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Article Review

Risk Factor Analysis of the Incidence of Hepatitis A in Indonesia: A Meta-Analysis

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ABSTRACT

Hepatitis transmission is still a global public health issue, including in Indonesia. Low personal hygiene and environmental sanitation are the contributing factors to hepatitis A. This study aimed to analyze the impact of hand-washing habits, cutlery exchange, food and snack hygiene, and latrine use on the incidence of Hepatitis A. The study used meta-analysis with the PICOS technique. The data from Google Scholar, Mendeley, and Research Gate by looking at keywords such as "risk factors" and "hepatitis A", which were then sorted according to the inclusion-exclusion criteria and obtained 16 full-text case-control articles. Data analysis used a fixed effect model through JASP software version 0.9.2. The meta-analysis found that hand-washing behavior had a risk of 1.131; food and snack hygiene had a risk of 6.233; the habit of exchanging cutlery had a risk of 10.17; and latrine utilization had the highest risk of 12.935 for the incidence of hepatitis A. The study found that the use of latrines is the most significant factor in the occurrence of hepatitis A due to open defecation. Furthermore, exchanging cutleries is rated as the second factor triggering hepatitis A transmission, followed by the consumption of snacks or other foods. The study also found that hand-washing behavior has the lowest risk of hepatitis A incidence. The study concludes that hand-washing behavior, latrine utilization, food and snack hygiene, and exchanges of cutlery increase the risk of hepatitis A at different levels. It is suggested that behavioral factors such as hand washing, the use of closed latrines, and the consumption of healthy snacks or foods are essential measures to educate the community about hepatitis A and reduce its transmission within the population.

Keywords: *Hepatitis A, Hand-washing, Food Hygiene, Exchanging Cutlery, Latrine Utilization*

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INTRODUCTION

Hepatitis is a public health problem worldwide, including in Indonesia. Five hepatitis viruses contribute to hepatitis cases, including Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis D virus (HDV), and Hepatitis E virus (HEV). All hepatitis viruses can cause acute hepatitis. Among the several types of hepatitis diseases, Hepatitis A often appears as an extraordinary event. This disease is closely related to environmental sanitation conditions, food hygiene and sanitation, and clean and healthy living behaviors that are not optimal, so Indonesians are at risk for contracting Hepatitis A and Hepatitis E[1,2,3].

World Health Organization (WHO) reported that 7.134 people died from Hepatitis A worldwide (accounting for 0.5% of deaths from viral hepatitis) in 2016[1]. Basic Health Research (Riset Kesehatan Dasar/Riskesdas) data in 2018 showed that 0.39% of the Indonesian population had hepatitis. The figure is a three-fold decrease compared to 2013 (1.2%)[4]. Despite the national decline, Hepatitis

A outbreaks occur in several regions. Ministry of Health of the Republic of Indonesia stated that Hepatitis A outbreaks had occurred throughout 2013 in East Java Province, in 6 districts, including Jombang, Lamongan, Pacitan, Sidoarjo, Ponorogo, and Pasuruan, with a total of 462 cases[3]. In 2014, it occurred in three districts, including Sidoarjo, Kediri, and Surabaya, with 59 cases[3]. The Hepatitis A outbreak in 2015 happened again in 3 districts, including Probolinggo, Lamongan, and Jember, with a total of 78 cases[5]. In 2019, Ministry of Health of the Republic of Indonesia reported a Hepatitis A outbreak in Pacitan District with a total of 957 cases[6].

Previous studies identified several things related to the incidence of hepatitis, especially extraordinary events (outbreaks) in specific communities and community groups, including boarding schools, dormitories, schools, and company employees, with a typical source pattern. Hepatitis A outbreaks often have an epidemic cycle of 5-10 years which usually occurs during the rainy season with an outbreak period lasting about 1-2 months[3]. The virus can be spread through food or drink contaminated with faecal-oral human faeces. One of the factors causing Hepatitis A is contaminated water sources, as happened in Pacitan in 2019. The outbreak occurred due to Hepatitis A virus contamination that may have originated from domestic waste in the Kaligoro River water in Sukorejo village. The river is the primary source of spring water for residents. The other contributing factors are poor environmental sanitation, including eating in unclean public spaces, sharing food on one plate, a cutlery exchange, and handling foods without washing hands[6–8].

When an HAV infection occurs, the patient will experience an incubation period of 18-50 days, with an average of 28 days. Symptoms include nausea, vomiting, decreased appetite, fever (temperature more than 390 Celsius), and discoloration of the skin; nails; and eyes to yellow, and yellow-brown urine due to bilirubin precipitation. Laboratory results show elevated Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT). Most acute hepatitis infections cause mild illness and even go undetected. However, in some cases, they can lead to complications and fatalities known as fulminant hepatitis A[6,8,9].

The first global health sector strategy in May 2016, the World Health Assembly (WHA) endorsed the Global Health Sector Strategy (GHSS) for viral hepatitis 2016-2021. The strategy proposes the elimination of viral hepatitis as a public health threat by 2030 through a 90% reduction in new chronic infections and a 65% reduction in deaths, compared to the 2015 baseline. WHO also sets out a roadmap towards elimination by implementing key prevention, diagnosis, treatment, and community intervention strategies. WHO supports its members to achieve global hepatitis goals through awareness raising, partnership promotion, resource mobilization, policy formulation, evidence-based data for action, improved health equity in hepatitis response, prevention of transmission, improved screening services, and care and treatment[1]. The Government of Indonesia through the Regulation of the Ministry of Health of the Republic of Indonesia No. 1501/ Menkes/Per/X/2010 on Certain Types of Infectious Diseases that Can Lead to Outbreaks and Their Management Efforts, and the Regulation of Ministry of Health of the Republic of Indonesia No. 53/2015 on Hepatitis Management. Those regulations stated that Hepatitis A outbreak/outbreak management can be carried out in five ways, namely 1) epidemiological investigation and surveillance, 2) management of patients in health facilities (case finding, examination, treatment, and care), 3) prevention and immunity (through vaccination), 4) destruction of the cause of the disease (through the provision of chlorine for clean water management; hand washing using soap; proper food processing; storing food at safe and appropriate temperatures; and using clean water), and 5) public education through health promotion[10,11].

This study aims to analyse the risk factors of handwashing habits, cutlery exchange, food and snack hygiene, and latrine utilization on the incidence of Hepatitis A in Indonesian communities.

METHODS

The study used meta-analysis with the PICOS technique, which combines several similar research results to obtain a blend of quantitative data with the same hypothesis to conclude by finding the effect size or summary value.[12] This research uses secondary data from

several electronic databases. The databases used are Google Scholar, Mendeley, and Research Gate (2012-2022). The keywords used in the search were "risk factors", and "Hepatitis A". The population of this study is sixty-seven international and national research articles with topics that match the research objectives. Fifty-seven articles was screening based on abstract review, then the full article was selected, and the exclusion of articles without full text. The next stage of the article was filtered again based on case-control research study designs. Forty-two journal articles were selected that examined the risk factors of hand washing habits, cutlery exchange, food and snack hygiene, latrine utilization, personal hygiene, and sanitation on the incidence of Hepatitis A in the Indonesian community. Finally, sixteen studies were selected that obtained a 2 x 2 table between exposure and outcome, discussed risk factor of Hepatitis A in Indonesia, and the number of articles in each variables was at least 6. The following is a PRISMA flowchart from this study.

The dependent variable was the incidence of Hepatitis A in Indonesia, while four risk factor includes handwashing habits; food and snack hygiene; cutlery exchange; and latrine utilization were independent variables. The process of doing a meta-analysis typically contains some parts, the first of which is formulating the study topic. The analysis was conducted to obtain the pooled odds ratio estimate value using the Mentel - Haenszel method for the fixed effect model analysis and the DerSimonian-Laind method for the random effect model analysis. If the variation between variables is homogeneous or the heterogeneity p-value is greater than 0.05, the analysis model used is the fixed effect model. Meanwhile, the random effect model analysis model is used if the variation between variables is heterogeneous or the heterogeneous p-value is smaller than 0.05. If the OR estimate value > 1 and the confidence interval range does not exceed 1, so the risk factors were hand washing habits, exchanging cutlery, food or snack hygiene, and latrine utilization on the incidence of Hepatitis A in Indonesian people. The following steps were literature gathering based on the planned objectives and evaluation.

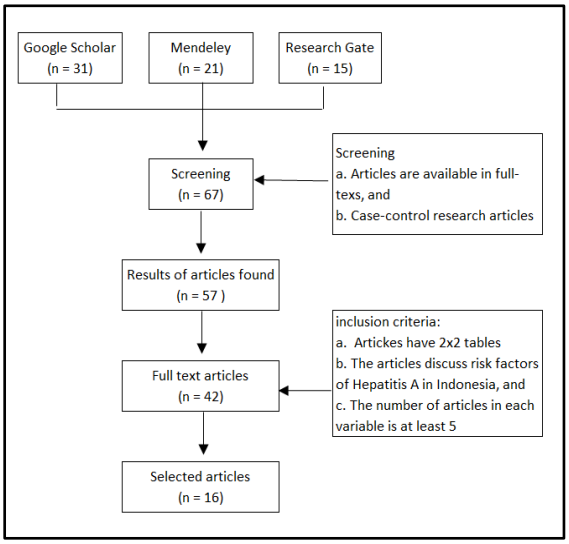
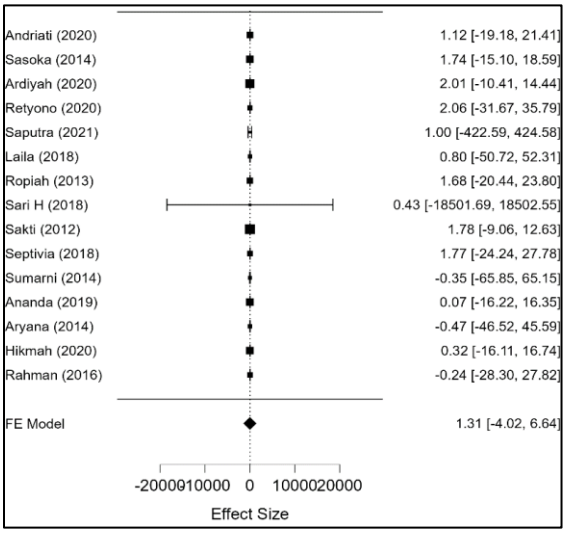
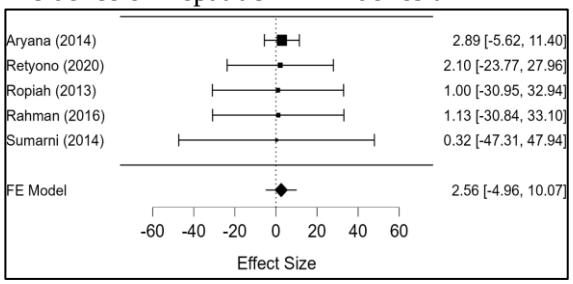


Figure 1. PRISMA Flowchart of Risk Factors of Hand-washing Habits, Cutlery Exchange, Food and Snack Hygiene, and Latrine Utilization on the Incidence of Hepatitis A in Indonesian communities.

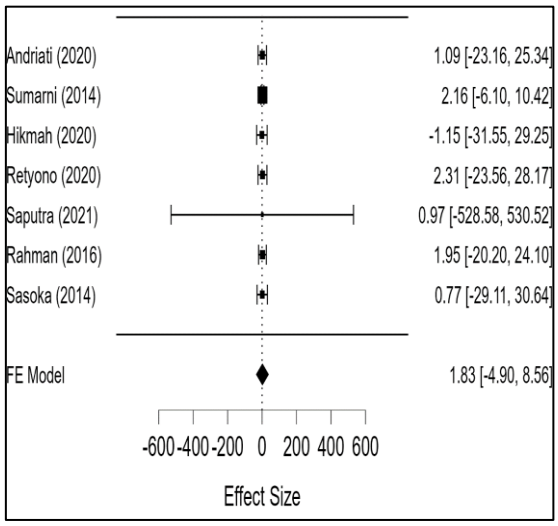
RESULTS



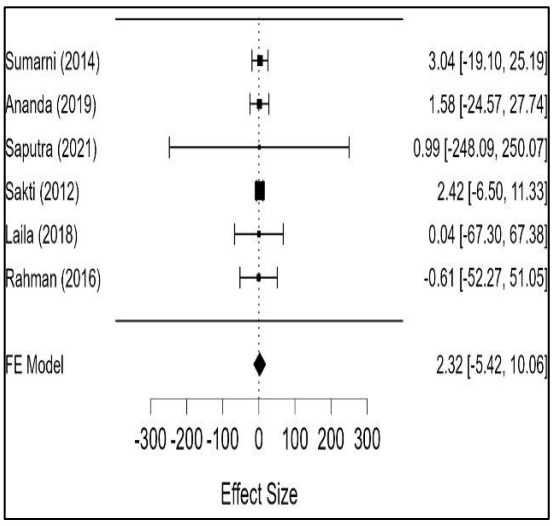
Risk Factors for Hand-washing Behavior on the Incidence of Hepatitis A in Indonesia



Risk Factors of Latrine Utilisation on the Incidence of Hepatitis A



Risk Factors for Food and Snack Hygiene on the Incidence of Hepatitis A in Indonesia



Risk Factors for the Habit of Exchanging Cutlery for the Incidence of Hepatitis A in Indonesia

Figure 2. Forrest Plot of Risk Factors of Hand-washing Habits, Food and Snack Hygiene, Cutlery Exchange, and Latrine Utilization on the Incidence of Hepatitis A in Indonesian communities

The Fixed Effect (FE) Model value of the Forrest plot on the hand-washing behavior represents the Odds Ratio (OR) estimate value showing a 95% CI of 1.31 with a range value of -4.02 - 6.64. The results of the forest plot in Figure 2 show that the pooled OR = $e^{1.31}$ = 3.706. So it can be concluded that personal hand-washing behavior has a 3.706 times greater risk of making Hepatitis A incident.

The Fixed Effect (FE) Model value of the Forrest plot on food and snack hygiene shows the estimated Odds Ratio (OR) with a 95% CI of 1.83. From the forest plot Figure 4. pooled OR value = $e^{1.83}$ = 6.233 (95% CI -4.90 - 8.56). It concludes that the food and snack hygiene variable has a 6.233 times greater risk of causing Hepatitis A incidents.

The Fixed Effect (FE) Model value of the Forrest plot on exchanging cutlery has an OR estimate with a 95% CI value of 2.32. Forest plot Figure 5. has a pooled OR value = $e^{2.32}$ = 10.175. The Habit of exchanging cutlery variable has a 10.175 times greater risk of experiencing the incidence of Hepatitis A. The confidence level of FE is 95% and has an interval range of -5.42 - 10.06.

The Fixed Effect (FE) Model value of the Forrest plot on use of latrines has an estimated OR 95% CI value of 2.56 with an interval range of -4.96 - 10.07. The results of the Forest Plot Figure 5. obtained a pooled OR value = $e^{2.56}$ = 12.935. It concludes that the use of latrines has a 12.935 times greater risk of experiencing Hepatitis A. This factor is most affected for Hepatitis A incidence in Indonesia.

Table 1. Heterogeneity Test of Meta-Analysis of Individual Hand-washing Behaviour, Food and Snack Hygiene, Exchanging Cutlery, and Latrine Utilisation on Hepatitis A Incidence

Varibales Independent	**Hand-washing Behaviour**			**Food and Snack Hygiene**			**Exchanging Cutlery**			**Latrine Utilisation**		
Fixed and Random Effects	**Q**	**df**	**p**	**Q**	**df**	**p**	**Q**	**df**	**p**	**Q**	**df**	**p**
Omnibus test of Model Coefficients	0.232	1	0.630	0.285	1	0.593	0.345	1	0.557	0.445	1	0.505
Test of Residual Heterogeneity	0.084	14	1.000	0.053	6	1.000	0.024	5	1.000	0.032	4	1.000

Table 1 shows that the p-value in the heterogeneity test of all factors (includes hand-

washing behaviour, food and snack hygiene, exchanging cutlery, and latrine utilisation) are greater than α (0.05), namely p = 1.000, which means that the variation between studies is homogeneous, so in this analysis, all variables is using the fixed effect method.

Table 2. Egger's Test of Risk Factors for Individual Han-dwashing Behaviour Food and Snack Hygiene, Cutlery Exchange, and Latrine Utilization on the Incidence of Hepatitis A in Indonesian communities

Regression test for Funnel plot asymmetry ("Egger's test")								
	Hand-washing Behaviour		**Food and Snack Hygiene**		**Cutlery Exchange**		**Latrine Utilisation**	
	z	p	z	p	z	p	z	p
sei	-0.088	0.930	-0.128	0.898	-0.095	0.924	-0.176	0.860

Based on Table 2, it is known that the p-value of Egger's Test of all vaiables > α (0.05). The variable hand-washing behaviour, food and snack hygiene, exchanging cutlery, and latrine utilisation on the incidence of Hepatitis A did not have publication bias.

Table 3. Results of Meta-Analysis of Individual Hand-washing Behaviour, Foodand Snack Hygiene, Cutlery Exchange, and Latrine Utilisation on the Incidence of Hepatitis A

No	**Variables**	**N**	***Fixed/Randomeffect Models***	
			OR	**95% CI**
1.	Hand-washing behavior	15	1,131	-4,02 – 6,64
2.	Food and Snack Hygiene	7	6,233	-4,90 – 8,56
3.	Cutlery Exchange	6	10,175	-5,42 – 10,06
4.	Latrine Utilisation	5	12,935	4,96 - 10,07

Based on the results of Table 6. which has the highest risk factor is the latrine utilization variable with a pooled OR value = e2.56 = 12.935 (95% CI 4.96 - 10.07), so it can be concluded that latrine utilization has a 12.935 times greater risk of experiencing Hepatitis A. Furthermore, the habit of exchanging cutlery variable with a risk of 10.175 times, and the food/snack hygiene variable with a risk of 6.233 times. The lowest risk factor was found in the individual handwashing/hygiene behavior variable, with a pooled OR = e1.31 = 1.131 (95% CI -4.02 - 6.64), so that poor individual handwashing/hygiene behavior has a 1.131 times greater risk of experiencing hepatitis A.

Table 4. Sensitivity Test Comparison of Pooled Odds Ratio Fixed Model and Random Model

Variables	**N**	***Hetero entity (p-value)***	***Fixed effect Models***		***Random Effect Model***	
			OR	**95% CI**	**OR**	**95% CI**
Risk Factors of Hand-washing Behaviour	15	1.000	1,131	-4,02 – 6,64	1,131	-4,02 – 6,64
Risk Factors of Food and Snack Hygiene	7	1.000	6,233	-4,90 – 8,56	6,233	-4,90 – 8,56
Risk Factors of Cutlery Exchange	6	1.000	10,175	-5,42 – 10,06	10,175	-5,42 – 10,06
Risk Factors of Latrine Utilisation	5	1.000	12,935	4,96 - 10,07	12,935	4,96 - 10,07

The four independent variables, there is no variation between studies, with no visible increase in the pooled OR value from the fixed effect model to the random effect model.

DISCUSSION

The results of the meta-analysis showed that the Hand-washing Behaviour variable had

a 3.706 times greater risk of experiencing the incidence of Hepatitis A in Indonesian society. Previous study claimed the risk ratio of Hepatitis A due to the habit of not washing hands before eating properly (using soap) is 2.19 (95%CI=1.32-3.65; p = 0.000), meaning that exposure to improper hand washing before eating will increase the risk of hepatitis incidence ($p < 0.05$)[13].

Proper handwashing before eating has a significant correlation with the incidence of hepatitis. A history of close contact with HAV-infected people allows for the transmission of Hepatitis A because the Hepatitis A virus can survive for several hours on fingertips and hands for up to two months on dry surfaces[8]. As a result, if a person has been in close contact with an infected person, transmission can occur directly through handshakes or indirectly through contaminated objects that are touched or shared. The unclean and unhealthy living behavior, before and after eating or defecating without washing hands with soap. The habit of washing hands with soap, especially before eating, and in several other conditions such as after defecating, after using the toilet, after touching garbage, and others, must become an internalized behavior in each individual as an effort to prevent disease, especially the category of fecal-oral infectious diseases[3,14].

Currently, the Indonesian government is intensively socializing Community-Based Total Sanitation (Sanitasi Total Berbasis Masyarakat/STBM), an approach to change hygiene and sanitation behavior through community empowerment with triggering methods. Hand-washing with soap is one of the STBM programs at the community level to promote hygiene (Cuci Tangan Pakai Sabun/CTPS)[3,15]. This program is expected to increase the achievement of CPTS, which is currently still low. The results of a survey of CTPS behavior in Indonesia on five critical CTPS times showed very low results, namely 12% after going to the toilet, 9% after washing children, 14% before eating, 7% before feeding children, and only 6% before preparing food[15].

The results showed that the incidence of Hepatitis A due to non-fulfillment of food hygiene or snacks consumed was 6.233 times greater. Previous research also concluded the same thing, namely, the serving of food in school canteens that did not meet the hygiene and sanitation of food/snacks triggered the outbreak of hepatitis in the school[16].

The results of a study of Food Service Companies in Central Kalimantan in 2016 showed that the level of fulfillment of sanitary hygiene principles in food management in the A2, A3, and B food service industries falls in the sufficient category. The food storage stage in the A2 food service industry and the food processing stage in the A2, A3, and B food service industries had a level of fulfillment of sanitary hygiene principles that was still lacking, so it needed to be further improved[17]. These conditions will contribute to states that do not maintain the cleanliness of food or beverages from possible biological, chemical, and other objects that can interfere with, harm, and endanger human health.[18] Other risk factors include the low quality of environmental sanitation, especially in the dining area. Hence, the risk of transmission of Hepatitis A and other diseases, such as E.Coli which causes diarrhea, is also higher[2,6,8].

Food sanitation efforts are needed to create and maintain healthy and hygienic food conditions free from the dangers of biological, chemical, and other objects as stipulated in Indonesian Law No. 18/2012.[18] These efforts must be carried out in a series of stages, starting from the selection and storage of food ingredients, food processing, cooking food, and transporting food to the final stage, namely serving food[19].

The meta-analyzes also show the risk of hepatitis A transmission through cutlery exchange. This habit has a 6.233 times greater risk of experiencing Hepatitis A in Indonesian people. Previous studies claimed that exchanging or using cutlery together has a 2.09 times increased risk of Hepatitis A transmission in Indonesian society (CI = 1.26-3.48; p = 0.00)[13].

Hepatitis transmission is very likely to occur indirectly through HAV-contaminated cutlery used together (exchanging cutlery). The Hepatitis A virus is relatively stable and can survive for up to two months on dry surfaces[20]. Eating and drinking utensils contaminated with the Hepatitis A virus, from the virus attached to the hands and fingers of sufferers and then shared with others, can be a medium for the transmission of Hepatitis A disease.

Education to the public regarding personal eating utensils needs to be carried out continuously, including introducing the habit of bringing eating utensils (spoons-forks) when traveling or consuming food outside the

home/public eating places/stalls. In this risk factor, it is also necessary to pay attention to the personal hygiene of food handlers in restaurants/stalls/restaurants, school canteens/offices, and food/snack sellers when working/touching the tools used when making / processing and serving food. The survey of handswashing with soap behavior (CTPS) in Indonesia on the five important times of CTPS showed the lowest result, only 6% before preparing food[15]. The importance of maintaining personal hygiene and environmental sanitation in food processing-storage and serving/consumption areas is the responsibility of all individuals in the area, especially catering workers (food handlers).

Using latrines that are not following sanitation standards also has a 12.935 times greater risk for the incidence of Hepatitis A transmission. Previous study found that an epidemiological investigation (case-control study) on a hepatitis A outbreak that occurred in one of the high schools in Jember Regency, East Java, showed that the behavior of students at risk included defecation, not in latrines[21]. Environmental conditions can affect the incidence of Hepatitis A, such as lack of clean water supply, unsanitary wastewater and garbage disposal, and personal hygiene. The incidence of Hepatitis A is influenced by a person's behavior, such as people living in areas with poor environmental conditions and people with low personal hygiene, such as lack of implementation of clean and healthy lifestyle (Perilaku Hidup Bersih dan Sehat/PHBS). Hepatitis A outbreaks due to HAV-contaminated water sources also occurred in Pacitan in 2019. The Hepatitis A virus contamination most likely came from domestic waste in the Kaligoro river water in Sukorejo Village, a spring water source for residents[6].

Efforts to continue to make people aware of Stop Open Defecation (Stop Buang Air Besar Sembarangan/Stop BABS) include the declaration of "Stop Open Defecation" in various regions in Indonesia, both in urban and rural areas. Stop Open Defecation behavioral efforts are part of Community-Based Total Sanitation (STBM), which requires commitment from all levels of society, the private sector, and the government. In addition to efforts to improve clean and healthy lifestyle (PHBS) through health education, other efforts are needed to overcome the physical constraints of the availability of latrine facilities. Triggering system of STBM through community empowerment (gotong royong system) is a solution to build latrines for people with limited funding. The provision/assistance of costs for the procurement of physical facilities for residents who cannot afford to provide latrine facilities that meet environmental health standards as has been implemented in various regions in Indonesia[22].

CONCLUSIONS

The meta-analysis results show that behavioral factors such as hand washing, unhygienic foods or snacks, the use of open latrines, and cutlery exchange may risk people to the exposure of hepatitis A transmission. However, there are variation on the level of risk among the behavioral factors where the use open latrine is the most significant contriubtor of the hepatitis A transmission. The study recommends that community empowerment through health education about hepatitis A transmission and contribution factors of the trnasmission is a crucial element to reduce the risk of transmission of the disease. The healthy life-styles need to be maintained by promoting community empowerment and the spirit of mutual cooperation by the community, the private sector, and the government in reducing/eliminating the incidence of Hepatitis A in Indonesia.

The study has some limitation includes only used quantitatif articles, just three data source, and the population of hepatitis A cases does not represent most of Indonesia. Further research is recommended to use qualitative data to look deeper into the intermediary factors that cause Hepatitis A, and look for articles from more data sources, and consider the population distribution that can represent all clusters/regions in Indonesia.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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