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THE EFFECT OF INTERVENTION PROGRAMS ON HOW TO WORK COMPLAINTS IN MECHANICAL WORKERS IN HEAVY EQUIPMENT COMPANIES

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ABSTRACT

Low back pain (LBP) is experienced by almost everyone during his life, and data in Indonesia ranged from 3-17% based on hospital records. LBP can occur due to awkward body postures and manual handling during working and need intervention to reduce complaints. This study to know intervention to reduce risk at ergonomic can induce LBP. This study uses a quasi-experimental design using control with a sample of 35 in each group. The intervention program monitoring was carried out by the SHE team at the work site based on conducting weekly observations regarding workers doing awkward work postures and manual handling activities and ensuring that mechanical workers receive ergonomics training. After one year of the intervention program, the data collection was carried out using a questionnaire to find out the changes in the length of the squat position, bending position, and manual handling activities in both groups. Significant differences between the two groups were obtained in the long work category with squat posture with p-value <0,001, bent posture with p-value 0.001, and a non-significant difference were found in the manual handling category with a p-value of 0.614. The intervention program can change manual handling in the intervention group 3.6 times at work duration more than 1 hour in a squatting position and decrease in the length of bending position more 1 hour by 1.4 times compared to control.

Keywords: ergonomic training, squatting position, bending position, manual handling.

INTRODUCTION

According to (Ministry of Health Republic of Indonesia, 2016) Occupational diseases are artificial diseases because they arise caused by human work. Progress in the industry has brought convenience to human life, however, there are still problems in the world of work that cannot be overcome by existing technology, so that interaction between workers and the environment and work tools can harm workers. One form of interference that can arise due to work is low back pain (LBP). Low back pain is a clinical syndrome characterized by the main symptoms of pain or other feelings that are uncomfortable in the lower back region. More than 70% of human beings have experienced LBP in their lives, with an average peak age of 35-55 years. Meanwhile, (Suma'mur, 2009) LBP is a pain in the back area between the lower angle of the rib to the lumbosacral. Pain can also spread to other areas such as the upper back and groin.

Ergonomic study results at PT X in 2018 found 61% of mechanical workers were at risk of low back pain (LBP), working in a squatting position more than one hour/day, 49% working in a bent position more than one hour/day and 39% lifting heavy objects manually (manual handling) more than 20 kg.

Analyze the level of ergonomic risk for manual handling activities using the Quick Exposure Check (QEC) tool by (Li and Buckle, 1998). obtained 59.6% of mechanical workers have a moderate to very high-risk level. Based on the overall data, 59% of mechanical workers have reported complaints of low back pain. The parts of the body that were most complained about related to

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musculoskeletal disorders (MSDs) during the last 7 days and 12 months showed that the highest prevalence of MSDs was found in the lower back.

In addition, efforts are made to diagnose occupational diseases by occupational specialists by (Directorate of Occupational Health and Sports, Ministry of Health of the Republic of Indonesia, 2018) and (Morris, 2013). This effort consists of seven steps of examination to assess whether the low back pain experienced by employees can be classified as work-related or not. The total number of employees who were physically examined by doctors was 253 people. Based on the results of the examination, 18 mechanical workers were diagnosed positive for LBP.

Based on these data, there were many complaints of low back pain suffered by mechanical workers, researchers assisted by an internal team at PT X took several corrective actions in the form of implementing intervention programs such as health promotion through the installation of low back pain awareness posters at the worksites of the intervention and control groups. At the work location, PT X internal team conducted other interventions towards the intervention group, namely education in the form of ergonomics training, stretching, and regular exercise in the workplace. This study was conducted to determine whether there was a change in working methods and a decrease in complaints of low back pain in mechanic workers after intervention in the intervention group and the control group.

METHOD

The design of this research was quasi-experimental. The study was conducted by comparing changes in complaints of low back pain in mechanical workers, namely between work locations that received an intervention program to change the way of working in the form of education with the installation of posters with low back pain awareness as control with work locations that received additional work change intervention programs in the form of ergonomic training, stretching muscle and regular exercise at work with a ratio of 1:1, namely 35 samples as a control group and 35 samples as the intervention group.

Prior to the study, researchers collected and analyzed secondary data from the results of the 2018 ergonomics study related to the prevalence of mechanical workers with LBP complaints in the locations carried out in the study, namely Samarinda, Tanjung Tabalong, and BSD Tangerang, after getting enough secondary data the researchers coordinated with management in Samarinda. as the location for the intervention and management group in Tanjong Tabalong and BSD Tangerang as the location for the control group either by telephone or by direct visit to the location. During the research, the researcher collected primary data through interviews with 70 research subjects using technology media in the form of Microsoft Team, WhatsApp, and Telephone applications because of the Covid-19 pandemic. Researchers also made visits every 4 months to the location of the intervention group to monitor the implementation of intervention programs in the workplace to ensure that intervention programs in the form of LBP awareness posters, ergonomics training, muscle stretching, and exercise were carried out regularly.

The method of selecting samples using convenience sampling technique where mechanical workers at heavy equipment company carried out an educational program in the form of health promotion through the installation of low back pain awareness posters, namely work location A from 23 samples selected 17 mechanical workers who participated in interviews in previous research and work location B from The 21 samples were selected as many as 18 mechanical workers who attended interviews in the previous

study. The location was chosen because it is the baseline research location.

In the intervention group, ergonomics training was carried out once a year and the installation of LBP prevention posters to change the way of working by avoiding hunchbacked squatting and lifting weights > 20 kg manually, stretching muscles 1x / day, and exercising once per month while in the control group only installing posters for the prevention of LBP. Ergonomics training was carried out directly by researchers assisted by Health Safety and Environmental (HSE) officers at worksites referring to the training syllabus, the making of LBP prevention posters was assisted by the Corporate Communication Department, and poster installation was carried out by HSE personnel at work sites, the muscle stretching method refers to the Machliss (2011). This muscle stretching is led by mechanic workers in turn and exercisers are led by an external professional instructor. Measurement of changes in working methods and complaints of LBP in both groups using a questionnaire. Ergonomics training is carried out directly by researchers assisted by HSE officers at worksites refer to the training syllabus matrix, LBP prevention poster postings are carried out by HSE personnel at work sites. Measurement of changes on how to work and LBP complaints in both groups using a questionnaire after one year intervention program.

Data processing was performed using the SPSS 20.0 program (Landau Sabine, 2001),(Bertani *et al.*, 2018). The data obtained will be entered into a computer and then analyzed by univariate and bivariate. Univariate analysis was carried out to see the frequency distribution of all the variables studied, including individual characteristics and occupation. In the univariate test, normality was assessed using the Kolmogorov Smirnov test. The bivariate analysis aims to see the relationship of each variable. The p-value which was considered significant was <0.05. The bivariate test used for categorical and categorical variable tests used Chi-Square or Fisher and for categorical and numeric variables tested by the Independent T-Test or Mann-Whitney test. The study protocol was approved by the ethics committee of the Faculty of Medicine, Universitas Indonesia (No: KET-388/UN2.F1/ETIK/PPM.00.02/2020).

RESULT

Mechanical workers by their assignments can be assigned to Heavy Equipment company's work location in a workshop or at a customer location in the field (field), assignments are carried out randomly according to operational needs. General working hours for mechanic workers in workshops are from 08.00 - 17.00 with 3 breaks from 10.00 - 10.15, 12.00 - 13.00 and 15.00 - 15.30 from Monday - Friday, while for mechanic workers in the field they follow customer work times well with shifts or without shift. Work shifts are divided into two shifts, namely morning shifts from 08.00 - 17.00 and night shifts from 20.00 - 05.00 hours with the same three break times for non-shift workers with five working days a week.

The workflow starts in the morning by conducting a toolbox meeting to discuss the work to be done at that time, the division of work, including ensuring that work is carried out with attention to the safety and health aspects of work. The job description of mechanical workers is generally divided into four, there are remove or install various components from or to the heavy equipment unit by the procedure, performing assembly and disassembly of various components of the machine according to the procedure, carry out maintenance activities of various types of heavy equipment units and machines and inspect and report using standard forms

After completing the toolbox meeting, each mechanical worker will prepare the necessary work equipment,

review the service manual for the type of work to be performed and review the Job safety assessment (JSA) to ensure the HSE aspects that need to be considered during the work process. After that, mechanical workers begin to carry out work processes according to the type of work assigned by their supervisor or foreman. Thirty minutes before the work time is over, mechanical workers stop doing the work process to tidy up the workplace and return work equipment to the counter.

The length of the work process required varies depending on the type of work being done. The fastest duration is one day for inspection, reporting using standard forms, and a maximum duration of six months for assembling and disassembling various engine components. Work was carried out continuously, for work that has not been completed will be resumed on the next day.

The results of the analysis of pre-intervention data in the age category for the intervention and control groups:

Table 1. Characteristic Demographic of Workers

Variable	Intervention (n= 35) n (%)	Control (n = 35) n (%)	Total	p Value
Age (*numeric*)	34.7 (23-48)	31.2 (23-55)	70	0.701[l]
Age (*category*)				
<35 years old	19 (54.3)	27 (77.1)	46	0.044[cs]
≥35 years old	16 (45.7)	8 (22.9)	24	
Years of Service				
<10 years	10 (28.6)	19 (54.3)	29	0.029[cs]
≥10 years	25 (71.4)	16 (45.7)	41	
LBP complaints (pre-intervention)				
Yes	24 (68.6)	20 (57.1)	44	0.322[cs]
No	11 (31.4)	15 (42.9)	26	

cs) Chi square
l) levene

Most of the workers' age was less than 35 years old, in the category of years of service for the intervention group the most in the years of the service period of ≥ 10 years and for the control group the most in the years of service period less than 10 years, at low back pain complaints category for the intervention and control group at most there are low back pain complaints. The results of the equality test on the pre-intervention data show that the data are not homogeneous at age (category), work period, and homogeneous data at age (numeric) and LBP complaints. The age distribution in the intervention group was dominated by those over 35 years old (54.3%) and had a work period of more than 10 years (71.4%). In contrast to the control group, the age was younger (77.1%) and the work period was under 10 years (54.3%).

Table 2. Changes in Occupational Risk Factors and LBP Complaints in the Intervention and Control Group

Variable	Intervention (n= 35) n (%)	Control (n = 35) n (%)	Total	p-Value	RR (CI 95%)
Length of work in squatting position					
≤1 hour	25 (71.4)	7 (20)	32	0.000[cs]	3.571 (1.738 – 7.156)
>1 hour	10 (28.6)	28 (80)	38		
Length of work in bending position					
≤1 hour	31(88.6)	22 (62.9)	53	0.012[cs]	1.409 (1.064 – 1.866)
>1 hour	4 (11.4)	13 (37.1)	17		
Manual handling (kg)					
≤20 kg	34 (97.1)	32 (91.4)	66	0.614[fe]	1.063 (0.946 – 1.194)
>20 kg	1 (2.9)	3 (8.6)	4		
Acute LBP complaints (last 7 days)					
Yes	4 (11.4)	9 (25.7)	13	0.124[cs]	0.444 (0.151 – 1.310)
No	31 (88.6)	26 (74.3)	57		
Chronic LBP complaints (last 1 year)					
Yes	16 (45.7)	28 (80)	44	0.003[cs]	0.571 (0.384 – 0.850)
No	19 (54.3)	7 (20)	26		
Acute LBP complaints (last 7 days)					
Improve	21 (60)	16 (45.7)	37	0.231[cs]	1.338 (0.822 – 2.177)
Fixed/worsened	14 (40)	19 (54.3)	33		

Variable	Intervention (n= 35) n (%)	Control (n = 35) n (%)	Total	p-Value	RR (CI 95%)
Chronic LBP complaints (last 1 year)					
Improve	9 (25.7)	4 (11.4)	13	0.124[cs]	1.518 (0.958 – 2.404)
Fixed/worsened	26 (74.3)	31 (88.6)	57		

[cs)] chi-square
[fe)] fisher exact

After the intervention, there were differences in results between the intervention group and the control group. In the intervention group, the habit of working in a squatting position was significantly reduced compared to the control group (p = 0.00). Likewise, the habit of working with a bent posture> 1 hour, obtained a significant difference between the intervention group and the control group, wherein for the intervention group the habit of working with a bent position was much less than the control group (p <0.01). (Bridger, 2018)

DISCUSSION

In the age category (categorical data) the results are not homogeneous while in the age category (numerical data) the results are homogeneous, in the years of service category the results are not homogeneous, and in the low back pain complaint category, the results are homogeneous. Based on these data this research was quite strong enough because it uses the same or homogeneous baseline data in the age category (numerical data) and LBP complaints. Research said LBP risk factors consisted of individual risk factors and occupational risk factors and also ergonomic risks (Sulaeman and Kunaefi, 2015). Jin said the most factor was overexertion in lifting and repetitive motion. (Jin *et al.*, 2011) This study examines both of these factors using post-intervention data where the individual factors of the researcher analyze the relationship of individual factors in the form of age, years of service, and smoking status with LBP complaints and for occupational risk factors the researcher analyses the relationship of occupational risk factors for length of work in squatting position, length of work in bending position and activity of lifting heavy objects> 20 kg (manual handling) manually with LBP complaints. This result is different from another research that stated a longer tenure can increase LBP complaints, as well as stated that increasing age can increase LBP complaints. (Rahayu, 2012), (Suma'mur, 2012)

This study also analyzed changes in occupational risk factors length of work in squatting position, length of work in bending position, and lifting activity> 20 kg in both groups for the intervention group and the control group. The results of data analysis in the category length of work in squatting position for the intervention and control group found a significant difference where the intervention can reduce the length of work in squatting position > one hour by 3.6 times, in the length of work in bending position category there was a significant difference with the value p 0.012 where the intervention can reduce the length of working bent position > 1 hour by 1.4 times, in the category of manual handling for the intervention and control groups found no significant relationship, where the intervention was not proven to

reduce the frequency of lifting heavy objects > 20 kg.

The intervention program carried out was proven to be able to change on mechanics ways of working who previously worked with squatting and bending positions more than one hour to less than one hour, where there is a decrease in all three categories in the intervention group and two categories in the control group compared with the results of a study conducted at Heavy equipment company in 2018. The intervention group for a long working squat position more than one hour from 61% decreased to 28.6%, while in the control group experienced an increase to 80% and in the intervention group for a long working bent position, more than one hour from 49% decreased to 11.4% while in the control group it decreased slightly to 37.1%. Changes in how mechanics work can occur due to interventions carried out in the intervention group in the form of training on ergonomics and posting LBP awareness posters, while the control group only posted LBP awareness posters. During the four hour duration of training for mechanical workers, researchers included in the training syllabus refer to (Koh *et al.*, 2017) who related to ergonomic risk factors which explain that working with awkward postures such as squatting and bending for a long time or > 1 hour could increase the risk of LBP.

According to (Bridger, 2018) and (Li and Buckle, 1998) work with squat and bent postures will increase the burden on the back muscles and can cause the structure of the spine to be overloaded and increase the activity of the entire muscle causing an increased risk of spinal cord injury. This program intervention on how to work is referred to as the behavior changes strategy. (Week, 2016) there are four behavioral changes strategies namely using power, providing information, discussing participation, and action. The intervention program was carried out using a behavioral change strategy approach where the intervention was carried out by providing information through the posting of awareness posters about LBP as well as discussion of participation through ergonomics training conducted to mechanical workers on the dangers of working with squatting, bending, and lifting heavy objects more than 20 kg.

There were changes in manual handling activities for lifting heavy objects manually more than 20 kg without tools in both groups, in the intervention group decreased from 39% to 2.9% while in the control group decreased to 8.6%. This is good because lifting heavy objects > 20 kg manually is a risk factor for LBP, according to (Widanarko *et al.*, 2015) and (Trippolini *et al.*, 2018) where a heavy burden will cause irritation, inflammation, muscle fatigue, damage to muscles, tendons, and other tissues. Although in the intervention group there was a higher decrease there was no significant difference between the two groups, this could be since both groups already had a good knowledge of manual handling as in both groups information was provided through LBP awareness posters media to avoid lifting objects manually, other than that for the intervention group got more information from ergonomic training and the control group can get this from other sources such as health talks, etc.

The results of the data analysis on the proportion category of acute LBP complaints about the intervention and control groups showed a high decrease, namely in the intervention group from 68.6% to 11.4% and in the control group from 57.1% to 25.7%, but significant in both groups found no significant difference with p-value 0.124, where the intervention was not proven to reduce complaints of acute LBP. Referring to these results, the first hypothesis is not proven that the intervention program changes the way of working by carrying out ergonomics education in the form of installing low back pain awareness posters, ergonomics training, and exercise in the form of muscle stretching, gymnastics will significantly reduce complaints of acute low back pain in

the intervention group mechanic workers. compared to the control group mechanic workers who only carried out an intervention program in the form of installing low back pain awareness posters.

(Larinier, Balaguier and Vuillerme, 2020) said that ergonomic training and exercise in the form of muscle stretching, gymnastics would significantly reduce complaints of acute low back pain in the intervention group mechanic workers compared to the control group mechanic workers who only carried out an intervention program in the form of installing low back pain awareness posters. This can occur because the effect of the interventions carried out is long-term, to prevent LBP complaints from disappearing from occurring for 12 months, so that the assessment was more accurate by knowing the complaints of LBP in the last 12 months, while for acute LBP complaints in the last seven days it is strongly influenced also with the workload in the last seven days where it is known that sampling was carried out in a pandemic situation. Workload during the last seven days was reduced in almost all work locations including intervention and control group work sites.

The results of data analysis on the proportion category of chronic LBP complaints about the intervention group showed a decrease from 68.6% to 45.7% and in the control group from 57.1% it increased to 80%, significantly in the chronic LBP proportion category for the intervention group and control found a significant difference with a p-value of 0.003, where the intervention was proven to reduce complaints of chronic LBP by 43%. Referring to these results, the second hypothesis is proven that the intervention program changes the way of working by carrying out ergonomics education in the form of installing low back pain awareness posters, ergonomics training, and exercise in the form of muscle stretching, gymnastics will significantly reduce complaints of low back pain in the intervention group mechanic workers compared to workers. the control group mechanic who only carried out an intervention program in the form of installing low back pain awareness posters.

This can happen because the effect of the intervention in the form of ergonomic training is carried out where there is a change in the way of work as evidenced by Umami (Umami and Hartanti, Ragil Ismi, 2014). The mechanical workers who work in a squatting position, hunched over > 1 hour and lift heavy objects > 20 kg manually decreased quite high compared to baseline data, The effect of the intervention was also seen where there were significant differences in the two groups for the length of time working in the squatting and hunched positions. Other interventions carried out are in the form of exercise by stretching muscles 1x/day and exercising once per month which can increase spinal muscle strength and improve blood circulation in the spinal area so that it can prevent LBP complaints from occurring within the last 12 months, referring to (Hasan, Ismail, and Raja Azidin, 2010). Physiologically, this activity can increase brain blood flow, especially to the spine and joints, strengthen the back muscles, increase the body's flexibility change in brain neurotransmitters (eg norepinephrine, endorphins, and serotonin) and develop structural changes in the body. brain. Meanwhile, in the psychological aspect, it can increase feelings of control, feelings of competence and self-confidence, relieve stress and depression as well as an opportunity to feel happier and feel more enjoyable.

These results are consistent with the reference in a study conducted by (Steffens *et al.*, 2016) which states that intervention in the form of a combination of exercise and education carried out for up to one year can reduce LBP complaints by 45% with RR 0.55 (0.41- 0.74). In a study conducted by (Huang *et al.*, 2020) Exercise alone and exercise combined with education both prevent episodes of low back pain and

related absenteeism, also concluded that the combination of exercise and education is the most effective method of preventing LBP.

The results of data analysis in the category of changes in acute LBP complaints in the intervention group found that 60% of complaints improved and in the control group as many as 45.7% of complaints were improved of acute LBP complaints improved in the higher intervention group could be an effect of the intervention carried out even though the significance was obtained a non-significant difference with a p-value of 0.231 where the intervention was not proven to change acute LBP complaints in both groups, as was the case previously discussed, this could be related to sampling carried out during the pandemic where the workload was reduced during the last seven days at the work location of the intervention and control groups.

In the category of changes in chronic LBP complaints in the intervention group, it was found that 25.7% of complaints improved, and in the control group, as much as 11.4% of complaints improved of chronic LBP complaints improved in the higher intervention group could be an effect of the intervention carried out although significant differences were not found. Significant with a p-value of 0.124 so that the intervention was not proven to change chronic LBP complaints.

This is different from the results of the previous analysis related to the proportion of chronic LBP complaints where the intervention was proven to significantly reduce the number of mechanical workers with chronic LBP complaints. This can occur because of the lack of strict supervision carried out on research subjects, so that improvements that can be made are to consider regular interviews, for example, once every three months to research subjects to ensure that the intervention program runs well by closely monitoring especially mechanical workers with complaints of LBP. Pre-intervention is to run the intervention program that has been determined.

In the analysis above, the results were not significant in several categories such as manual handling acute LBP complaints, changes in acute and chronic LBP complaints. Several things need to be considered to improve the intervention program to get better results, namely by implementing additional program interventions, according to (Slovak, 2012) said the most important ergonomic intervention programs are to reduce workplace exposures, by doing engineering in the form of changes in the workplace design, changes in work processes and replacement or adjustment of tools used by workers. In this recent study, researchers intervened to change the way of working by doing ergonomics training to avoid awkward postures at work, namely squatting and hunched over positions, while other interventions such as changes in workplace design, replacement or adjustment of tools needed in the workplace have not been carried out.

Some limitations that were difficult to overcome by researchers related to the COVID-19 pandemic situation is that interviews cannot be conducted directly at the worksite, so this method is replaced with interviews through Microsoft teams, WhatsApp, and telephone applications that are sometimes constrained by networks or signals. Another limitation is that in this study to find out LBP complaints only use questionnaires with yes or no answers and are not equipped with more complete tools.

CONCLUSION

Intervention program on how to work by conducting ergonomics education in the form of installing low back pain awareness posters and ergonomics training found significant differences in changes the ways of working for the length of work in squatting position, bending position in the intervention group compared to the control group, and no significant differences in

manual handling activities in the two groups.

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THE ASSESSMENT OF HEALTH PROTOCOL IMPLEMENTATION IN FOOD AND BEVERAGES BUSINESS DURING COVID-19 PANDEMIC ERA

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ABSTRACT

During the COVID-19 pandemic era, the government has implemented a new strategy of health protocol called Adaptation of New Habits to prevent COVID -19 virus spread. By implementing such protocol, it is expected that health and economic sectors can be handled well. The research aims to discover the implementation of health protocol in Indonesia's food and beverage business, and to analyze factors that support and hamper its implementation. This research was cross-sectional research with direct observation and brief interviews with 16 food and beverage business places. Observations and interviews were guided using a checklist derived from government policies set by the ministry of health and commerce then the data will be analyzed descriptively. This research shows that the implementation health protocol remained far from expectations. Moreover, business activity, management system, and the awareness of employers, employees, as well as consumers, became a critical key in health protocol implementation. Comprehending the dangers of COVID-19 and committing to comply with health protocols are imperatives to succeed in the health protocol implementation.

Keywords: Adaptation of New Habits, Health Protocol of COVID-19 Pandemic, evaluating health protocols implementation

INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemic causes changes of habits and lifestyles. Such changes are attempts to minimize the virus spread and to make life back to normal as before the pandemic era. Responding to those efforts, the government has been actively socializing the Adaptation of New Habits (ANH) to decrease the spread of the COVID-19 virus (Indonesia, 2020). The policy stipulated by several Ministries, such as The Ministry of Health and The Ministry of Commerce. They expected that the wheels of the economy remain spinning without forfeiting health sectors (Ministry of Finance of the Republic of Indonesia, 2020) (Ministry of Health of the Republic of Indonesia, 2020) (Ministry of Trade, 2020).

To date, there is not any evidence stating that the COVID-19 virus can be transmitted through food. The risk of transmitting COVID-19 through food and food packaging is very low as long as the Good Processed Food Production Method is undertaken by all industrial sectors in every food supply chain. However, the implementation of health protocols in preventing transmission of COVID-19 must remain undertook due to the social and physical interactions between individuals in food and beverage business (National Agency of Drug and Food Control, 2020).

Research undertaken by federal researchers in 3,076 (97.9%) countries in the United States stated that subsequent to the reoperation of restaurants and on-site dining service, regions that open restaurants to eat

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on the premises - indoors or outdoors - had an increase in daily infections about six weeks later, and an increase in the COVID-19 mortality two months later (Guy, Massetti and Sauber-Schatz, 2021). The state of Los Angeles claimed that restaurants have contributed less than 4% of the COVID-19 outbreak virus in non-residential environments. In Indonesia, eating outside the house certainly reflects the contribution in increasing the spread of the COVID-19 virus. The magnitude of the effect from eating in restaurants or other food businesses emerge from two matters: (1) the movement to release masks during meals and (2) contact among workers, consumers, and workers and consumers due to the limited space and poor air circulation (ABC, 2021) (Guy, Massetti and Sauber-Schatz, 2021).

A policy stipulation constitutes a good initial step, yet it should be followed by further actions to ensure its effectivity and well-implementation throughout Indonesian society. Its workability needs to be reviewed to make it applicable and appropriate in such condition, considering the owners of food and beverage businesses are being forced to survive with declined earnings while this health protocol application raises expenses which includes the provision of PPE, extensive materials, and other supporting equipment that must be adjusted to the type of business activities (Burki, 2020) (Central Bureau of Statistics, 2020). This research aims to discover the implementation of ANH health protocol in the food and beverage business as well as to analyze factors that play as supports and obstacles of the policy implementation.

METHODS

The study was cross-sectional, through direct observation towards activities and health protocol implementation at food and beverage business places during operational hours and brief interviews both to business owners and employees at one time (Setia, 2016). Data collection was derived during October-November 2020 in Jakarta Capital Special Region, Tangerang, and Medan, the observation was held at hours when most visitors came and the interview was adjusted to the condition of busyness. The population of this study was all food and beverage businesses that remain operated during the pandemic, affordable places of business located in the cities of Jakarta, Tangerang, Depok, Bogor, and Medan. After acquiring their consent, 16 business places were willing to be research subjects. Observations and interviews were guided using a checklist derived from government policies set by the ministry of health and The Ministry of Commerce (Ministry of Health of the Republic of Indonesia, 2020) (Ministry of Trade, 2020) (OSHA, 2020).

The observation was undertaken in 16 food and beverage businesses consisting of Micro, Small, and Medium Enterprises, franchises, and restaurants which divided equally into 4 risk criteria based on risk scale classification for restaurants by the *Centers For Disease Control And Prevention* (CDC) in The United States of America (CDC, 2020). Low Risk was described as limited food services at a drive-through, delivery, take-out, such as restaurants that provide delivery orders through the online application as well as order by phone. Medium Risk was described as besides providing means such as *drive-through*, delivery, picking up, and roadside buying, the place/restaurant also provided the dine-in facility with limited capacity compared to the one before a pandemic or offered seats outdoor. The seating capacity was decreased to keep the distance at least 1 meter. High Risk was described as dine-in both indoor and outdoor. The capacity was decreased to keep distance between the tables and visitors. Very High Risk was described as dine-in both indoor

and outdoor. The capacity was not decreased and the distance between the tables and visitors was less than one meter such as *warung Tegal* and other traditional restaurants.

The data was analyzed using Risk Rating with formulas (Peters *et al.*, 2019):

Risk Rating = Consequences x *Probability*

Whereas:

Consequences were set as a constant with equal value in each policy since it has equal risk: being exposed to COVID-19 virus. Therefore, the score will be given.

Probability constituted a percentage derived from the number of business places to every risk group that did not implement health protocols as appropriate to the government policy.

Then the data was analyzed by using *Health Risk Assessment (HRA)* to know risk levels of every category of food and beverage business place (National Research Council, 2003). Then, the derived risk rating was classified based on cross points adjusted to the assessment system, therefore it was found factors that supported and hampered the program implementation. the assessment results from the risk assessment have a range of values from 0 to 400. To facilitate the grouping, it will be divided into 4 categories: good, fair, poor, and very poor.

This study has passed the ethical review of the Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia - RSUPN. Dr. Cipto Mangunkusumo with number KET-355 / UN2.F1 / ETIK.PPM.00.02 / 2021.

RESULTS

Based on the results of observation guided using check-list point, 30 policies became the focus of observation in implementing health protocols, whereas the first 20 targets for business owners and the next 10 targets for employees as mentioned in Table 3. The research subjects consist of 16 places of business which are divided into 4 categories of risk rating. Each category consists of 4 places of business.

Table 1. Results of Walk Through Survey Implementation of Health Protocol Policy

Total Score Of Risk Assessment	Result Of Observation Implementation Of Each Policy	Category Implementaion In Site
0-99	0	Good
100-199	7	Fair
200-299	17	Poor
300-400	8	Very Poor

Based on HRA, by calculating the Risk Rating of each risk group of business place (calculation horizontally to every policy), the result showed that none of the health protocol policies was categorized as well-implemented. The calculation was undertaken for every risk group (calculation vertically to every risk group), whereas those having the smallest score constitute a group of business places that implemented the best health protocols compared to other groups with the bigger total score.

Table 2. Health Risk Assessment (HRA) results of walkthrough survey at 16 places of food and beverage business

Targets	Policies	The score of Risk Rating				Total Score Of Risk Assessment
		Low Risk	Medium Risk	High Risk	Very High Risk	
Business Owners	Provide facilities for washing hands using soaps and hand sanitizer					
	Entrance	0	50	50	100	200
	Strategic Places	50	50	75	75	250
	Require every person who wants to get in, to wash hands with soaps water, or use hand sanitizer.	75	25	75	100	275
	Require employees to wear masks during working.	25	25	25	75	150
	Prohibit to get in for employees and visitors who have symptoms of fever, cough, cold, sore throat, shortness of breath, and/or diarrhea or those have history contacted to persons exposed to COVID-19.	75	75	75	100	325
	Do checking up body temperature at the entrance. When founding employees or visitors with temperature > 37.3^{o} C (twice checking with interval 5 minutes) they are not allowed to get in.	100	25	25	100	250
	Require all those touching food or employees who have direct contact with food, to wear masks, gloves, or tongs when touching fast food, and wear head covers and apron while preparing, cooking, and serving food. Using gloves as adjusted to the prevailing food safety standard.	50	25	25	75	175
	Provide aids such as gloves and/or tongs to minimize direct contact with fast food during the	75	25	75	75	250

Targets	Policies	The score of Risk Rating				Total Score Of Risk Assessment
		Low Risk	Medium Risk	High Risk	Very High Risk	
	process of preparation, cooking, and serving.					
	Do not provide a buffet. When providing buffet then recommended to employ service officers at the stalls and they wear masks and gloves. They serve taking foods for the visitors and keep distancing at a minimum of 1 meter. All cutleries must be rinsed and disinfected before re-use.	50	25	50	75	200
	Keep the air quality at businesses or workplaces by optimizing air circulation and sunlight coming in and also cleaning AC filters.	50	50	50	75	225
	Procure payment through cashless by providing disinfection to payment machine. When having a transaction with cash use hand sanitizer after doing it.	50	25	50	75	200
	Make sure that all surroundings of restaurants are clean and sanitized, by doing cleanup and disinfection periodically at least twice a day (before open and close) with appropriate cleaner and disinfectant.	25	25	25	25	100
	Increase frequencies of cleanup and disinfection (st 3 times a day) mainly the surfaces of area and facilities frequently touched/passed by people such as tables and seats in the dining room, door handles, toilet flush handles, teller machine, and others.	75	50	50	100	275

Targets	Policies	The score of Risk Rating				Total Score Of Risk Assessment
		Low Risk	Medium Risk	High Risk	Very High Risk	
	Cover cutlery placed on the dining tables (spoons, forks, knives wrapped with tissue).	100	25	50	100	275
	Do not use cutlery jointly. The frequently touched cutlery on the dining table should be changed into a one-used sachet or given to the visitors if requested.	0	25	50	100	175
	Apply to keep a distance with various techniques such as:					
	a. Maintaining a distance of at least 1 meter while queuing up to enter restaurants and similar ones, ordering and paying at the cashier by providing marks on the floor. When possible, providing borders between visitors and cashiers such as control partition or glass.	25	25	50	75	175
	b. Maintaining distance between seats at a minimum of 1 meter and not face to face, or installing partitions (glass, mica, or plastic) between guests on dining tables**.**	100	0	75	75	250
	Increase service for food and beverage orders through online or delivery service or drive-thru, and others.	50	50	75	75	250
	Apply to maintain circulation and limitation for visiting time and number of visitors maximum 40% of visits at normal condition by implementing strict control at the entrance and exit in such a way so that not to occur crowd by health protocols.	75	25	50	75	225

Targets	Policies	The score of Risk Rating				Total Score Of Risk Assessment
		Low Risk	Medium Risk	High Risk	Very High Risk	
	Make sure that all officers, managers, and waitresses of restaurants are negative COVID-19 based on results of PCR/*Rapid Test* which were conducted by the restaurant owner, or local health unit, and wear masks, face shields, and gloves while having activities.	100	75	100	100	375
	Before restaurants open, conduct early screening to make sure that the body temperatures of all officers, managers, and waitresses of the restaurants are below 37.3^0C (adjusted to WHO regulation).	75	50	50	100	275
	Sell clean and healthy food.	25	0	25	50	100
Workers	Make sure themselves in healthy condition before leaving their house. If having symptoms such as fever, cough, cold, sore throat, and/or shortness of breath they must stay at home and check up to health service if the symptoms keep running, and report to leaders of the workplace.	75	75	75	100	325
	Wear masks during the journey and while in the workplace.	50	50	50	50	200
	Avoid touching face, eyes, nose, and mouth.	50	50	50	50	200
	Care to keep distance at a minimum of 1 meter with other people.	50	25	50	75	200
	Wear specific clothes during work.	0	0	0	100	100
	Avoid using personal belongings jointly such as equipment for doing s*halat*, cutlery, and others.	75	75	75	75	300

Targets	Policies	The score of Risk Rating				Total Score Of Risk Assessment
		Low Risk	Medium Risk	High Risk	Very High Risk	
	Immediately take a bath and change clothes before having contact with family members at home.	75	75	75	75	300
	If needed, clean mobile phone, glasses, bag, and other stuff with disinfectant liquid.	75	75	75	75	300
	When arriving home, immediately take a bath and change clothes before having contact with family members at home. Clean mobile phone, glasses, bag, and other stuff with disinfectant liquid.	75	75	75	75	300
	Increase the body stamina by applying Clean and Healthy Lifestyle (PHBS) such as consuming balanced nutrition, physical activities minimum of 30 minutes a day and have enough rest with sleep minimum of 7 hours, and avoid factors of disease risks.	75	75	75	75	300
		LOW RISK III 1.850	MEDIUM RISK I 1.325	HIGH RISK II 1.775	VERY HIGH RISK IV 2.550	

DISCUSSION

Based on the Table 1, it can be concluded that generally there was not any health protocol policy that was well-implemented by food business places in Indonesia. However, there are some policies that have been fairly implemented due to previously good socialization and had been being implemented when the pandemic occurred. Policies that categorized as poorly implemented were commonly dealed with new habits or protocols which were newly socialized during the COVID-19 pandemic. In short, it was less socialized and required awareness of the employers, workers, and

consumers as well (Ministry of Health of the Republic of Indonesia, 2020) (OSHA, 2020). Policies that categorized as very poor generally had several difficulties in the implementation, such as constituted a binding protocol and had to be implemented strictly and required high understanding and commitment. Any matters happening outside the workplaces and impossible to be directly monitored by the business owner (Food Standard Agency, 2020). They required an amount of financial support thus strong willingness and high commitment from the business owner were strongly advised.

Based on the result in Table 2, it showed that there was a significant incompatibility between the expected results from risk assessment of business places based on types of business activities (delivery order, *dine-in* or *take away*) and the observation results of health protocol implementation in line with the policy stipulated by the government (Agency, 2020). Based on risk grouping from CDC, the business places which only served delivery orders had lower risks than the other risk groups, however, the business places with low risk constituted the second-worst business place that implemented health protocols, therefore they exactly riskier than the business places which provided dine-in system (CDC, 2020)(Han *et al.*, 2021). It occurred since the assessed factors were not only comprising aspects of business types and physical distancing but also the awareness of business owners and workers. This result brought awareness that prevention of virus spread at food and beverages business, the preventive actions should not only rely on types of business activities and physical distancing but also include other factors such as wearing properly Personal Protective Equipment (PPE), habits of washing hands and keeping cleanliness, and strong commitment from the business owner and workers (WHO, 2020) (Anelich *et al.*, 2020).

From the research, it can be concluded that food and beverage business places in Indonesia are still very low in implementing health protocols. The low awareness and understanding of COVID-19 danger influence the low commitment of business owners, workers, and consumers in implementing health protocols (Bazaid *et al.*, 2020). The stipulation of a health protocol policy for every industrial activity is a good initial step to prevent transmission of the COVID-19 virus, yet it should be continued with farther steps including socialization, implementation, supervision, and evaluation of this policy (Zhang *et al.*, 2021). Some policies remain ineffective since they need huge financial supports, such as obligating the business owners to ensure all workers in condition negative COVID-19 based on evidence of test result PCR/Rapid Test required huge amount of money since it is mandatory periodically (Ministry of Health of the Republic of Indonesia, 2020). On the other hand, at the same time, the business owners were struggling to survive their business facing uncertain economic conditions (Indonesia, 2021).

Based on the result of the research, it is necessary to establish the effective health protocols and adjusted them to each site condition and business scale, such as Micro, Small, Medium Enterprises. They possses limited resources yet they contribute significantly on Indonesia's economy (Ministry of National Development Planning of the Republic of Indonesia, 2017).

CONCLUSION

Based on the research, it was found that the distribution of the risk scale based on the CDC was remain inappropriate (CDC, 2020). In Indonesia, where food providers that serve delivery services are mostly a

micro-business scale, they have a greater risk of transmitting the covid-19 virus compared to other business places that serve dine-in. This is in contrary to the division set by the CDC which stated that restaurants that serve dine-in become restaurants that have a high risk of transmitting the COVID-19 virus. Analyzing the existing data, several factors that led to this can be explained. The main factor was that food service establishments that only serve delivery services are generally micro-scale businesses that have many limited resources, such as a small business area which makes it difficult to maintain physical distance between workers and consumers as well as poor air circulation. The minimal provision of PPE was also a factor that increases the spread of the COVID-19 virus in the work environment.

The poor application of health protocols in food supply businesses was generally caused by a lack of awareness, understanding, and commitment of business owners and workers in implementing proper and correct health protocols on an ongoing basis.

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RELATIONSHIP BETWEEN NUTRITION INTAKE AND THE FITNESS OF MANUFACTURING WORKERS IN INDONESIA

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ABSTRACK

Indonesia ranks fourth in the world out of 15 countries whose manufacturing industries contribute more than 10% to the Gross Domestic Product (GDP). Nowadays, one of the consequences of the rapid development of the manufacturing industry in Indonesia is related to work productivity. Each person's work productivity is not the same, one of them depends on the availability of nutrients in the body. Lack of nutritional consumption for someone from standard needs will affect health conditions, activities, and work productivity. Nutritional substances in workers also affect fitness in addition to other factors such as age, health status, nutritional status, nutritional status, gender, and psychological conditions. Based on the description above, it is necessary to study the relationship between nutritional status and physical fitness of workers in manufacturing companies in Indonesia. The study was cross sectional on 120 workers from 6 manufacturing companies in Indonesia which was conducted using cluster sampling. Assessment of individual characteristics was conducted by direct interview. Assessment of nutritional intake uses the Food Frequency Questionnaire (FFQ) and the results were categorized as appropriate and inappropriate based on the 2019 nutritional adequacy figure for the Indonesian population. The fitness assessment (physical capacity) used a six-minute walking test by an occupational specialist and was converted to Meters and categorized with a cut off of 4.5 Mets to be sufficient or insufficient. About one third of manufacturing workers were centrally obese. Characteristics The dietary intake according to the recommendation were only about 10%, namely the appropriate carbohydrate intake 11.7% (Frequency 8.46 times (533.22 gr)), suitable fat 12.5% (Frequency 2.75 times (57.14 gr)), and suitable protein 10% (Frequency 6.55 times (101.77 gr)). The physical capacity of manufacturing workers in Indonesia was categorized as sufficient as much as 75.8% of their workload. Factors that affect physical capacity, namely age ≥ 40 years have 4.37 times less physical capacity and protein intake affected physical capacity / fitness for workers (p = 0.02). About a third of manufacturing workers were centrally obese. The characteristic of food intake in accordance with the recommended nutritional adequacy of the Indonesian population was only about 10%. The physical capacity of manufacturing workers in Indonesia was categorized as sufficient as much as 75.8% of their workload. Factors that affected physical capacity were age and protein intake.

Keywords: Food Intake, Food Frequency Questionnaire (FFQ), Manufacturing Worker, Fitness, Six-Minute Walking Test.

INTRODUCTION

Based on data released by (Basic Health Research, 2018), Indonesia was ranked fourth in the world out of 15 countries whose manufacturing industries contribute more than 10% to Gross Domestic Product (GDP). The development of the industrial sector cannot be separated from the role of the workforce even though many companies use sophisticated machines and technology in their production processes. One of the consequences of the rapid industrial development and intense competition between companies are the productivity of workers. Productivity is a universal concept that creates more goods and services for human needs, using limited resources. Basically, (Yuan *et al.*, 2018) said productivity was influenced by three factors, namely workload, work capacity and additional load due to the work environment. Workload relates to physical,

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mental and social loads that affect labor. Work capacity relates to the ability to complete work at a certain time. Meanwhile, the additional burden due to the work environment includes physical, chemical and labor factors, which include biological, physiological, and psychological factors. Each person's work productivity is not the same, one of them depends on the availability of nutrients in the body. Lack of nutritional consumption for someone from the minimum standard will generally affect physical fitness, work activities, and productivity.

Physical fitness is the main asset for all human life. Labor requires good physical fitness to work, thus it can increase work power and high productivity. According to (Grimani, Aboagye and Kwak, 2019) "physical fitness is the ability of a person to do daily work efficiently without excessive fatigue thus he can enjoy his spare time". Physical fitness is one aspect of total fitness.

Physical fitness is important for everyone to live their daily life. (Shearer, Graham and Skinner, 2016) said the role of other factors that may influence the health and productivity of workers, such as nutrition, is generally overlooked. Based on the above opinion, it is clear that every physical activity (physical activity is subject to a load) requires a level of physical fitness which is supported by nutrition.

Overall physical fitness (total fitness). Physical fitness gives a person the ability to do daily productive work without excessive fatigue and still has reserves of energy to enjoy his free time well or do sudden work.

Good physical fitness is the main basic capital for workers to do physical activity repeatedly in a relatively long time without causing significant fatigue. By having good physical fitness, it is hoped that workers will be able to work productively and efficiently. Factors that support physical fitness in the industry vary widely, influenced by workload, work environment, physical problems, and health conditions. Physical fitness can also be influenced by individual factors such as age, health status, nutritional status, nutritional status, gender, and psychological conditions. Based on the description above, it is necessary to study the relationship between nutritional status and physical fitness of workers in companies in Indonesia.

METHOD

This research was using cross sectional study design (cross-sectional) on manufacturing workers in 6 companies spread over the areas of Bandung, Surabaya, Medan, Semarang, Makassar, and Samarinda which were determined based on cluster sampling. The number of samples in this study were 120 people. The research instrument used in this study was a respondent characteristic questionnaire to see individual factors written in numerical and categorical form. For food intake using (Fahmida Umi, 2011), the Food Frequency Questionnaire (FFQ) was written in grams, then compared to the 2019 Nutritional Adequacy Rate of the Indonesian population (Ministry of Health Republic of Indonesia, 2019) and categorized as appropriate and inappropriate (more and less). The fitness assessment was conducted by means of a six-minute walking test by (Issues *et al.*, 2002) which was converted into Mets and categorized as being insufficient and sufficient with a cut-off value of 4.5 Mets. This research was assisted by enumerators from each region with a minimum requirement of a S1 nutrition education and the previous perceptions were equated. The Six-minute walking test was performed by an occupational specialist. This research has passed the ethical test from the Faculty of Medicine, University of Indonesia with No: 007/UN.2.F1/ETIK/2019.

Inclusion criteria was being with a manufacturing company for at least three months and willing to participate in research and have signed an informed consent and for exclusion only not willing to take part in research.

Data collection was collected by researchers on weekdays from 08.00-16.00 WIB for approximately three weeks. Respondents were manufacturing workers who work in manufacturing companies spread across six regions in Indonesia. The process of selecting prospective respondents began with providing information about the aims and objectives of the study, then continued with a short interview for respondent selection, and approval of prospective respondents according to the criteria of the research subject will be asked to participate in the research. Furthermore, an interview was conducted and given an explanation of how to fill out the questionnaire and how to do the 6 minutes walking test. Respondents will fill out a questionnaire accompanied by a researcher and a research assistant, namely a doctor who has been trained and will undergo a fitness test.

Data processing was performed using the SPSS 20.0 program. Data obtained will be entered into a computer and then analyzed by univariate and bivariate. Univariate analysis was conducted to see the frequency distribution of all the variables studied, including: demographic characteristics, individual characteristics, occupation. In the univariate test, normality was assessed using the Kolmogorov Smirnov test. Bivariate analysis aims to see the relationship of each variable. The p value which was considered significant was <0.05. The bivariate test used for categorical and categorical variable tests used Chi-Square or Fisher and for categorical and numeric variables tested by the Independent T-Test or Mann-Whitney test.

RESULT

Data collection in this study took 2 weeks in 6 types of manufacturing companies in Indonesia. These three types of companies are engaged in food, vehicles, and goods. It was obtained the distribution of individual characteristics as follow:

Table 1. Individual Characteristics in the Numeric Variable of Research Subjects

No	Variable	Mean/Median
1	Age	35.5 (21-56) years
2	Years of service	11.5 (1-39) years
3	Length of Sleep	6.54 (+/- 1.61) hours
4	Weight	64.5 (33-127) kg
5	Height	164.44 (+/- 6.48) cm
6	Abdominal Circumference	84.96 (+/- 12.54) cm
7	Road Test Mileage 6 Minutes	449. 55 (300-730) m
8	Mets	5.67 (2.97 -9.97) Mets
9	Total Carbohydrates Consumption	533.22 (233.87- 3534.75) gr
10	Total Protein Consumption	101.77 (26.84-723.94) gr
11	Total Fat Consumption	57.14 (12.84-430.14) gr
12	Frequency of Carbohydrate Consumption	8.46 (3.57-20.89) kali
13	Frequency of Protein Consumption	6.55 (1.2-45.71) times
14	Frequency of Fat Consumption	2.75 (0.29-22.5) times

Table 1 was found that the characteristics of manufacturing workers have an age with a mean value of 35 years, a work period with a mean value of 11.5 years. For physical capacity (fitness) the value of strength was 5.67 Mets. The average circumference of workers was 84.96 cm, but some reach 97 cm. The height of manufacturing workers in Indonesia ranges from 155-170 cm and weighs varying from 33 to 127 kg. Manufacturing workers sleep an average of 6.5 hours a day, but some only sleep about 4 hours per day. Carbohydrate, Protein, and Fat Intake with mean 533.22 gr, 101.77 gr and 57.14 gr. Manufacturing workers consumed more high-carbohydrate foods with an average of 8.5 times per day, even up to 20 times per day. However, for fat aspuan less frequently with an average of 3 times a day and some even less than once a day.

Table 2. Individuals Characteristics in the Category Variable in the Research Subjects

No	Variable	Number	(%)
1	Sex		
	a. Male	113	94.2
	b. Female	7	5.8
2	Age		
	Adult (≥ 40 Years)	36	30
	Adolescent (<40 Years)	84	70
3	Married Status		
	a. Married	33	27.5
	b. Single	87	72.5
4	Habit of Drinking Tea (Cup)		
	a. Not	47	39.2
	b. 1-2	66	45
	c. > 2	7	5.8
5	Frequency of Physical Activity		
	a. Good (≥ 3 times / week)	114	95
	b. Poor (<3 times / week)	6	5
6	Sleep Duration		
	a. Good (≥ 6 hours)	101	84.2
	b. Poor (<6 hours)	19	15.8
7	Years of service		
	31-40	3	2.5
	21-30	24	20
	(11-20)	33	27.5
	(1-10)	58	48.3

No	Variable	Number	(%)
8	Weight		
	a. Normal	34	28.3
	b. Sufficient	11	9.2
	c. Over (Overweight and Obesity)	74	61.7
9	Blood pressure		
	Normal	32	26.7
	Pre Hypertension	65	54.2
	Grade I Hypertension	17	14.2
	Grade II Hypertension	6	5
10	Central Obesity		
	a. Normal	82	68.3
	b. Central Obesity	38	31.7
11	Protein Category		
	a. Appropriate	12	10
	b. Less	16	13.3
	c. Over	92	76.7
12	Carbohydrate category		
	a. Appropriate	14	11.7
	b. Less	17	14.2
	c. Over	88	73.3
13	Fat Intake		
	a. Appropriate	15	12.5
	b. Less	64	53.3
	c. Over	41	43.2
16	Physical Capacity Category		
	a. Less	29	24.2
	b. Enough	91	75.8

Based on Table 2, it was found that 94.2% (117 people) were male workers with 72.5% unmarried. The age of manufacturing workers was 70% (84 people) under 40 years. The work period was about half as low as 10 years, but there are also those who work for more than 20 years. The physical condition 61.7% of workers were overweight, but the physical capacity based on the workload (4.5 meters) was sufficient, namely 75.8%. Among workers, it was found that about 80% had normal blood pressure or pre-hypertension in manufacturing workers, it was found that 31.7% had a large abdominal circumference. Adequate intake of carbohydrates, protein, and fat were around 10%. As much as 73.3% excess carbohydrate intake as well as 76.7% excess protein intake. In contrast to fat intake, there was 43.2% excess but there is 53.3% less.

Table 3. Relationship of Physical Capacity (Fitness) in Numeric Variable with Other Risk Factors

Variable Dependent	Variable Independent	N	P*
Physical Capacity (METS) 5.67 (2.97 -9.97)	**Years of service**		
	Working period> 15 years	47	0.259
	Service Period ≤15	71	
	Age		
	Old Age (≥ 40 Years)	36	0.005
	Young Age (<40 Years)	84	
	Sports Activity		
	Less exercise (<3x / week)	40	0.207
	Enough Exercise (≥ 3x / week)	18	
	Carbohydrate intake		
	Not Appropriate	105	0.934
	Appropriate	14	
	Protein Intake		
	Not Appropriate	108	0.02
	Appropriate	12	
	Fat intake		
	Not Appropriate	105	0.12
	Appropriate	15	

* Mann Whitney

Table 3 showed that the physical capacity of manufacturing workers has met value between 3-10 meters and a mean value of 5.67 meters. Physical Capacity was affected by age (p = 0.0045) while the influential intake was protein (p = 0.02). Other statistical tests showed that the physical capacity of workers was not related to length of work and physical activity.

Table 4. Relation of Physical Capacity (Fitness) in Category Variable with Other Risk Factors

No	Category	Physical Capacity		p*	OR (95% CI)
		Inappropriate	Appropriate		
1	Age				
	Adult (≥ 40 Years)	16	20	0.01	4.37 (1.81-10.58)
	Adolescent (<40 Years)	13	71		
2	Sex				
	Female	1	6	1	0.51 (0.05-4.38)
	Male	28	85		
3	Years of service				
	> 15 years	15	14	0.13	1.91 (0.82-4.45)
	≤15 years	32	57		

No	Category	Physical Capacity		p*	OR (95% CI)
		Inappropriate	Appropriate		
4	Duration of Sleep				
	Good (<6 hours)	5	10	0.52	1.60 (0.49-5.15)
	Poor (≥ 6 hours)	24	77		
5	Sports				
	Poor (<3x / week)	27	87	0.63	0.62 (0.11-3.58)
	Good (≥ 3x / week)	2	4		
7	Married Status				
	Single	6	27	0.34	0.61 (0.23-1.68)
	Married	23	64		
8	Category of Carbohydrate Intake				
	Inappropriate	27	78	0.51	2.08 (0.44-9.88)
	Appropriate	2	12		
9	Protein Intake Category				
	Inappropriate	25	83	0.48	0.60 (0.17-2.16)
	Appropriate	4	8		
10	Fat Intake Category				
	Inappropriate	27	78	0.52	2.25 (0.48-10.61)
	Appropriate	2	13		

*Chi-Square

Statistical calculations to find the relationship between physical capacity and other factors found that age was significant to physical capacity with p = 0.01 with OR (95% CI) 4.37 (1.81-10.58).

The effect of intake on physical capacity was found to be unrelated. In Carbohydrates, Protein, and Fat intake, it was found that there was no significant difference between workers and sufficient physical capacity or those with less physical capacity. Besides that, there was no relationship between individual factors such as marital status, sleep duration, and sports activities among workers.

DISSCUSION

Data distribution in six manufacturing companies throughout Indonesia was found not homogeneous. This can be due to the inconsistencies in policies in each company, regional characteristics, and regional economy. The applicable government standards were still indicated by the existence of healthy information. Some large manufacturing companies have thought about hiring workers based on their workload. Another cause of the inhomogeneity of manufacturing workers in Indonesia is that the work system in companies is still familial and semi-formal.

Of the age distribution, all enter productive age, however, there were some workers above the productive age (56 years old). However, thirty percentages of manufacturing workers were over 40 years old. Yong Kang Cheah, 2014 said that younger people are more active than older people with an OR of 0.985 (0.985- 0.990) with the main factor being the degeneration process of body metabolism and degradation. The working period that spreads from 1 year to 39 years can affect workers in diet and fitness. Sagara *et al.*, (2009) said that the longer middle age

workers work, the lazier they are to exercise, a diet high in calories and low in carbohydrates.

In addition, manufacturing workers are dominated by male sex (94.2%), this condition was in accordance with the workload in manufacturing (4.5 Mets). As many as 72.5% were unmarried, this condition led to an irregular eating pattern and uncontrolled intake. Win *et al.*, (2015) said that physical activity were influenced by several factors such as age, gender, education level, and income level. Worker habits such as exercise and sleep duration were relatively good, namely 95% and 84.2%. This good daily habit was able to support the physical capacity of workers by being shown the Physical Capacity category, the category was quite 75.8%. Some workers only sleep for about 4 hours a day even though their workload was in the medium category and the working hours are usually long. This situation can affect the health conditions for manufacturing workers.

This study also found that manufacturing workers have tension in the normal category and prehypertension was 80.9%. This is in accordance with Jakicic *et al.*,(2019) in their meta-analysis, stated that people who have moderate activity will increase their health status such as fitness, protection from high blood pressure, etc. In addition, many manufacturing workers have a smoking habit. This study was more than 50% smoked. This needs to be a concern because research conducted by Lestari, (2017) found that smoking is a risk factor for metabolic disorders in workers.

In manufacturing workers, it was found that 61.7% were overweight or obese, but did not have central obesity (68.3%). In contrast to the research of Sangroula and Uprety, (2020) said manufacturing workers in India were 31% obese. This may occur because according to research by Zhou *et al.*, (2017) conducted in China, it was suggested that a person's nutritional knowledge did not related to the incidence of obesity in adults. According to this study, one of the reasons is because in that country, the guidelines regarding the relationship between nutritional knowledge, nutritional status, and the factors that influence it were still limited and not systematically arranged thus a person with good nutritional knowledge cannot combine diet with physical activity, which was regularly proven. increasing their weight.

Diets vary widely where the intake of macronutrients varies widely, but according to government recommendations only about 10%, namely, carbohydrates according to 11.7%, frequency 8.46 times (533.22 gr), fat according to 12.5%, frequency 2.75 times (57.14 gr), and protein according to 10%, Frequency 6.55 times (101.77 gr). This is in accordance with Levesque, (2011) calorie intake was influenced by one person's workload. Win *et al.*, (2015) also said that her calorie intake was due to work factors which would later lead to weight gain and decreased fitness for workers. Another factor that can cause an increase in food intake is excess body weight. Rogers and Brunstrom, (2016) said that people who are overweight are more likely to eat more.

Theoretically, physical capacity was influenced by several factors such as individual characteristics, exercise habits, intake factors, and illnesses. In this study, the relationship between physical capacity and numerical or categorical variables (sufficient and insufficient) was sought with other factors. Based on the results of the Spearmen test between physical capacity (numerical) and related factors, there is no correlation and meaning. Factors of age, years of work, length of sleep, total calorie intake, and work climate did not affect the value of physical capacity.

This condition is possible because the age of the workers is relatively young compared to the workload which is only moderate (4.5 meters). For the tenure, due to no new employees, it is possible to adapt the workers. Adaptation can occur after 10-12 weeks of work. The length of sleep is sufficient to cause the physical capacity of

the workers is not disturbed. Besides that, excessive intake of workers causes workers not to lack energy for their workload.

According to the Mann Whitney test, the significance of protein intake was p = 0.02 and age p = 0.005. The intake of protein that is inappropriate (insufficient or excessive) can lead to reduced physical capacity. This situation is possible because protein is a substance that cannot be stored, if too much is removed by the body. This disposal also requires energy for metabolism and a considerable amount of water. However, protein is the body's last reserve in forming energy if needed. The age factor has an effect, with increasing age, naturally the organ function (respiration, heart, and muscles) decreases hence physical capacity also decreases. However, the Chi-Square test found that age had an effect on physical capacity with p = 0.01. This is in accordance with the body's physiology. The number of meaningless results is in accordance with the literature that a person's physical capacity is influenced by many factors and no factor is dominant.

The description of macronutrient intake in this study compared to (Ministry of Health Republic of Indonesia, 2019) shows that many workers have excess carbohydrates, protein and fat. The intake of carbohydrates and fats in this study was higher than protein. Research conducted by Kim and Song, (2019) stated that variations in both low and high macronutrient intake are associated with body fat levels and the risk of obesity. Moreover, variations in macronutrient intake are associated with metabolic abnormalities that can increase the risk of heart and blood vessel disease. Thus, the identification of macronutrients in obese people is quite important for an individual approach regarding an appropriate diet.

Eliane A.Castro, Eliana V. Carraca, Rocio Cupeiro, Bricia Lipez-Plaza, (2020) said that obesity is influenced by the number of calories in. It was not found that when balanced macronutrients can lead to obesity. This is consistent with this study which shows that the large amount of carbohydrate, fat, and protein consumption is the main cause of obesity in manufacturing workers.

This study found that protein intake can affect physical capacity. The intake of protein that was inappropriate (insufficient or excessive) can lead to reduced physical capacity. This situation was possible because protein is a substance that cannot be stored, if too much will be removed by the body. This disposal also requires energy for metabolism and a considerable amount of water. However, protein is the body's last reserve in forming energy if needed. The age factor has an effect, with increasing age, naturally the organ function (respiration, heart, and muscles) decreases thus physical capacity also decreases. The majority of protein consumed by manufacturing workers was vegetable originating from nuts such as tempeh and tofu. This protein in Indonesia is easy to obtain and the price is relatively cheap compared to animal protein.

In contrast to fat intake, there is 43.2% excess but there is 53.3% less. This situation is in accordance with the research conducted by Arheart and Lee, (2013). Research shows that food intake is influenced by a person's level of production. In most manufacturing workers, workers are not high income earners, this condition results in low fat intake for them. In addition, low fat intake is also possible because it is not easy to get fatty foods while working. Some workers prefer to bring perishable food items or food stalls provide low-fat but high-carbohydrate menu.

CONCLUSION

The majority of manufacturing workers are male and under 30 years of age. About a third of manufacturing workers are centrally obese. The characteristics of food intake that are in accordance with the nutritional adequacy recommended by the Indonesian population are only about 10%.

Half of the fat intake in manufacturing workers is less, this is different from the intake of carbohydrates and protein which tends to be excess. The physical capacity of the manufacturing workforce in Indonesia is categorized as sufficient as much as three-quarter of the workload. Factors that influence physical capacity are age and adequate protein intake.

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BONE ALUMINUM AS A BIOLOGICAL MONITORING OF OCCUPATIONAL EXPOSURE TO ALUMINUM

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ABSTRACT

The current proposed biological monitoring of aluminum is based on the analysis of aluminum concentration in blood/serum or in urine, but both considered to be reflective of short-term exposure. Based on its toxic kinetics, aluminum has been demonstrated to be accumulated in the bone. The aim of this study is to find out whether by analyzing bone aluminum, we might have an overview of aluminum accumulation that might cause health problems in the future. This review was conducted through a method of search and selection of articles from Pubmed, Cochrane Library, and Google Scholar databases aimed to answer question rising from the problem statement of this study. The process of searching articles used the keywords "occupational aluminum" OR "bone aluminum" AND "biological monitoring" OR "biomonitoring". The selection of articles was performed using the defined inclusion and exclusion criteria. Initially, 61 articles were obtained, but after the selection process and hand searching, four articles remained consisting of two case reports and two cross sectional studies. Based on the selected evidence-based resources, bone can be a promising potential biomarker of aluminum, especially for cumulative exposure assessment. The use of in vivo neutron activation analysis (IVNAA) or X-ray fluorescence (XRF) technology for the purpose of noninvasively quantifying aluminum concentration in the bone, is suitable enough to be performed in occupational settings.

Keywords: Bone aluminum, occupational exposure, IVNAA, XRF, biomonitoring, biological monitoring

INTRODUCTION

Aluminum (Al) is used in many industries to make millions of different products and for Indonesia, Al is one of the potential export commodities (Roesfitawati, 2017; Müller, 2020). Since in the global market, the demand of Al is predicted to keep growing until 2035, the Indonesian state-owned company specialized in aluminum smelting has set a long-term goal of tripling its production capacity by expanding the operations. The plan is also supported by the Nation's President and Ministry of Industry as the goal is to shift the country from an exporter of minerals into a major producer of processed metals (INALUM, 2019). By all means, more workers are needed to objectify the vision and more are prone to the health effects of aluminum.

Aluminum occurs naturally in soil, water, and air as one of the most common metal in the earth' crust. Despite of it is typical used in a huge variety of products, Al is considered unsafe to humans when the body burden achieved high levels. It is known to target the nervous system, bone, and affect respiratory function. Workers are usually exposed through breathing Al containing dusts or fumes (Agency for Toxic Substances and Disease Registry (ATSDR), 2008; Igbokwe, Igwenagu and Igbokwe, 2019). Unfortunately, the national occupational disease prevalence data related to Al exposure in Indonesia has not been well established. Only two studies were found, with both could barely describe effects other than respiratory symptoms (Suwanto, 2018; Hutapea, 2019). Urine and blood aluminum are being used as the biomarkers to determine the exposure of Al, but both considered to be reflective of short-term exposure. Based on the toxic kinetics,

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Al has been demonstrated to be accumulated in the bone (ATSDR, 2008). The purpose of this review was to evaluate whether any method of bone aluminum measurement can be utilized as a biomonitoring to reflect the cumulative occupational exposure to aluminum.

METHOD

Following the search of articles used the keywords (Table 1), the selection was conducted based on the inclusion and exclusion criteria (Figure 1). The inclusion criteria were human studies, in occupational settings, and in English language. Articles that were irrelevant to the purpose of this review were excluded. The authors decided not to favor articles that were published only in the last few years, as the information regarding this topic was limited. Apart from the electronic database, hand searching was also performed. Four articles remained for appraisal, consisting of two case reports and two cross sectional studies.

The cross-sectional studies were critically appraised based on the Center of Evidence-Based Medicine, Oxford University {Formatting Citation}, while case report studies using the Joanna Briggs Institute's Checklist for Case Reports (Joanna Briggs Institute, 2017). The level of evidence was also determined based on the Center of Evidence-Based Medicine, Oxford University (CEBM, 2009). The results of the appraisal were presented in Tables 2, 3, 4, 5.

RESULT

The study by Elinder et al. (1991) found bone aluminum concentrations in two workers who had been exposed with aluminum for 20 years were 29 and 18 μg Al/g dry weight, which were higher than previous studies in subjects without renal disorder (average 7.6 μg Al/g). The upper limits of normal Al content in bone are below 10 mg/g dry weight (Klein, 2019). The results suggest that the welders' bone aluminum was about 10 times higher than normal but about 10 times lower than in patients with dialysis encephalopathy (ranged from 12 to 100 μg Al/g). Unfortunately, this study did not perform either bivariate or multivariate analysis between bone aluminum, urinary aluminum concentrations and years of exposure. The method was performed using invasive biopsy, which might limit further investigations due to ethical reasons and also likely be the reason why only two subjects were examined. This study was probably the initial study and the result was used to promote more studies on the evidence of aluminum accumulation in the bone (Elinder *et al.*, 1991).

Aslam et al. (2009) was first intended to describe the measurement of manganese accumulation in the human bone, but the authors expanded the research with technical improvements to the in vivo neutron activation analysis (IVNAA) and adjusting it for the purpose of bone aluminum detection. The population of this study comes from a group of manganese welders prior to their previous study. The occupational exposure to aluminum is only recorded in the crudest manner, namely "yes" or "no" without specific measurement, which might affect the precision of the analysis consequently. The result of this study indicated that there was a significant mean difference between the exposed and unexposed group (14.1 ± 6.7 μg Al/gCa). Although this study did not provide a correlation between the bone aluminum level and exposure period, as it was a preliminary human study, it should be considered as an encouragement to proceed to further studies directed specifically at aluminum accumulation in human bone due to long-term occupational exposures. The non-invasive properties and minimal radiation dose of this bone aluminum detection method allowed us to take this method into account for conducting a routine biomonitoring analysis to workers who will be exposed to aluminum for some period of time. As this method was also

successfully conducted to determine manganese concentrations in the bone, it may be used for the purpose of differentiating the metal that majorly responsible for developing metal-induced health effects in the case of multiple exposure (Aslam *et al.*, 2009).

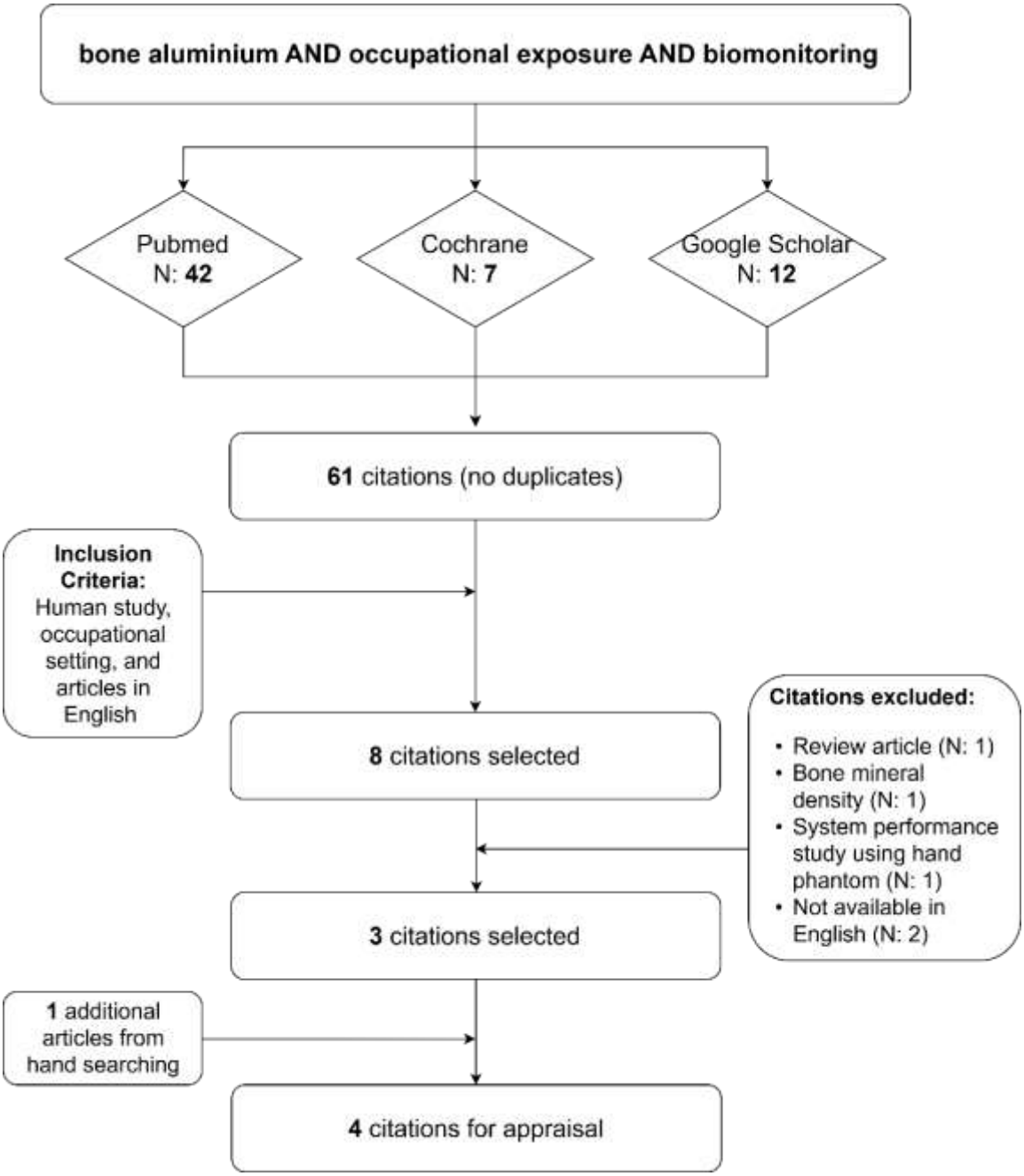

Figure 1. The Process of Article Selection

Hasan et al. (2020) performed the bone aluminum measurement on the right hand of the subject for 10 minutes and used deuterium-deuterium accelerator-based IVNAA system. The authors did not use the reference standard test (serum and urine aluminum analysis) probably based on the understanding that both of these tests only reflect short-term exposure. As a comparative indicator, they used fingernail aluminum and an environmental index (cumulative exposure indices, CEI). Fingernail was used because evidences suggested that the metal in nail presents the prior 2-12 months of exposure, hence it can be used in comparison to the years of metal exposure that can be stored in the bone. The CEI was determined to ensure that the chronic exposure was cumulatively caused in the occupational setting. The limitations of this study were that the sample size was relatively small and the CEI was relied on work history, rather than specific measurement (such as air sampling evidence). But the authors claimed that the use of work history to compose the CEI was an established method which was sufficiently strong and précised enough to estimate the relative ranking of exposure within their study population over the working lifetime (Hasan *et al.*, 2020).

Table 1. Search Strategy Using Keywords

Database	Keyword	Found	Selected	Filter
PubMed	Search: ((occupational aluminum[MeSH Terms]) OR (occupational aluminum[Title/Abstract])) AND ((bone[Title/Abstract]) OR (bone[MeSH Terms]))	42	2	Title/ Abstract
Cochrane	#1 MeSH descriptor: [bone aluminum] explode all trees #2 MeSH descriptor: [biomarker OR biological monitoring OR biomonitoring] explode all trees #3 #1 AND #2	178 13491 7	0	Title/ Abstract
Google Scholar	"bone aluminum" AND "occupational exposure" AND "biomonitoring"	12	1	Title/ Abstract

Table 2. Critical Appraisal Checklist for Case Report (Article 1)

Article	Evidence of aluminum accumulation in aluminum welders
Author(s)	Elinder et al. (1991)
Level of Evidence	4
Were patient's demographic characteristics clearly described?	Age, work history and duration of exposure were described, but medical history was not mentioned.

Article	**Evidence of aluminum accumulation in aluminum welders**
Was the patient's history clearly described and presented as a timeline?	Their work histories were mentioned, but nothing about their medical, family, and psychosocial history including relevant genetic information
Was the current clinical condition of the patient on presentation clearly described?	Inapplicable, because the subjects were considered healthy
Were diagnostic tests or assessment methods and the results clearly described?	Yes, the method of sampling and analysis for urine, blood, and bone biopsies were described in detail.
Was the intervention(s) or treatment procedure(s) clearly described?	Inapplicable, because no treatment applied on both of the subjects.
Was the post-intervention clinical condition clearly described?	Inapplicable
Were adverse events (harms) or unanticipated events identified and described?	Inapplicable
Did the case report provide takeaway lessons?	Yes, the report provided further evidence that long term exposure to aluminum by inhalation gives rise to accumulation of aluminum in the body of healthy persons, and that the elimination of aluminum was very slow

The result of Hasan et al. (2020) study suggested that there was a significant association between elevated bone Al with 15-year CEI (p = 0,02) and approaching significance for 20-year CEI (p = 0,07). Although a significant association between BnAl and lifetime CEI was not observed, it is considered that aluminum accumulation might not reflect multiple decades of exposure even when the half-life is relatively long. The association between BnAl and FnAl could not be observed as well, but the result was consistent with evidence suggesting that nail and bone represent very different time periods with regards to exposure and metal accumulation in the body. (Hasan *et al.*, 2020).

Table 3. Critical Appraisal Checklist for Diagnostic Study (Article 2)

Title	**Noninvasive measurement of aluminum in human bone: Preliminary human study and improved system performance**
Author(s)	Aslam et al. (2009)
Level of Evidence	3b

Title	**Noninvasive measurement of aluminum in human bone: Preliminary human study and improved system performance**
Was the diagnostic test evaluated in a representative spectrum of patients (like those in whom it would be used in practice)?	Yes, this study involved 6 male subjects who self-reported some exposure to aluminum through welding, either presently or in the past. Therefore, this article was compatible with the main purpose of this scientific review in which to find out if bone aluminum could be used as a biomonitoring in occupational settings.
Was the reference standard applied regardless of the index test result?	No, other reference standard test such as serum or urine aluminum measurement was not performed, but the authors compared bone aluminum measurement between the exposed and unexposed group (general population).
Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?	Unclear, this study did not explain whether the process of bone aluminum determination was done differently or blindly between the two groups.
Are test characteristics presented?	Although two types of results commonly reported in diagnostic test studies (accuracy and predictive values) were not presented in this study, the authors provided a comparison of estimated aluminum concentration between the two groups. A significant mean difference was established.
Were the methods for performing the test described in sufficient detail to permit replication?	Yes, the method of bone aluminum determination in this study was using the technique of in vivo neutron activation analysis. It is non-invasive and has an effective dose that is similar to a chest radiograph examination dose, thus might be applicable in occupational settings.

The case report by Assunção (2017) claimed to present an unprecedented case of multifocal osteonecrosis secondary to chronic occupational exposure to aluminum. The pathophysiology was because of the aluminum effect on inhibition of osteoid tissue calcification of the trabecular bone, thus resulting in osteomalacia that makes the bone tissue more fragile and susceptible to osteonecrosis from micro trauma. This proposed mechanism was proved in the patient as high concentration aluminum was related to the low concentration of calcium, which in a healthy individual the levels were inversed. This disease has been described more commonly in patients with chronic renal failure or persons with regular intake of aluminum containing medicines. The author provided a sufficient information regarding patient's history of work, which can benefit us as the reader to draw a correlation between his occupational exposure and the disease. The diagnostic studies in the patient were completed thoroughly. Bone aluminum in this case report were determined using biopsy and x-ray fluorescence spectrometry.

Table 4. Critical Appraisal Checklist for Diagnostic Study (Article 3)

Title	**Characterization of bone aluminum, a potential biomarker of cumulative exposure, within an occupational population from Zunyi, China**
Author(s)	Hasan et al. (2020)
Level of Evidence	3b
Was the diagnostic test evaluated in a representative spectrum of patients (like those in whom it would be used in practice)?	Yes, this study was performed to adult (≥18 years) employed at manufacturing facility or a ferroalloy smelting factory in Zunyi, China, thus compatible with the main purpose of this scientific review in which to find out if bone aluminum could be used as a biomonitoring in occupational settings.
Was the reference standard applied regardless of the index test result?	No, the reference standard test (serum or urine aluminum measurement) was not performed, but instead the researchers used fingernail Al (FnAl) and a semi-quantitative methods namely cumulative exposure indices (CEIs), which incorporate a combination of air sampling and work history data to summarize the total inhaled concentration over time. CEI was based on distinct exposure group (ranking exposure) rather than specific measurement, while FnAl was measured using ICP-MS analysis.
Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?	Unclear, the reference standard test (serum or urine aluminum measurement) was not performed. FnAl analysis was conducted at the Purdue Campus wide Mass Spectrometry Center without any information on who was performing the analysis. Determination of CEI was performed by constructing several CEIs over the prior 5, 10, 15, 20 years and lifetime exposure. The subjects were put into different group based on low, moderate, and high exposure that came with their job. Previously published Al exposure data for similar job titles in the literature were used to determine group assignment. It was not stated whether the CEI determination was blinded or conducted by someone other than the authors.
Are test characteristics presented?	Although two types of results commonly reported in diagnostic test studies (accuracy and predictive values) were not presented in this study, the association between BnAl with FnAl and CEI measures was determined using multiple linear regression models, to reflect the correlation of chronic Al exposure.
Were the methods for performing the test described in sufficient detail to permit replication?	Yes, the BnAl measurements were assessed with a compact deuterium-deuterium accelerator-based IVNAA system, which is non-invasive and posed minimal radiation risk. The research team has developed a transportable version of this technology and the procedure during the sampling was stated.

High aluminum level remained in the patient's bone tissue, even after 3-years period of exposure cessation, about 2-fold compared to a healthy sample control. This result was suspected taking major part in causing symptoms of polyarthralgia related to osteonecrosis. Arthralgia was a usual symptom complained middle age adults, and often underrated (Assunção *et al.*, 2017). Therefore, this case report has given us an insight that a proper history taking, including history of occupation must be assessed comprehensively.

Table 5. Critical Appraisal Checklist for Case Report (Article 4)

Title	Multifocal osteonecrosis secondary to occupational exposure to aluminum
Author(s)	Assunção et al. (2017)
Level of Evidence	4
Were patient's demographic characteristics clearly described?	Yes, the patient was a black male, 39 years old, worked for eight years in a plant refining bauxite and producing aluminum.
Was the patient's history clearly described and presented as a timeline?	Yes, it was stated that the symptoms started for years prior. A complete history of his work was also provided.
Was the current clinical condition of the patient on presentation clearly described?	Yes, his symptoms were presented.
Were diagnostic tests or assessment methods and the results clearly described?	Yes, the type of diagnostic tests, the location, and the result were well-defined.
Was the intervention(s) or treatment procedure(s) clearly described?	Yes, the patient was treated conservatively in this case report.
Was the post-intervention clinical condition clearly described?	Yes, within 6 years of follow-up, the pain improved partially and no collapse reported.
Were adverse events (harms) or unanticipated events identified and described?	No, the patient chose to take opioids regularly rather than having a surgery, but the adverse events relating to this were not elaborated.
Does the case report provide takeaway lessons?	Yes, this case reported provides a novel case of a patient with multifocal osteonecrosis associated with chronic occupational exposure to aluminum. No other reports found associating the occurrence of osteonecrosis with occupational exposure to aluminum.

DISCUSSION

The proposed mechanism is that aluminum can accumulate at the mineralization front of the bone surface and occupies the unmineralized type I collagen. Thus, aluminum act as a competitor to calcium, impairing calcification and resulting in osteomalacia. Aluminum also impair the secretion of parathyroid hormone which will result in a functional hypoparathyroidism with consequent hypercalciuria. It also inhibits renal enzyme 25 hydroxyvitamin D-1 alpha hydroxylase (25(OH)D-1-alpha hydroxylase), which converts 25(OH)D to 1 alpha, 25 dihydroxyvitamin D, resulting an alteration in calcium homeostasis, and bone cell differentiation (Klein, 2019).

During the past years, the only known method for bone aluminum measurement was performed with biopsy, which was implemented in the study of Elinder et al. **(**1991). Although the correlation between bone aluminum level and exposure time could not be determined by then, the result suggested more studies to prove more evidence. Both of Aslam et al. (2009) and Hasan et al. (2020) studies were using the technique of in vivo neutron activation analysis (IVNAA) for bone aluminum detection. This method was developed decades ago and had been used to measure certain elements in human body such as calcium, phosphorus, sodium, and chlorins (Shulyakova, Avtonomov and Kornienko, 2015). Both studies used hand bone as the site of detection, as it can be easily extended and not particularly sensitive to radiation-induced damage. Long half-times retention for aluminum were recognized for 29 years in cortical bone and 500 days in trabecular bone. The long half-time in bone is related to the slow rate of bone turnover, about 3% per year in cortical bone and 20% per year in trabecular bone. Human hand bone accounts for 1.5% of the skeleton and mainly consists of cortical bone, which makes it a suitable site of choice for irradiation (Riihimäki and Aitio, 2012). Based on a systematic review of published articles between 1985 and 2016, only one cross-sectional study assessed the effect of aluminum exposure to the bone (Ferguson *et al.*, 2018). However, the study used bone mineral content and density rather than the concentration of aluminum, so it is considered irrelevant to the purpose of this review. This result suggest that the use of IVNAA for bone aluminum detection, probably other elements as well, has not been widely implemented in occupational practices. IVNAA is available in Indonesia under the supervision of National Nuclear Energy Agency of Indonesia (Badan Tenaga Nuklir Nasional, BATAN), but more commonly used for environmental sampling (Dwijananti *et al.*, 2018).

Out of the four journals appraised in this scientific review, unfortunately, none of them was a cohort study providing the exact relationship between aluminum accumulation in the bone and duration of exposure. This finding was expected as seen on a systematic review mentioned before, only 8 cohort studies were found with none of them analyzed bone aluminum concentrations (Ferguson *et al.*, 2018). Bone aluminum studies were more common to be assessed in populations with renal failure. Hasan et al. (2020) probably has the closest effort, as it compared BnAl with cumulative exposure indices (CEIs). However, the CEI as the potray of occupational exposure to aluminum, was only recorded in the crudest manner in this study, without specific measurement. This lack of available study is somehow understandable, as cohort studies might be time-consuming and not feasible. At the present, our information regarding the effectiveness of bone aluminum assessment as a biomonitoring for chronic exposure is still limited.

Nervous system has been known as the most sensitive target of aluminum exposure. Although the relation still controversial, aluminum has been associated with some neurodegenerative

disorders such as Alzheimer's disease, Parkinon's disease, and multiple sclerosis. Aluminum may not be the only causative agent of the diseases, but it is possible that it may play a role in the disease progression (ATSDR, 2008; Inan-Eroglu and Ayaz, 2018). The chronic effects of aluminum are linked to the retention of aluminum in the depot (most probably in bone) from which it is slowly eliminated. The slow release and ongoing exposure can result in an increased aluminum body load (Klein, 2019). Assunção et al. (2017) provided us with a novel case of aluminum-induced bone toxicity, affirming us that the bone accumulation of aluminum may still pose a risk of health effect, even after the exposure had been stopped for years. The patient presented with arthralgia, which is a usual symptom complained middle age adults, and often underrated. Occupational specialists have to pay extra attention to any symptoms that may seemed common in regular setting.

Bone aluminum level in Assunção et al. (2017) study was determined using biopsy and x-ray fluorescence (XRF) spectrometry. Although biopsy may not be suitable, XRF is another method that may be feasible to be applied in occupational settings for routine monitoring. Like IVNAA, this XRF method is also available in Indonesia under the supervision of Indonesian Institute of Sciences (Lembaga Ilmu Pengetahuan Indonesia, LIPI) but it is currently used for environmental sampling.

CONCLUSION

In regard to around one-half of the total body burden of aluminum is stored in the bone (ATSDR, 2008), bone is a promising potential biomarker of aluminum, especially for cumulative exposure assessment. Using IVNAA or XRF technology to quantify aluminum concentration in the bone noninvasively, it is considered reliable enough to be performed in occupational settings. Although resulting in some radiation exposure, the dose is minimal and may not posed health risks. IVNAA and XRF methods are both available in Indonesia but it's currently used for environmental sampling (Dwijananti *et al.,* 2018). There are wide opportunities in the future for the utilization of this method, especially in the occupational settings that we should look forward to.

Based on the knowledge from this scientific review, some recommendation can be applied for practices. Bone aluminum level should be assessed initially as a baseline, prior to a worker's employment or assignation to a high-risk occupational environment of aluminum. Whenever it is necessary, routine analysis can be implemented along with environmental monitoring and other supportive biomarkers, as a medical surveillance of aluminum-induced health effect. More evidence is still needed to compare bone aluminum measurement with other biomarkers and enviromental sampling in larger working populations. Performance study for optimization and improvement of IVNAA or XRF to be a routine monitoring of bone aluminum is also necessary. Further studies are also required regarding the correlatoin between bone aluminum accumulation and years of exposure, as well as the chronically emerging health effects long after the cessation of exposure. The workers should be encouraged to get the bone aluminum measurement because the data acquired may benefit the workers and their families who seek compensation after suffering aluminum health related problems that may develop long after the occupational exposure had been halted.

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LUNG CANCER ASSOCIATED WITH CARBON BLACK EXPOSURE ON BRICK WORKERS

Evidence-Based Case Report

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ABSTRACT

Carbon black aerosol has potential risks to human health. It has been acknowledged to cause cardiovascular and respiratory diseases in human**s.** International Agency for Research on Cancer (IARC) 2010 stated that carbon black classification is 2b, which is carcinogenic. This research explains a case of lung cancer due to carbon black exposure and reviews the literature of occupational cases to get the answers about the effects of carbon black exposure and the increasing risk of lung cancer for workers exposed to carbon black. The literature review was performed to answer the clinical question via electronic databases: PubMed and Google Scholar. The keywords used were 'carbon black' and 'lung cancer' and 'workers'. The inclusion criteria of this searching strategy were the workers which exposed to carbon black, meta-analysis, randomized controlled trial, systematic reviews, cohort. The exclusion criteria of this article were inaccessible articles, RCTs that have been used in the recent systematic reviews. The selected articles were then critically appraised using relevant criteria by the Oxford Center for Evidence-based Medicine. This study reviews the literature by Rota Matteo; The epidemiological evidence on the polyaromatic hydrocarbon (PAH) high exposed, perspective cohort study by Delli LD, and the control case study by Marie EPt. All the researches above showed that carbon black carcinogenic potential is the same as the IARC monograph statement that the epidemiological studies of carbon black provide possible carcinogenicity (Group of 2B).

Keywords: carbon black, lung cancer, workers

INTRODUCTION

Carbon black, an important aerosol in the atmosphere, is generally produced by weathering of graphitic carbon in rocks and the incomplete combustion of fossil fuels, vegetation, biofuels, and biomass. Carbon black's nature has a distinctive form, with nanometer to micrometer particle size, and layered structure. Recently, carbon black has had an enormous contribution to global climate change and is related to a persistent organic pollutant and affects human health (Wu *et al.*, 2018). Carbon black aerosol has potential risks to human health. It has been acknowledged to cause cardiovascular and respiratory diseases in humans. Carbon black potentially induces cardiovascular morbidity and mortality. Its particle size and its catastrophic effects are strongly connected. Polyaromatic hydrocarbon (PAH) carcinogenicity activity is primarily explained by the diolepoxide process, i.e. the production of intermediate PAH metabolites (diols and diolepoxides) as a result of DNA reaction and DNA adduct formation was known to be genotoxic and carcinogenic. (*International Agency for Research on Cancer (IARC) Monographs on the evaluation of Carcinogenic Risks to Human volume*, 2018). Other possible pathways include orthoquinone and the formation of reactive oxygen species, aryl-hydrocarbon, immunosuppression, and epigenetic processes (Sharma, 2010). Agency for Research on Cancer (IARC) stated that the carcinogenic effect of carbon black on human is still a controversy. Hence, it is important to research with literatures review to have the answer about carbon black exposure effects and the increasing risk of lung cancer among carbon

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black exposed workers (Hancock DG, 2014).

The finding on this case explains the relationship of lung cancer with carbon black exposure through the literature review on the occupational case report.

The case description of this research was taken from a patient in A 47-year-old man who came to the hospital with complaints of breathing shortness and chest pain. The pain spread to the upper left abdomen. The patient felt pain and tight every time he breathed. Breath is felt rather tight. This complaint has been felt since approximately 3 months ago and started to get heavy in recent weeks. Coughing of blood since 6 months ago, history of completed tuberculosis treatment, diabetes, and hypertension were denied. History of the family with diabetes and hypertension was denied, smoking over 35 years, 1-2 packs/day. (index brickman: heavy). Based on the physical examination, there were signs of hypotension and uninodular firm elastic lymphatic node enlargement with 0,5 cm in diameter in the left neck. Based on the thorax examination, there were asymmetrical left and right chest, dimmed right lung percussion, and diminished vesicular breath sound. Based on the radiology examination, there were a quite massive right pleural effusion and swelling of antebrachial soft tissue with intact visualized bone and good joints. The biopsy result showed it as squamous cell carcinoma. The occupational history of this patient has been working as a brickmaker in his home industry since 20 years ago and works 8 hours per day, 6 days per week. For making much brick, he uses combustion material from charcoal which produces carbon black. He never uses personal protective equipment such as masks, boots, google glasses, and gloves. The clinical diagnosis for this patient is squamous cell carcinoma of lung cancer. Based on the 7 steps of occupational diagnosis, it was determined as lung cancer aggravated by work.

This research aims to get the answers about the effects of carbon black exposure and the increasing risk of lung cancer for workers exposed to carbon black.

METHODS

The literature search was performed to answer the clinical question via electronic databases: PubMed and Google Scholar. The keywords used were 'carbon black' AND 'lung cancer' AND 'workers' (table 1). The inclusion criteria of this searching strategy were the workers which exposed to carbon black, meta analysis, randomized controlled trial, systematic reviews, cohort. The exclusion criteria of this article were inaccessible articles, RCTs that have been used in the recent systematic review (figure1). The searching was done on March 23th 2019.

The selected articles were then critically appraised to determine whether the article is valid, important, and applicable to the patient using relevant criteria for etiological study by the Oxford Center for Evidence-based Medicine. (*Oxford Centre for Evidence-Based Medicine (CEBM). Critical Appraisal Tools.*, 2019).

From online search results, three selected articles fit the inclusion and exclusion criteria: A systematic review; Occupational exposures to polycyclic aromatic hydrocarbons and respiratory and urinary tract cancers: an updated systematic review and a meta-analysis to 2014 (Rota *et al.*, 2014), a prospective cohort study; Cohort Study of Carbon Black Exposure and Risk of Malignant and Nonmalignant Respiratory Disease Mortality in the US Carbon Black Industry (Dell *et al.*, 2015), and case-control study; Case-Control Study of Exposure to Carbon Black in the Occupational Setting and Risk of Lung Cancer (Marie EP, 1996).

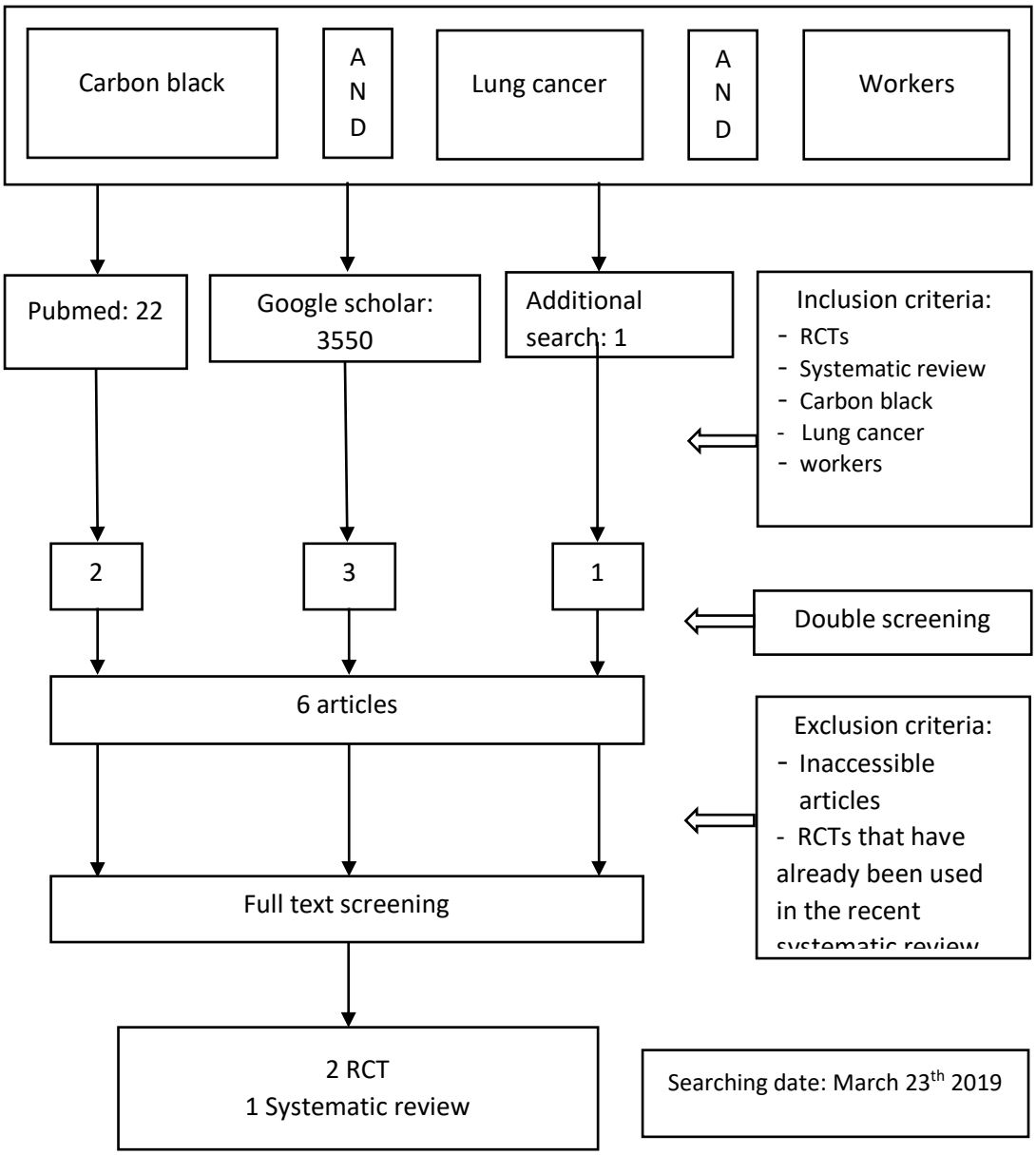

Figure 1. Literature searching chart

Table 1. Searching strategy using the database from PubMed AND Google Scholar

Database	**Search strategy**	**Hits**	**Selection**
PubMed	Carbon black AND Lung cancer AND workers	22	2
Google Scholar	Carbon black AND Lung cancer AND workers	3550	3
Additional Search (reference)	Carbon black AND Lung cancer AND workers	2	1

RESULT

The first study Rota *et al.*, (2014) found 62 out of 474 non-specific journals identified through eligibility standard for literature searching and a complete text evaluation, 49 out of 62 articles are not included because of different occupation or peculiar cancer, control case study, investigated mortality or incident quantitative estimation, or several publications on the same cohort. Thus, there are 13 articles assessed in this review.

This systematic review assessed 13 articles that showed that polycyclic aromatic hydrocarbons (PAH) exposure among the alumunium workers was showed insignificantly related to lung cancer (including other non-specified respiratory cancers) (RR 1.08 95% CI 0.95 to 1.23). The study shows that the iron and steel factory workers were insignificantly related with lung cancer (including other non-specified respiratory cancers) (RR 1.31 95% CI 1.08 to 1.59), in three cohort studies on asphalt workers, showed insignificant results with RR for lung cancer was 1.59 (95 % CI 0.68–3.76).

Table 2. Critical appraisal checklist for systematic review

Article	Occupational exposures to polycyclic aromatic hydrocarbons and respiratory and urinary tract cancers: an updated systematic review and a meta-analysis to 2014		Level: 1a (Systematic review of clinical trials, meta-analysis)
Question	What question (PICO) did the systematic review address?	Yes	according to the abstract and the final paragraph of the introduction the article, the PICO was P: the workers in selected industries; I : polycyclic hydrocarbons; C: unexposed workers; O:respiratory and urinary tract cancers
find	Is it unlikely that important, relevant studies were missed?	Yes	The search technique, including the words used, is evidence in some detail. The number of titles and abstracts checked, the number of full-text studies retrieved, the number of omitted studies and the exclusion grounds.
Appraise	Were the criteria used to select articles for inclusion appropriate?	Yes	Yes, they were appropriate. Inclusion criteria; cohort studies, the study of workers from selected industries characterized by PAH exposure, providing standardized mortality ratios (SMRs) and/or standardized incidence ratios

			(SIRs) of respiratory and urinary tract neoplasms.
Synthesize	Were the included studies sufficiently valid for the type of question asked	Unclear	The description of how the quality of each study was assessed using predetermined quality criteria relevant to a clinical questioning method (e.g. randomization, blinding and thorough investigation) was not found in the method or result section.
	Were the results similar from study to study?	No	The assessment of heterogeneity between studies was focused on the chi-square test, according to the method portion. The findings of the numerous cohort studies under review were substantially heterogeneous in many cases.
Result	What is The result of the articles?		The forest plot shows that the exposure to polycyclic hydrocarbons **amid** aluminium workers was negligible concerning lung cancer (including other non-specified respiratory cancers) ((RR 1.08 95 percent CI 0.95 to 1.23) and significant to lung cancer (including other non-specified respiratory cancers) among iron and steel smelting workers (including other non-specified respiratory cancers) (RR 1.31 95 percent CI 1.08 to 1.59)

The second study (Dell et al., 2015) found that there was no clear association in the full-time or hourly worker community between the mortality risk of lung cancer and carbon black exposure.

Even though there is no excess lung cancer mortality in this cohort study, the lack of connection between carbon black exposure and lung cancer is persistent with the studies of the same field in the UK and Germany.

Cancer mortality in this cohort is different (RR: 2,781 CI 95%1,923 to 4,022). Concerning carbon black exposure estimates, this study concluded that no clear trends of increased lung cancer were found. No clear association was found between the risk of mortality from lung cancer with lagged or lugged carbon black exposure in the full cohort or the entry cohort of hourly male workers.

Table 3. Critical appraisal checklist for a prospective cohort study

Article	Cohort Study of Carbon Black Exposure and Risk of Malignant and Nonmalignant Respiratory Disease Mortality in the US Carbon Black Industry		Level: (3) prospective cohort study
Validity	Was the objective of the study clearly stated?	Yes	To know if there was a correlation between cumulative inhalable carbon black exposure and lung cancer and respiratory disease mortality among 6634 US carbon black employees.
	Were exposures and results measured in the same method in the patient groups?	Yes	The measurement is the same method for exposure of black carbon and the result (standardized mortality ratio) for each group of patients.
	were there clearly defined groups of patients. similar in all important ways other than exposure to the treatment or other cause?	Yes	Employees at 18 carbon black facilities in the United States are groups of patients (of a total of 20 that were working with carbon black as of January 1, 2000)
	was the investigation of the patients complete and long enough?	Yes	Yes, the investigation of the patients is complete and long enough. The analysis aimed to determine whether carbon black exposures were predictive of risk in the 15 years preceding the death of lung cancer to allow for direct comparisons of outcomes between the cohorts.
	did the study have a sufficiently large sample size?	Yes	The sample size is 6634 subjects. It is sufficient.
	was there a statistical adjustment for the important difference between patient groups?	Yes	Cumulative inhalable carbon black exposure was modeled as both a continuous and a categorical component. Continuous cumulative inhalable carbon black exposure was modeled in increments of 100 mg/m3.yr.
		Yes	

	is it clear that the exposure preceded the onset of the outcome?		The onset of the outcome was preceded by exposure.
	is there a dose-response gradient?	Yes	It is shown in Table 4. For the entire cohort of 6634 workers, inhalable carbon black exposure influenced hazard ratios and 95 percent confidence intervals for lung cancer.
	is the association consistent from study to study?	Yes	No clear association was found between the risk of mortality from lung cancer and lagging or lugging carbon black exposure in the full cohort or the entry cohort of male freelance workers. The lack of connection between carbon black exposure and lung cancer is persistent with the studies of the same field in the UK and Germany. Even though there is a huge difference in the lack of an excess of lung cancer mortality in this cohort.
	is the biological relationship plausible?	Yes	Inhalation is the main route of exposure to black carbon, and the lung is considered the target organ of concern, similar to other particles.
Clinical importance	how strong is the association between exposure and outcome, and how precise?		Total patient for lung cancer : 184 Total patient : 6634 Total reference patient : 2565 Relative Risk for kohort: 2,781 CI 95% (1,923 – 4,022)
Aplicability	were the study patient and their management similar to those in my practice ?	Yes	This patient has the same exposure, the other risk factor are similar

The result of the third study Marie EP, 1996) is compatible with the hypothesis of the high risk of lung cancer due to black carbon exposure, yet only in the “higher” exposure group. Moreover, this study provides evidence on the risk that can occur from carbon black exposure in a wide range of occupations, compared to cohort studies carried out in specific industries. the results from the present in-depth analyses are compatible with the hypothesis of excess risk of lung cancer with exposure to carbon black, but only in the "higher" exposure group. These findings must be interpreted cautiously, given the limited number of exposed cases in this exposure category

(n:18). The conclusion is that the evidence for carbon black's role is inadequate and contradictory. This study provides some additional evidence for an association between exposure to carbon black and lung cancer.

Table 4. Critical checklist for case control study

Article	Case-Control Study of Exposure to Carbon Black in the Occupational Setting and Risk of Lung Cancer		Level: (3a) a case control study
Validity	are the objective of the study clearly stated?	Yes	To investigate the association between carbon black exposure in the workplace and risk of lung cancer
	were exposures and outcomes measured in the same way in the patient groups	Yes	The measurement is the same way for exposure of carbon black (the synthetic index of cumulative exposure to carbon black) and the outcome (estimated odds ratios)
	were there clearly defined groups of patients. similar in all important ways other than exposure to the treatment or other cause?	Yes	Male residents from the greater Montreal area aged 35-70 years were recently diagnosed with one of 19 histologically confirmed cancer types comprised the case series. The ascertainment of cases was carried out in all large hospitals in the area over 6 years
	was the follow-up of study patients complete and long enough?	unclear	The follow-up study is complete but it wasn't mentioned about the duration of follow up
	did the study have a sufficiently large sample size?	Yes	The sample size is 3730 subjects. It is sufficient
	was there a statistical adjustment for important differences between patient groups?	Yes	Exposure of carbon black was expressed in three categories, that is, unexposed, lower, and higher exposure, corresponding to the lower two-thirds and upper third of the distribution of the index of cumulative exposure described previously. This allowed for an examination of the exposure-response relationship. Adjusted regression models included linear terms for age, socioeconomic status as measured

			by self-reported income, job dirtiness, and alcohol intake, and categorical terms for ethnicity (French, Anglo, other) and respondent status (self, proxy). Asbestos and chromium compounds are recognized lung carcinogens and were incorporated as continuous variables, using the same type of synthetic index described earlier for carbon black.
	is it clear that the exposure preceded the onset of the outcome?	Yes	It is clear that exposure preceded the onset of the outcome
	is there a dose-response gradient?	Yes	It is shown in TABLE 5. Odds Ratio between exposure to carbon black and Lung cancer for the main histologic Subtypes, using two control groups, Montreal, 1979-1985
	is the association persistent from research to research?	Yes	According to some research, carbon black exposure is related to non-carcinogenic diseases of the respiratory system. [Gardiner et a]., 1993; Gardiner, 1995; IARC,19841, while other studies have found no such deleterious effect [Crosbie, 1986; Robertson and Ingalls, 1989; Indirect evidence pointing to carbon black as a lung carcinogen comes from studies focusing on industries.
	is the association consistent from study to study?	Yes	Some researchers mentioned that carbon black exposures are related to non malignant diseases of the respiratory system.
Clinical importance	how strong is the association between exposure and outcome, and how precise?		Low Exposure :OR 1.08 CI95% 0.66 – 1.76. Higher exposure : OR 2.17 CI95% 0,95 – 4,91. The assosiation is not strong enough.
Applicability	were the study patient and their management similar to those in my practice?	Yes	This patient has the same exposure, the other risk factor are similar

DISCUSSION

The studies above showed that the relation between carbon black and lung cancer was still not clear. A systematic review about occupational exposures to polycyclic aromatic hydrocarbons and the health effect on respiratory and urinary tract cancers showed that carbon black which is a group of polyaromatic hydrocarbon (PAH) has an insignificant related to lung cancer for alumunium workers (RR 1,08 95%CI 0,095 T0 1,23), the iron and steel foundry workers (RR 1,31 95%CI 1,08 to 1,59), asphalt worker (RR 1,59 95%CI 0,68-3,76). The conclusion is there is no indication of high risk discovered in coal tar and carbon black employees.

In the study of meta-analysis, coal gasification, coke production, and carbon electrode production were observed to find the high risk of respiratory tract cancer among workers in these sectors. It revealed that there was no high risk of respiratory tract cancers in employees. The study of meta-analysis confirmed workers engaged in the manufacturing of carbon electrodes had a potential excess risk of respiratory cancer**.** (Rota *et al.*, 2014).

The other paper, a prospective cohort (Dell et al., 2015), concluded that to estimate carbon black exposure, there were no clear trends of increased lung cancer**.** There was no direct connection between lagged or lugged carbon black exposure and lung cancer mortality in the full cohort or the entry cohort of hourly male workers.

The last article of case control study (Marie EP, 1996), reported that the results from the present in-depth analyses are compatible with the hypothesis of excess risk of lung cancer with exposure to carbon black, but only in the "higher" exposure group. The quality of job histories may differ depending on whether they are obtained directly from the subjects or by proxy interviews. The interviews had to be carried out for some lung cancer cases as well as for an appreciable proportion of cancer controls. Since there was little difference (10%) in the proportions of proxies in the two groups, there was little opportunity for bias in the comparison. The inclusion of proxies may have resulted in some misclassification and have minimized the differences between groups, but not in an inflation of the risk estimates. Along with inaccurate recall of work histories and misclassification in the attribution of exposures by chemists, the use of proxy respondents is one of the factors that may have attenuated the relationships observed if there was a true association (Sorahan and Harrington, 2007).

The result from these three studies is contributed for several reasons that in the West where the three studies had been done, especially in US and UK where they have standard regulation of harmful exposure effect protection. They use standard engineering control to limit the exposure and also management early detecting management for workers' health. However, it is important to remember that each country has its medical regulation on a surveillance system that can influence the implementation, accessibility ,and effectiveness of lung cancer prevention, such as the quantity examination of polyaromatic hydrocarbon (PAH) especially carbon black in the working environment and workers health by biological monitoring of carbon black exposure (Sorahan and Harrington, 2007).

The eminence of this study is a large number of research samples in a systematic review, prospective cohort study, and control cases. The study is complete with adequate quantitative data and cost-efficient data collecting by compiling cohort studies from original articles. Of course, there are weaknesses of this research, such as the heterogeneous data that reflects the varied pattern of exposure in some cohorts and the difference of period that can be a bias and confounding factor. This study did not analyze the dose–response relation between carbon black and lung cancer.

Information from the above literature study on the review of this patient

case explains that carbon black exposure causing lung cancer is still not clear. Moreover, for his patient, Other factors can contribute to lung diseases (especially lung cancer) such as smoking habits, other working process exposure, and pollutant from where he lives in.

It is important to manage carbon black exposure by medical surveillance especially in home industries in Indonesia where there is a lack of regulation, controlling and protection from exposure. Home industries like as charcoal industries, tofu industries, extraction of nutmeg oils and clove oils, food industries which are exposed by carbon black should get attention for safe and healthy workers with the hierarchy of control such as; 1) Elimination or substitution by change charcoal burning to gas which is healthier and safe. 2) If elimination and substitution can't be realized, get engineering control to enclose operations and/or provide appropriate local exhaust ventilation at machinery and at places where dust can be generated to flow away air pollutant direction and make a chimney or closed burn setting/isolating operation. 3) Administration control to lead the regulation of job procedure, health promotion to prevent the health risk for the workers, Medical surveillance to determinate the quantity of carbon black in air workplace, early detection by biomonitoring of carbon black to the workers; by examining the metabolic of hydroxypyrene (in urine) by using the high performance of liquid chromatography (HPLC)and enzyme-linked immunosorbent assay (ELISA) and periodic medical examination (Angerer J, Mannschreck C, 1997). 4) Personal protective equipment (carbon black; 1750 mg/m^3) by using respirators such as respirators operated in a pressure-demand or other positive-pressure mode. For research; Advanced studies of the carbon black exposure to lung cancer in Indonesia, and the research of grading dose cumulative inhalable carbon black exposure as cancer's variable cause to human's other organs, especially in workers (Borm and Driscoll, 2019)(McCunney RJ.et al, 2012).

CONCLUSION

This research showed there was no strong relation between carbon black and lung cancer risk. The three types of research showed that carbon black carcinogenic potential is the same as the IARC monograph statement that the epidemiological studies of carbon black provide lack indication to the notation of carcinogenicity (Group of 2B).

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BIOMONITORING OF SEVOFLURANE EXPOSURE IN ANESTHESIOLOGIST

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ABSTRACT

Sevoflurane is used by anesthetists for the induction and maintenance of general anesthesia. This causes the anesthetist to get daily exposures. This will be a potential hazard for exposed operating room personnel, especially anesthetists. The adverse health effects of sevoflurane as hepatotoxic, nephrotoxic and neurotoxic in the human body can be a risk for anaesthetists. Biological monitoring can be done by measuring the levels of sevoflurane and its metabolites or by looking at biomarkers for their effects on health effects. The aim of this study was to seek a literature review on the biomonitoring of sevoflurane exposure in anaesthetists. We searched the literature review using the PRISMA method in PubMed and Google scholar using the following keywords "occupational disease" "chronic effects" "anaesthetist" "sevoflurane exposure" "inorganic fluoride" "biomarkers" previously using the term MeSH and combined with Boolen "OR" and AND". We obtain 75 articles taken from the database, excluded 35 articles, and selected 5 articles. The results of the review articles showed that there were health effects, especially on liver and kidney function in chronic exposure. Biological monitoring can be undertaken by detecting sevoflurane and its metabolites in the urine during work and function of the liver and kidneys. The evidence for biological monitoring as surveillance in anaesthesiologists remain inconsistent due to limited studies. We recommend to measure sevoflurane in ambient air using a hierarchy of controls, such as elimination, replacement, engineering, administrative and personal protective equipment. We need to undertaken environmental and biological monitoring in order to acquire a safe and healthy work environment.

Keywords: sevoflurane exposure, occupational health, anesthesiologist

INTRODUCTION

Prior to the invention of intravenous drug administration, the first anaesthetics (diethyl ether) were delivered through inhalation and used as a general anaesthetic by Long in the 1840s. Classification of inhaled anaesthetic drugs are ethers, alkanes, and gases. The drugs have an unconscious and immobile effect in patient. The pharmacokinetic of drugs relies on their physical properties. Most of the absorption of inhalation anaesthetics and the rate of elimination from the alveoli are determined by solubility in blood where the soluble substance has a faster rate than the less soluble substance. The effect of inhalation anaesthetics depends on the alveolar concentration not on the dose of the anesthetic absorbed. Wells first used nitrous oxide in 1844 for dental analgesia, and chloroform (trichloromethane) was developed by Simpson in 1847 as a non-explosive alternative to ether. These medicines, of which only nitrous oxide is still commonly used, dominated the first century of anaesthesia. Ethers include diethyl ether, methoxy propane, vinyl ether, enflurane, methoxyflurane, isoflurane, sevoflurane, and desflurane (Hemmings and Egan, 2019).

Sevoflurane, a halogenated inhalational anaesthetic, used for the induction and maintenance of general anaesthesia in adult and paediatric patients that more than 20 years. The character of sevoflurane is volatile, non-flammable, non-irritant, and easy to provide, with low solubility profile and blood-to-gas partition coefficient (Brioni *et al.*, 2017).

Sevoflurane, a fluorinated methyl isopropyl ether has very poor blood solubility. Sevoflurane is a volatile anaesthetic with smells sweet and

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minimally pungent that used during surgical procedures offers hypnosis, amnesia, analgesia, akinesia, and autonomic blockade. Sevoflurane causes modern agents with the least cerebral vasodilation, thus it is favourable in neurosurgical patients with elevated intracranial pressure (Edgington, Muco and Maani, 2007; Hemmings and Egan, 2019).

Inhaled anaesthetics can result in brain damage that can be a trigger the onset of Alzheimer's disease. It can be a potential risk factor for cognitive decline. Inhaled anaesthetics in human cell cultures cause amyloid β accumulation and cell death, suggesting a possible molecular mechanism of cognitive decline related to anaesthesia. The researchers found that more plaques were created by the transgenic mice exposed to inhalation anaesthetics (Kubota, 1992; İnan and Özköse Şatirlar, 2015).

Sevoflurane triggers health effects in high and low concentrations. Headache, fatigue, disorder coordination, liver and kidney disease are common symptoms that occur at high concentrations. Generally, chronic effects with small concentrations do not cause health problems. However, several study showed the relationship between the incidence of miscarriage, genetic mutations, and cancer among workers in the operating room. In addition, workers exposed to anaesthetic gases have an increased incidence of chronic headaches, peripheral neuropathy, anemia , multiple sclerosis and depression (Dalagkozi *et al.*, 2018).

The main effects of sevoflurane exposures are nephrotoxic, hepatotoxic, and neurotoxic. The aim of this review is to provide an understanding to the specific biological monitoring and systemic health effect of sevoflurane exposure in anaesthesiologist.

METHOD

We undertook the literature searching strategies for answering the clinical question performed on December 14, 2020 with the PRISMA method that used electronic database in Google Scholar and PubMed. Keywords used were “chronic effect of sevoflurane for occupational disease” and “biomarker of sevoflurane exposure in anaesthesiologist” in google scholar. Keywords in PubMed has been used “occupational disease” “chronic effect” “anaesthesiologist” “sevoflurane exposure” “inorganic fluoride” “biomarker” which previously used the MeSH term and combined with Boolen operation “OR” and “AND”. Our goal was to find answers to the question 'What is the specificity of biological monitoring and health effect in anaesthesiologist with sevoflurane exposure.

Table 1. Searching strategy using database from PubMed and Google Scholar

Database	Keyword	Finding	Selected
Google scholar	chronic effect of sevoflurane for occupational disease	20	2
Google scholar	biomarker of sevoflurane exposure in anesthesiologist	20	2
Pubmed	Search ((((occupational disease) OR chronic effect)) AND anesthesiologist) AND (((((sevoflurane exposure) OR inorganic flouride) OR inorganic flouride[MeSH Terms]) OR biomarker) OR biomarker[MeSH Terms])	35	1

The inclusion criteria of this searching strategy were research in anaesthesiologist, occupational exposure, biomonitoring, full text article available. The exclusion criteria of this article were inaccessible articles. We critical appraisal article according to the systematic review, observational study, and case study. The authors concluded that this literature review did not require approval by the Ethics Committee.

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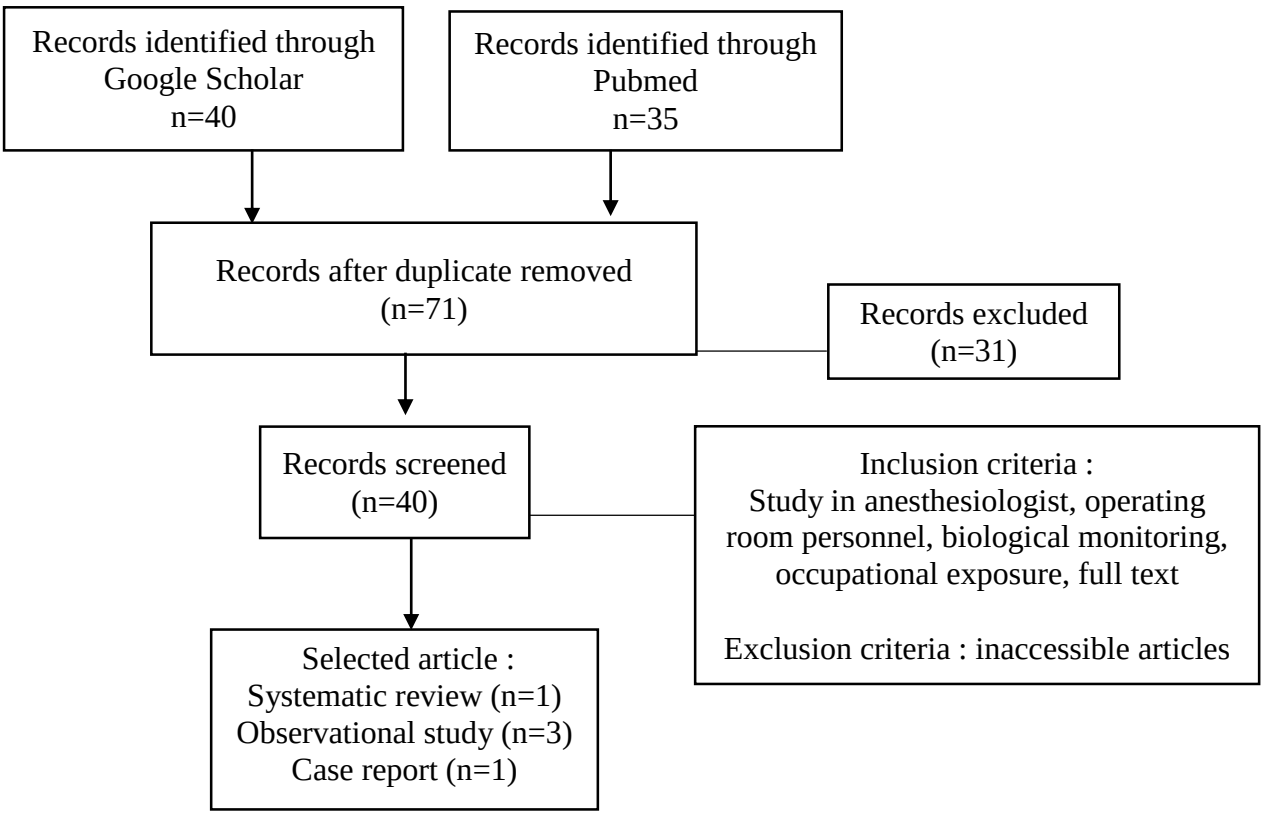

Diagram 1. Searching diagram on finding literatures

RESULT

A total of 75 articles were initially retrieved from online database. A total of 31 articles (41 %) were excluded because did not relate to the aims of study. The study was explained about the other inhaled anaesthetic agent without sevoflurane. We eliminated the article from abstract. Then, we screened the 40 article that have inclusion criteria like study in anaesthesiologist, operating room personnel, biological monitoring, occupational exposure, and full text.

Table 2. Critical appraisal systematic review

Appraisal question	Answer
What was the issue PICO in the systematic review?	What is the impact of occupational exposure to volatile anesthetics exposure and the best health surveillance for exposed personnel?
F- Is it doubtful that important and substantial studies have been missed?	Unclear, because only use 2 database, in the Medline and Cochrane Library databases.

A- Are the criteria used to select articles appropriate?	Unclear, inclusion study just only depend on title, language, and population like anesthetists, surgeons, nurses and auxiliary personnel
A- Do the included studies have good validity to answer the questions posed?	Unclear, because no specific information or resume of validation the study in this review
T- Do have similar results from one study to another?	Yes
What is the results?	Evidence of the adverse effects on exposed workers of volatile anesthetics is contradictory since there is no evidence of adverse effects when the level of the monitoring environment is held below the legal threshold values. It is still very few reliable details exist in this systematic analysis and may involve reviewing and revising surveillance guidelines and procedures for exposed employees. No clinical signs or biomarkers have been established as appropriate for the use of exposed workers in surveillance.

A systematic review containing seventeen studies on the impact of sevoflurane was conducted by Molina Aragonés *et al.*, 2016 to address their concern about the effect of occupational exposure to volatile anaesthetics and the best of health monitoring for exposed staff?' They found that sevoflurane exposure, depend on the dose, can adversely affect the liver and kidney. Some authors said that sevoflurane can make a DNA damage when the sevoflurane exposure in workplace above 4 ppm and no impact of DNA when the sevoflurane exposure under 0,5 ppm. They believe if the air monitoring level under of 2 ppm would be the safety workplace. The effect of the currently used volatile anaesthetic on the population exposed has been routinely studied and very few reliable data have been collected. Therefore, review surveillance guidelines and procedures for exposed employees is unclear. No clinical sign or biomarker has been established as appropriate for use in surveillance in exposed staff (Molina Aragonés *et al.*, 2016).

The other research involved anaesthesiologists in 52 operating room workers who had been randomly chosen for at least one year of exposure as a case group and fifty two administrative staff as a control group. The measure of outcome was concentrations of nitrous oxide, isoflurane, and sevoflurane in urine sampling that had taken in morning shift/ at least three hours of exposure in operating room. Liver and kidney function are calculated by mean levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, alpha-glutathione-s-transferase, and serum levels of kidney injury molecules-1, creatinine, and calcium (Neghab *et al.*, 2020).

In the result of this study showed that the non exposed group have lower risk

than the exposed group in aspartate aminotransferase (p value 0.04), alanine aminotransferase (p value 0.01), gamma glutamyl transferase (p value 0,003), alpha glutathione s-transferase (p value 0.04), serum creatinine (p value 0.03), kidney injury molecule (p value 0.003),calcium (p value <0.001) (Neghab *et al.*, 2020) .

Table 3. Critical appraisal observational study

Articles	study design	Number of subject	Randomiza	Similiarity treatment	Blinding	Domain	Deteminan	Measurement of outcome	Result	Level of evidence
Toxic Responses Of The Liver And Kidneys Following Occupational Exposure To Anesthetic Gases	case contrl ol	52 exposed and 52 unexposed group	Yes	Yes	Unclear	Population at risk in exposed group (operating room personnel)	yes, as in practice (exposure/ risk factor)	Yes, urinary and blood sampleuse the same equipment	Exposed group have a higher risk to renal and liver function than unexposed group	3 b
Biomonitoring occupational sevoflurane exposure at low levels by urinary	Observational study	Individual sevoflurane exposure	Unclear	Yes	Unclear	Population at risk	Yes, as in practice (exposure/	Yes, the passive air sampling device Radiello, and assaying Sev-	In this research, the exposure biomarker (urinary sevoflurane and hexafluoroisopropanol)	3 b
Articles	Study design	Number of subject	Randomiza	Similiarity treatment	Blinding	Domain	Deteminan	Measurement of outcome	Result	Level of evidence
sevoflurane and hexafluoroisopropanol		r was measued in 100 health care operators					risk factor	U and HFIP concentrations. The environmental levels of sevoflurane in workplace	used to assess occupational exposure to sevoflurane has been found to	

		(physicians, anaesthetists, instrumentalists and nurses) at five hospitals						were also tracked	correspond with the anaesthetic levels measured in the air.	
Urinary sevoflurane and hexafluoro-isopropanol as biomarkers of low-level occupational exposure to sevoflurane	Observational study	A group of 36 subjects (13 male, 23 female) occupationally exposed to volatile anaesthetics in paediatric operating	unclear	yes	unclear	Population at risk	Yes, as in practice (exposure/risk factor)	Yes, Individual passive sampler cartridges and urinary morning post-shift urine samples were collected . GC-MS method is used to quantitate environmental sevoflurane, urinary sevoflurane and total urinary HFIP. Breathing	Correlation between breathing area sevoflurane and total urinary HFIP with r=0,749 p value <0.0005 ; correlation between breathing area sevoflurane and urinary sevoflurane with r =0.835 p value p<0.0005	3 b
Articles	Study design	Number of subject	Randomiza	Similiarity treatment	Blinding	Domain	Deteminan	Measurement of ourcome	Result	Level of evidence
		rooms was studied in a 2-week survey						zone sevoflurane. Levels of concentration were expressed in parts per million, and		

			analyte urine concentrations were expressed in micrograms per liter of urine and in milligrams per liter of urine (for sevoflurane and HFIP)

In order to evaluate and analyze the best biomarker of exposure to sevoflurane, Maria et al have examined the relationship of sevoflurane levels with urinary concentration or hexafluoroisopropanol (HFIP) with the corresponding biological equivalent exposure limit values. The measure applied to 100 healthcare in operating room in five hospitals in north-eastern Italy who were exposed to sevoflurane by passive air sampling in breathing zone personnel and by assessing the levels of Sev-U (sevoflurane-urine) and HFIP in urine sampling obtained at the end of shift work in operating room (Scapellato *et al.*, 2014).

Gas chromatography-mass spectrometry was used for their research. They reported very low levels in personal exposure, typically under 0.5 ppm (mean 0.116 ppm; range 0.007–0.940 ppm), as a result. The concentrations of sevoflurane (Sev-U) and HFIP from urine sampling were between 0.1-17.28 mg/L and 5-550 mg/L, respectively. There was a statistically important association between the two biomarkers and workplace exposure levels (Sev-U, r=0.49; HFIP, r=0.52), but there was an abnormal distribution of value. Sevoflurane in urine (Sev-U values) appears to be affected at the end of the shift as a peak value of exposure, while HFIP on the day before. In conclusion, both Sev-U and HFIP are suitable biomarkers to determine the exposure of sevoflurane in this analysis (Scapellato *et al.*, 2014).

Antonio et al studied in 36 subjects (13 male, 23 female) occupationally exposed to volatile anaesthetics in paediatric operating rooms in a 2-week survey. The objective of the study is to quantify environmental sevoflurane, urinary sevoflurane and total urinary HFIP, using a previously mentioned GC-MS technique such as Maria et al (Accorsi *et al.*, 2005).

Table 3. Critical appraisal for case studies

Appraisal questions	Answer
Does the research answer the problem clearly?	Yes. Responding to anesthetic gas exposure as a potential risk of Parkinson's Disease (PD)
Is the study design appropriate for answering research questions??	Yes. The results of hexafluoroisopropanol was 483.4 μg/liter (over the 465 μg/liter threshold) in May 2007 and 535.6 μg/liter on next week.

Are the background and subject criteria related to the population to be referenced?	Yes, The subject has worked as a anesthesiologist for 30 years, exposing nitrous oxide for 22 years and sevoflurane for 23 years.
Is the researcher's perspective clearly explained??	Yes. Differential diagnosis is also considered. Sevoflurane has been shown to increase TNF-alpha and beta-amyloid development by activating caspases and apoptotic cascades, which are the key characteristics of PD that activation of caspases and apoptotic cascade
Is the data collection method clear??	Unclear Beginning with the individual evaluation (clinical, laboratory and electrophysiology) and the workplace obtained by individual samples of anesthetist in general hospitals in Veneto from 1990 to 1999.
Do the methods for analyzing data have good validity and are reliable? Are there any quality control measures??	unclear. The excessive exposure to the subject's anesthetic gases may have exacerbated parkinson's disease, given the limited evidence from human studies and sufficient evidence from laboratory studies.
Was the analysis repeated by more than one researcher to ensure reliability?	Unclear. The research was carried out by a team. No repeat and no repetition
Are the results credible, and if so, are they relevant to the practitioner?	Unclear Due to insufficient data from human studies
Are the conclusions drawn justified by the results?	Yes. To the results, the conclusion was appropriate .
Can the study findings be used in different practitioners?	Yes, at least for the personnel in the operating room

Sevoflurane concentration levels in the breathing zone were expressed in ppm and analyte urine concentrations were expressed in mcg dan mg per litre of urine (sevoflurane and HFIP). There was a correlation between sevoflurane breathing area and total urinary HFIP with a p-value of r=0.749 <0.0005; correlation between sevoflurane breathing area and urinary sevoflurane with a p-value of r=0.835 p<0.00055 (Accorsi *et al.*, 2005).

A case was underwent by an anaesthesiologist, 59 years old, and 23 years exposed to sevoflurane. The absence of family history of Parkinson's disease or tremors, mood disorders, a bronchial asthma and high blood pressure (use drug like beta blocker or calcium channel blocker) are not likely to lead to a non-occupational disease. There is no history of chemicals, rural living or use of water contaminated with pesticides. The patient is a smoker and a moderate drinker, but in theory that practices protect him from the disease of Parkinson (Mastrangelo *et al.*, 2013).

This case report want to know about how an anesthetic gasses are relatively

rarely associated with Parkinson's disease in several epidemiological studies. However, exposure in workplace to inhaled gases (nitrous oxide, halothane, isoflurane, levoflurane) with the risk of Parkinson's disease have been related by a number of recent mechanistic studies. It confirmed the assumption of an association between anaesthetic gas exposure and Parkinson's disease risk with a little evidence (Mastrangelo *et al.*, 2013).

DISCUSSION

Sevoflurane is the first choice of inhaled gases for general anaesthesia because it has a more rapid of induction, lower effect of airway irritation, respiratory depression, and arrhythmia potential than the other anaesthetic gases. Sevoflurane is often combined with other anesthetic gases for example nitrous oxide for analgesic effects and desflurane for maintenance of anesthesia. According to some literature, health effect of sevoflurane can be a nephrotoxin and hepatotoxicity because of chronic exposure in occupational health. The neurotoxicity of sevoflurane is unclear because there have not a specific effect of sevoflurane exposure but some researcher believe that sevoflurane has be a trigger effect to β accumulation like in Alzheimer's disease. In the case study, Parkinson's disease as multifactorial causes have a limited correlation with sevoflurane exposure since the level of HFIP above a normal reference. It remains unclear because limited evidence said that sevoflurane triggers a Parkinson's disease directly, especially in epidemiology study (Mastrangelo *et al.*, 2013).

Sevoflurane will be around 2-5 percent metabolism to a metabolite, fluoroacetic acid in the liver by a particular enzyme of cytochrome P450 (2E1). This particular metabolite has been discovered to alter microsomal liver proteins. subsequently function as hapten, activating antigens for an immune-mediated antibody response. With acyl halides attached to liver proteins, the antibody will react to hapten. In several case, like paediatric anaesthesiologists who were regularly exposed to halothane, the same autoantibodies were identified, indicating that these CYP2E1 antibodies do not have a pathogenic function. Although this response was unusual due to the low percentage of metabolized sevoflurane, but it still has health effect risk (Edgington, Muco and Maani, 2007; Hemmings and Egan, 2019).

Waste anaesthetic gases can cause health effect in anaesthesiologists that have chronic exposure, such as DNA damage and increased micronucleus. In addition, oxidative stress is often correlated with anaesthetic gas waste since it causes lipid peroxidation, DNA oxidative damage, and antioxidant protection system damage in such a way that genotoxicity and mutagenicity in anaesthesiologists. However, low occupational exposure to sevoflurane did not show a major impact on the peripheral blood lymphocytes of operating room workers, but further research in the long-term are warranted (Lucio *et al.*, 2018; zhimin ji *et al.*, 2020). long term exposed inhaled anaesthesia (Türkan, Aydin and Sayal, 2005).

Formation of free radicals was one of the effects induced by long-term exposure to sevoflurane. It is necessary to preserve antioxidants by taking antioxidant supplements in order to resolve this problem. Pathogenic processes associated with cancer, degeneration disease, cardiovascular disease, which are the responsibility of free radicals, must also be prevented and may boost the immune function of anaesthesia workers who are

Sevoflurane induced apoptosis and elevated levels of the level-site amyloid precursor protein-cleaving enzyme and Aβ. In exchange, Sevoflurane stimulated caspase, which raised the levels of amyloid precursor protein and Aβ at the enzyme breakdown site. Further apoptosis is caused by the rise in Aβ levels (Dong *et al.*, 2009).

Minor injury is characterized by a small increase in aminotransferase serum activity, while fulminant hepatic failure is associated with a substantial increase in liver enzyme activity and bilirubin levels, resulting in extreme liver necrosis. The study showed that some liver function biomarkers in the non-exposed group were lower than in the exposed group, especially aspartateaminotransferase, alanine aminotransferase, and gamma glutathione S transferase (Neghab *et al.*, 2020).

There are two suspected mechanisms for the potential nephrotoxic activity of sevoflurane. The metabolite, fluoroacetic acid, which has shown nephrotoxicity as well as hepatotoxicity, is the first element. The second is compound A's formation. Compound A is another fluorinated substance formed by an exothermic reaction between the absorbents of sevoflurane and carbon dioxide used in anesthetic delivery systems, which in animal studies can reportedly trigger mild and reversible injury. The theoretical risk of nephrotoxicity caused by compound A in humans can be time-dependent on dosage and exposure (Edgington, Muco and Maani, 2007).

Compound A (fluoromethyl-2,2-difluoro-1-[trifluoromethyl] vinyl ether) is the result of the metabolism of sevoflurane, formed by its interaction with carbon monoxide absorbents. The mechanism leading to renal toxicity is still debated, with the renal cysteine conjugate β-lyase pathway (involved in compound A biotransformation). Human beings may be less prone to compound A renal toxicity than rats if this pathway is responsible. Human studies have shown that long exposures (8 hours) to sevoflurane and low fresh gas flow rates can lead to substantial output of compound A. A low risk of biochemical changes in kidney injury occurs when the flow is low from sevoflurane administration (Hemmings and Egan, 2018).

As far as their demographic characteristics concerned, no major variations between the revealed and referent subjects were noted. Furthermore, none of the studied subjects had a history of hepatotoxic and/or nephrotoxic that caused by material exposure. The result was that the biomarker of renal function in the exposed group was significantly different from the non-exposed group, particularly in the serum creatinine, kidney injury molecule-1, and calcium (Neghab *et al.*, 2020).

Recommended exposure limit values of 2 ppm have been recommended by NIOSH for all halogenated agents, including sevoflurane and 25 ppm for nitrous oxide. While biological exposure indices levels were not calculated for these anaesthetic gases by ACGIH and 3.6 μg/l for sevoflurane, respectively, based on the NIOSH exposure limit of 2 ppm (Hoerauf *et al.*, 1996, 1999; Neghab *et al.*, 2020).

The degree of exposure to sevoflurane depends on a variety of parameters, including the absence or existence of sufficient ventilation and scavenging systems in the operating room, the form of operation, the extent of anaesthesia face mask leaks during anaesthetic gas administration, cylindrical leakage, whether gas leakage from the anaesthetic machine is regularly verified or not. In this case, dangerous working practices such as triggering the flow of anaesthetic gas before applying a mask to the patient's face or closing the flow of anaesthetic gas after removing a face mask and improperly fitting face masks also play an important role (Neghab *et al.*, 2020).

Accorsi *et al.*, 2005 examined operating room workers post-shift urine by gas chromatography-mass spectrometry coupled. Subjects' levels of urinary anaesthetic gases ranged from 0.4 to 1415.9 μg/l for nitrous oxide, 0.0 to 36 μg/l for isoflurane, and 0.0 to 46 μg/l for sevoflurane. Similarly, the concentration of anaesthetic gases in the urine of forty workers was measured by Al-Ghanem et al. The mean urinary concentrations of nitrous oxide, isoflurane and sevoflurane were

respectively 1234, 3.75 and 4.3 μg/l (Hoerauf *et al.*, 1999).

At the beginning of an operating room shift or a work shift, operating room personnel exposed to sevoflurane during the previous work day had accumulated high HFIP values in their urine, indicating that 24 hours was not sufficient for HFIP elimination. As for Sev-U, our findings indicate that peaks of exposure in the end operating room session is especially influenced by this biomarker (2.8 h). The study showed there were a statistically significant correlation between sevoflurane urine and HFIP. The variation factor can be influenced by the biological factors, which tends to be greater even at minimal exposure (with sevoflurane exposure under 1 ppm), as well as by the presence of a group of subjects with low Sev-U but relatively high HFIP levels, presumably as exposure from the day before due exposure from the previous day (Scapellato *et al.*, 2014).

Based on the results of this analysis, the measured urinary biomarker concentrations according to the workplace exposure in 2 and 0.5 ppm were 318 and 131 mg/L for metabolite of sevoflurane (lower 95 % CL: 133 and 72 mg/L respectively) and 3.7 and 2.1 mg/L for sevoflurane urine (lower 95 % CL: 2.0 and 1.4 mg/L respectively). The biological equivalent concentrations of Imbriani et al for urinary HFIP were 488 and 160 mg/L, according to safe value of NIOSH exposure for airborne sevoflurane of 2 and 0.5 ppm, which some researchers proposed as a particular measure of occupational exposure to sevoflurane. Different HFIP values of 800 mg/L and 2772.7 mg/L for exposure to sevoflurane at 2 ppm. At the end of the operating session, the other study had substantial peak levels of sevoflurane exposure; the values were slightly lower (1.9 and 1.3 mg/L for 2 and 0.5 ppm environmental sevoflurane exposure, respectively) (Scapellato *et al.*, 2014).

Sevoflurane exposure to HFIP was more stable, with a longer half-life than the urinary sevoflurane biomarker (2.8 and 19 hours, respectively, for sevoflurane and HFIP). However, this value indicates several factors that can affect sevoflurane metabolism such as smoking, alcohol consumption and genetic metabolic polymorphisms. HFIP is produced from the metabolism of the CYP2E1 enzyme, where its function can be established by smoking and alcohol habits (Scapellato *et al.*, 2014).

In addition to monitoring, according to a study conducted by Jenifer et al., environmental monitoring with multi-capillary column-ion mobility spectrometry (MCC-IMS) method is also needed. There was a higher risk of turbulent flow compared to laminar flow in the operating room (Herzog-Niescery *et al.*, 2015; Kunze *et al.*, 2015; Neisi *et al.*, 2019).

Due to the hazards posed by sevoflurane, it is possible to undertake a risk assessment, thus possible threats to health conditions can be anticipated. Exposure to anaesthetic gases in the workplace damage operating room personnel. Health care and environmental control, such as anaesthesia equipment maintenance, breathing system efficacy and anaesthetic gas removal procedures, and regular staff training are also highly recommended (Dehghani *et al.*, 2020).

In order to develop an effective workplace, monitoring of occupational hazards for anaesthetists who are exposed on a daily basis is important to minimizes risks and generates a successful anaesthesiology practice. This will result in less absenteeism, better patient care, and better improvement of the anaesthesiologist's quality of life (Hoerauf *et al.*, 1999; Volquind *et al.*, 2013).

CONCLUSION

Sevoflurane is an inhalational anaesthetic agent that is used to induce and maintain the patient under anaesthesia during surgery. Health effects of sevoflurane as hepatotoxic, nephrotoxic and neurotoxic in the human body pose as a

health risk for anaesthesiologist. We need to environmental and biological monitoring to create a safe and healthy workplace. We need more data to discover about a specific monitoring to supervise each anaesthesiologist that has sevoflurane exposure.

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