eISSN: 2620-7869
HEARTY
Jurnal Kesehatan Masyarakat
Vol. 12 No. 3, Agustus 2024, Hal. 518-523

THE IMPACT OF CHRONIC PESTICIDE ON INCIDENCE OF GASTRIC CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS

Mukhammad Arif Hadi Khoiruddin [*], Jasmine Tartila, Wiwien Sugih Utami, Irawan Fajar Kusuma
Faculty of medicine, Universitas Jember,
Jl. Kalimantan Tegalboto No.37, Krajan Timur, Sumbersari, Jember, 68121, Jember, Indonesia
Email: *arifhakz08@gmail.com*

Abstract

Indonesia as an agricultural country relies heavily on its corps as the main sector of nation's development. On daily basis, many farmers use pesticide to increase corps productivity. However, pesticides were known to induce malignancy, one of them being gastric cancer; the fourth most mortal cancer in the world, with less than 12 month life expectancy on advanced stage, thereby making it a global health problem. This research used systematic review and meta-analysis methods to examine pesticide exposure variables on gastric cancer cases. Three journals were found, and meta-analysis results showed that there was a significant increase in the risk of gastric cancer in respondents who experienced pesticide exposure, especially with prolonged exposure with an odds ratio of 1.47 (more than two years). However, this review cannot explain the toxicity dose of pesticides and the nutritional status of respondents which can increase the incidence of gastric cancer due to the lack of research on related variables.

Keywords: pesticides, Incidence, Gastric Cancer

Introduction

Indonesia is a large agricultural country, which means that the agricultural sector is the main sector in the country's development. In carrying out their work, many farmers use pesticides to increase their production. This is proven by data from the Ministry of Agriculture, there were 3,207 pesticides that were registered in Indonesia in 2016 [(1)]. Even though pesticides were considered useful, they have the potential to be toxic to other living creatures, including humans. This is because the active ingredients contained that can affect the ecosystem as a whole [(2)]. One of the side effects of pesticides exposure is gastric cancer. According to epidemiological studies, gastric cancer is the fourth cause of cancer deaths worldwide with survival of less than 12 months for advanced stages making it a global health problem [(3,4)]. However, there has not been enough research discussing the impact of pesticides exposure on the incidence of gastric cancer. Based on the description above, the aim of this article is to determine the impact of pesticide exposure on the incidence of gastric cancer.

Methods

The research was carried out in a systematic review and meta-analysis. Research data is secondary data taken from national and international research articles. The article search process was carried out in August 2022. Sources were taken from various PubMed databases, Science Direct, Google Scholar, and other trusted sources. The article search technique uses eligibility criteria with

Submitted: June-2023 Received: December-2023 Available online: August-2024

PICOS (Population/patients, Intervention, Comparison, Outcome, and Study Design) through keywords and their synonyms. Keyword synonyms were searched using the help of Medical Subjects Headings (MeSH) which was displayed using the Preferred Reporting Systematic Review and Meta Analysis (PRISMA) flow diagram. The PRISMA of this research is listed in Figure 1.

Results

The articles used are published in 2012-2022. After reviewing the overall quality of the journal, three articles were found that met the final inclusion criteria. The characteristics of these journals are listed in Table 1.

Each article discusses exposure to various pesticides, starting from organochlorines, methyl bromide, and exposure to pesticides in general. However, these three journals have objective and fulfilled systematic assessment so that the results can represent the research criteria well.

Yi, et al (2014) reported an increase in gastric cancer cases in Vietnam war veterans from Korea in 1999-2003 who were exposed to pesticides with a p-value of 0.004 and an adjusted hazard ratio (aHR) 1,14 (CI: 1.04 – 1.24)[5]. Research by Luce, et al (2020) showed that there is an increase in incidence among respondents with a standardized mortality ratio (SMR) of 1.08 (CI: 0.86 – 1.34) in men and 1.94% (CI: 1.24-2.89) in women[6]. Barry, et al (2012) showed that exposure to methyl bromide over a period of fifteen years can increase the incidence of mortality due to stomach cancer with a risk ratio of 3.33% (CI: 1.3 - 8.51)[7]. These three journals have the same variable duration of exposure of at least 2 years of use. Based on this data, a meta-analysis carried out obtained an odds ratio (OR) of 1.47, which means that exposure to pesticides causes a 1.47x greater incidence of stomach cancer as shown in Figure 2.

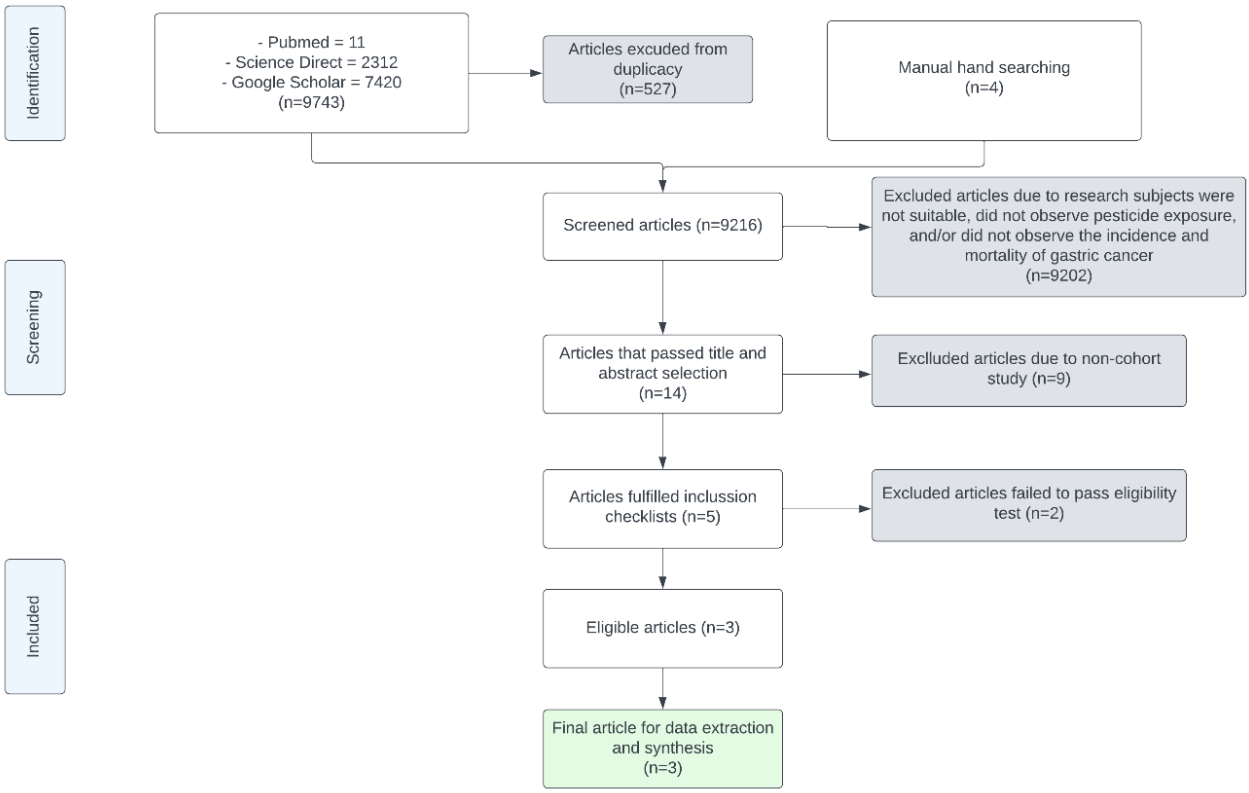

Figure 1. PRISMA flow chart

Table 1. Characteristics of the articles studied.

Researcher, Year	Methods	Exposure*	Results
Luce, 2020	Cohort	Organochlorine (Chlordecone)	There was an insignificant relationship caused by organochlorines
Barry, 2012	Cohort	Methyl bromide	There is an increased risk of gastric cancer in farmers who used methyl bromide
Yi, 2014	Cohort	Agent Orange (2,4,5-trichloropjenoxyacetic acid)	There is a significant relationship between the use of pesticides and the incidence of stomach cancer

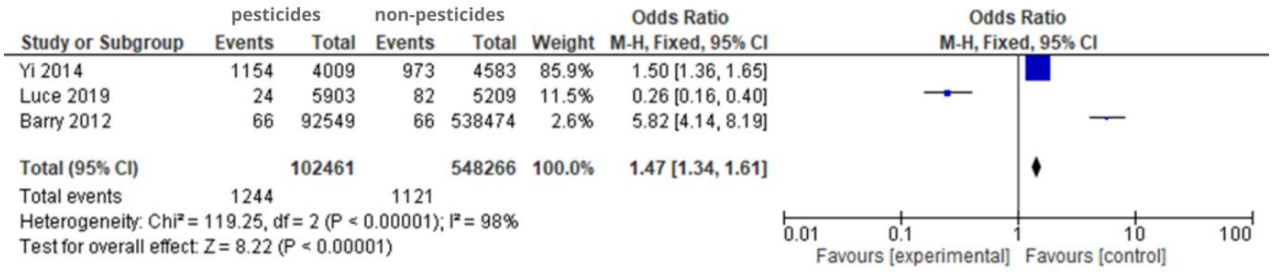

Figure 2. Meta-analysis

Discussion

This comprehensive investigation of 102.461 of pesticide subjects and 548.474 control from three journals of gastric cancer, we recognized several occupational exposure that were related with gastric cancer. we found that all of journals described an increase in gastric cancer due to pesticides. Pesticide regularly utilized in agriculture activity.

The residue of pesticides may be found in various foods and drinks, including juice and livestock feed [8]. In addition, Reiler et al., 2015 found that pesticide residues still remained and could not be removed even after washing and peeling [9]. If accidentally consumed in a long term, may possibly driven to health problem.

Human exposure to pesticides can happen through several pathways, including work activities involving production, transportation, shipping, application of pesticides, as well as repeated exposure due to living in areas with high levels of contamination and accumulation in food [10]. Health problems arose from skin contact, ingestion, and inhalation. In addition, the type of pesticide, duration, route of exposure, and a person's health status (for example nutritional deficiencies) are influencing factors [11,12]. In the human body, pesticides can be metabolized, excreted, stored, or biologically accumulated in body fat [13,14].

The analysis in this study showed an odds ratio (OR) of 1.47, which means that exposure to pesticides causes a 1.47x greater incidence of gastric cancer. Gastric cancer cases due to pesticides are thought to occur due to cellular changes involving deoxyribo nucleic acid (DNA) methylation, histone/chromatin structure, nucleoson placement, and non-coding RNA due to reactive oxygen spesies (ROS) [15,16].

Human oxoguanine glycosylase 1 (hOGG1) is responsible for repairing 8-hydroxy-deoxyguanosine residue, which is the major form of oxidative DNA damage initiated by ROS. hOGG1 decreased DNA repair activity, and might increase of gastric cancer risk due to micro RNA(miRNA) aberrations [17]. Aberrant expression of miRNAs could inhibit tumour suppressor genes or inappropriately activate oncogenes resulting in cancer, increased invasion and metastasis [18].

Several studies have observed dysregulation of the expression of different miRNAs. At this stage, there are three mechanisms at play: co-localization of miRNA-coding genes, epigenetic regulation, and altered protein expression involving miRNA processing and biogenesis [19,20]. Specifically these chemicals induce tumors after prolonged administration [21–23].

These data might have important implications for individual risk stratification, consideration of selected screening or surveillance, and counseling regarding risk factor modification to attenuate gastric cancer risk in susceptible individuals, and should serve as a basis for future investigations.

Conclussion

Based on this study, a significant relationship was found between chronic exposure to pesticides (more than two years) and cases of gastric cancer with an odds ratio (OR) of 1.47. This is thought to be due to the action of pesticides which can cause cell mutations through several mechanisms. However, this review cannot explain the toxicity dose of pesticides and the nutritional status of respondents that can increase gastric cancer due to the lack of available research. Hence, a comprehensive approach is needed regarding exposure assessment, integration of epidemiology and biological toxicology to better assess the relationship between gastric cancer and pesticides.

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