip osteoarthritis (HR 4.20) for

male farmers who had worked for more than 20 years. Male farmers were also associated with the risk of undergoing TKR (total knee replacement) and THR (total hip replacement) due to osteoarthritis. This study also mentioned that work with heavy physical loads is associated with TKR and THR due to osteoarthritis (Franklin et al., 2010). So, it can be concluded that a long working period with a heavy physical burden, such as farmers, is an independent predictor of osteoarthritis. In addition, continuous use of joints in heavy work also causes traumatic injuries such as meniscus tears and ligament instability, which predisposes to osteoarthritis (Soeroso et al., 2014).

Research by Webber et al. (2020) and Franklin et al. (2010) has met all the criteria in the JBI critical appraisal tool, and it can be concluded that the quality of the study is good. Research Andersen et al. (2012) are also of good quality but do not meet one of the criteria because this study has not included an exploration plan for respondents who have lost to follow-up.

The Relationship between Lifting Heavy Weights and Osteoarthritis in Farmers

Research by Do et al. (2020) on female farmers in Korea reported that cumulative heavy lifting working time (CLWT) lowers the femoral bowing angle (FBA). The longer was lifting heavy loads, the smaller the FBA. It is because lifting heavy weights is done in a standing position and places the load along the axis of the long bones. In addition, weightlifting is an endurance exercise that increases lower extremity muscle strength, thereby positively affecting bone density (Shanb and Youssef, 2014). This supports the conclusion that lifting heavy weights serves to maintain or strengthen muscles and is a protective factor against femoral bowing.

Research by Hong et al. (2020) on farmers in Korea proved that the cumulative heavy lifting working time (CLWT) was not significantly related to meniscus tears. These results are supported by a large-scale cohort study of workers handling airport baggage, which found that lifting weights alone did not cause meniscus tears. The risk increases when weightlifting is combined with squatting or kneeling (Mikkelsen et al., 2016).

The research of Muraki et al. (2011) examines the activities of lifting weights that are often carried out by agricultural, forestry, and

fishery workers. Lifting weights were significantly associated with a smaller minimum vertical joint space width (mJSW) but not with osteophyte area or osteophyte area (OPA). This result was no more significant than kneeling and squatting activities associated with both variables simultaneously (mJSW and OPA). Research by Rachmi et al. (2018) on dairy farmers in Indonesia also concluded that lifting weights is associated with knee pain as measured by the Knee Injury and Osteoarthritis Outcome Score (KOOS) according to bivariate analysis, but results were not found in multivariate analysis.

Study Limitation

This review takes the latest journals in the last ten years (2010-2020) and with the subject of farmers to put forward research novelty. However, the journals obtained with the farmer as subjects displayed various osteoarthritis-related variables. Osteoarthritis in a recent study was not only shown in the ICD-10 diagnostic criteria or Kellgren-Lawrence grading but other radiological assessments such as femoral bowing angle (FBA), meniscus tear, minimum joint space width (mJSW), and osteophyte area (OPA). In addition, it is also expressed as knee pain as assessed by the Knee Injury and Osteoarthritis Outcome Score (KOOS) and TKR (total knee replacement) and THR (total hip replacement) status due to osteoarthritis. Research on the effect of pesticides on osteoarthritis in farmers was not found directly. Recent research by Li et al. (2020) studied pesticide serum in patients with osteoarthritis. The results of this review should also be interpreted with caution, given the small sample size.

CONCLUSION

This study concludes that there is no relationship between pesticide use and osteoarthritis. However, there is a relationship between attitude/work posture and tenure with osteoarthritis in farmers. The results of this study can be used as a source of education to reduce the prevalence of farmers' osteoarthritis. Further research is needed to focus on the risk factors use of pesticides in osteoarthritis with a larger sample and using a follow-up study.

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