

The Effects of Bacille Calmette-Guerin Immunization and Contact History on the Risk of Leprosy: Meta Analysis of Case Control Study

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ABSTRACT

Background: Leprosy or Hansen's is an infectious disease caused by Mycobacterium leprosy. The incubation period is 3 to 20 years and affects the skin, peripheral nerves, mucosa of the upper respiratory tract, and eyes. Based on research in leprosy endemic areas, BCG immunization provides protection against the risk of developing disease. Contact with untreated sufferers can lead to leprosy. This study aims to see how much influence BCG immunization and contact history have on the risk of leprosy by meta-analysis.

Subjects and Method: This was a systematic review and meta-analysis. The study was carried out by collecting articles from PubMed, ProQuest, Science Direct, Scopus, Spinger Link, EBSCO, Google Scholar, Embase, LILACS, Embase, Emerald, PLOS, and *Perpusnas* databases. The key words are "leprosy OR" hansen disease "AND" risk factor "AND" immunization BCG "OR" vaccine BCG "AND" household contacts "AND" odds ratio". The inclusion criterion was a full text study. Article searches from 1949 to 2020 used English and Indonesian. The study design was case control and the results are reported in Adjusted Odd Ratio (aOR). Articles that meet the requirements

are analyzed using the Revman 5.4 application.

Results: Fifteen articles were reviewed in this study with a total of 2,435 case subjects and 4,212 controls. The results of the meta-analysis showed that getting BCG immunization reduced the risk of leprosy by 0.77 times compared to not getting BCG immunization (aOR= 0.77; 95% CI= 0.40 to 1.49; p= 0.43), having a history of contact with lepers increased the risk of leprosy by 3.55 times compared to do not have a history of contact with leprosy patients (aOR = 3.55 95% CI = 1.86 to 6.76; p<0.001).

Conclusion: The risk of leprosy decreases by getting BCG immunization, having a history of contact with lepers increases the risk of leprosy.

Keywords: leprosy, BCG immunization, contact history, meta-analysis

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BACKGROUND

Leprosy is a chronic granulo-matrix infection caused by the obligate intracellular organism Mycobacterium leprosy. Leprosy

will first attack the peripheral nervous system, skin, mucosa, respiratory tract, reticuloendothelial system, muscles, eyes, bones and testes. Leprosy is also known as

Leprosy, Morbus Hansen, Lepra, Hanseniasis, Mal de San Lazaro, Judham, Aussatz, Mafung, Kustha, LepraArabum (Amiruddin, 2019).

Leprosy is unique because in the explanation of the characteristics, modes of transmission, prevention and quarantine of lepers, it has also been recorded around 1512 BC by the prophet Moses in the holy book of Leviticus 13: 1-45. After more than 3000 years have passed, the spread of leprosy has not been eliminated (Bible, 2019; Sehgal., Et al 2006).

WHO has been doing treatment since 1981 by providing 3 types of drug therapy or Multi Drug Therapy (MDT), namely dapson, rifampin, and clofazimine. This therapy is successful for healing but leprosy has not been eliminated from all over the world, especially in developing countries and tropical climates (WHO, 2016, 2019a).

Report of leprosy cases from 152 countries to WHO in 2018 from Africa Region 42, American Region 32, Southeast Asia Region 11, Eastern Mediterranean Region 18, European Region 32 and Western Pacific Region 26. New cases detected were 208,613 and the prevalence of leprosy registered was 184,194 cases. The countries with the highest leprosy burden in 2018 were India with 120,334 cases, Brazil with 28,660 cases, Indonesia with 17,017 cases, Bangladesh 3,729 cases (WHO, 2019b).

Turankar et al., (2016) found that active M. leprosy from environmental soil samples specifically came from public bathing places, washing places used by patients, around the patient's house, ward or hospital where patients were receiving patients.

A retrospective cohort study for 16 years and a follow-up of 7 years evaluating the presence or absence of BCG immunization scars against leprosy by Gomes et al., (2019) concluded that BCG vaccination at

the time provided a protective effect with a risk 0.42 times lower than that. didn't receive the vaccine.

A study by Ratnawati (2016) concluded that people who live with leprosy sufferers with unsanitary home sanitation conditions have a risk of contracting 7.85 times than healthy home sanitation. Different research results reported by Aprizal et al., (2017) state that individual characteristic factors, household contact, neighbor contact, home physical environment and occupant density are statistically proven to have no effect on the incidence of leprosy.

The purpose of this study is to draw conclusions by conducting systematic studies and meta-analyzes. By collecting and combining all relevant and pre-existing research results regarding BCG immunization and contact history with leprosy sufferers against the risk of leprosy.

SUBJECTS AND METHOD

1. Study Design

This research is a systematic review and meta-analysis conducted by following the PRISMA flow diagram. The article search databases are presented as follows: PubMed, ProQuest, Science Direct, Scopus, Springer Link, EBSCO, Google Scholar, Embase, LILACS, Embase, Emerald, PLOS, Perpustakaan. The key words are "leprosy OR" hansen disease "OR" leprosy "OR" leprosy ", AND" risk factor "AND" immunization BCG "OR" vaccine BCG "AND" household contacts "AND" odds ratio, AND "leprosy and odds ratio".

2. Inclusion Criteria

The inclusion criteria in this research are full text articles, in English and Indonesian. The articles were published from 1949 to 2020. The study design was an observational with case-control study. The article discusses the history of BCG immunization against leprosy risk and contact history

against leprosy risk. The sample in the case study is an individual diagnosed positive for leprosy, while the control is an individual without symptoms of leprosy with negative results. Study articles were those that were conducted by multivariate analysis and reported results in adjusted odds ratio (aOR).

3. Exclusion Criteria

The exclusion criteria in this study were research articles on quasi experimental trials, RCT, study protocol, pilot study, animal studies. Research articles were those that were performed by univariate, bivariate or non-adjusted odds ratio (aOR) analysis.

4. Operational Definition

Leprosy sufferers are all people who experience symptoms of leprosy and are diagnosed by health personnel.

BCG Immunization History is all people who have received BCG vaccine immunization with scars or without scars who have been checked for correctness.

Contact History is a track record of an individual in the form of a statement of having had physical contact with a person with leprosy.

5. Instruments

The study was conducted by following the PRISMA flow diagram and assessing the quality of research articles, using the Critical Appraisal Check List For Study from the Center for Evidence Based Management, (2014) for a case control study.

6. Data Analysis

The data analysis process in this study was carried out using the Review Manager application (RevMan 5.3), to determine the effect size and heterogeneity of the study. The results of meta-analysis data processing are presented in the form of a forest plot and a funnel plot.

RESULTS

The process of searching for articles on an electronic data base according to PRISMA flow diagrams can be seen in Figure 1.

Fifteen articles out of 9,878 were reviewed in this study with a total of 2,435 case subjects and 4,212 controls. Five of the articles were research conducted on the South American continent and eleven research articles were conducted in the Asian continent. Next, the researchers conducted an assessment of the quality of the articles (Table 1).

1. The effect of BCG immunization on the risk of leprosy.

Table 2 provides information on 6 articles with a case-control study design as a meta-analysis source of the effect of BCG immunization on leprosy risk.

a. Forest plot

Figure 2. Forest plot shows that getting BCG immunization reduces the risk of leprosy by 0.77 times compared to not getting BCG immunization, but this is not statistically significant. The distribution of data is stated to be heterogeneous (random effect model), $I^2 = 91\%$.

b. Funnel Plot

Figure 3 funnel plot of the effect of BCG immunization on the risk of leprosy, there is no publication bias, it is shown by the symmetrical plot right and left. The number of left-sided plots is 3 with a graph showing a standard error between 0.4 and 0. The right-sided plot is 3 with the graph showing that the SE is between 0.6 and 0.2.

2. Effect of contact history on leprosy

Table 2 provides information on 12 articles with a case-control study design as a source of meta-analysis of contact history on leprosy risk.

a. Forest plot

Figure 4. The forest plot shows that a history of contact with leprosy patients increase the risk of leprosy by 3.55 times

compared to no contact with leprosy patients and it is statistically significant ($p < 0.001$).

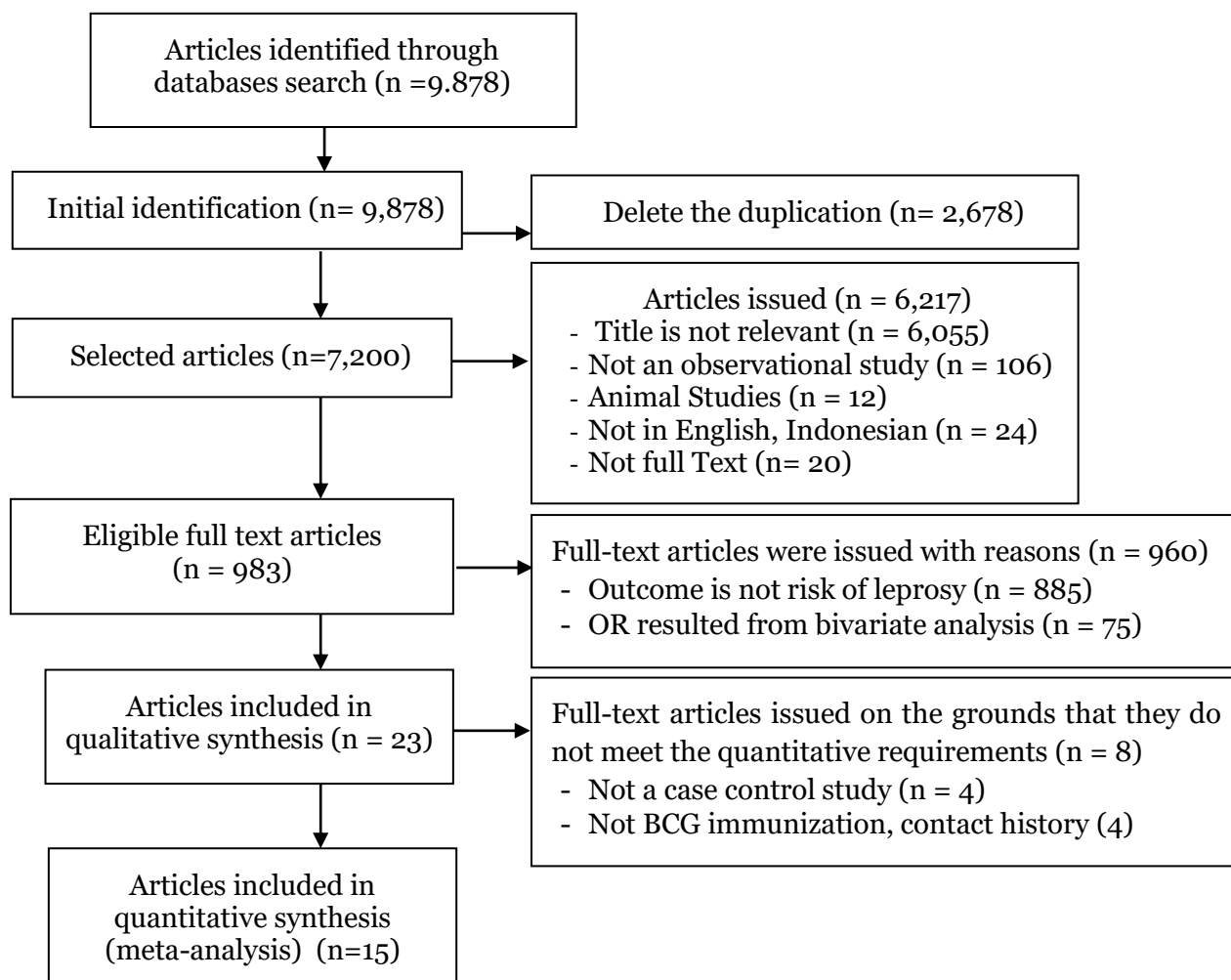


Figure 1. PRISMA flow chart

The heterogeneity value of I^2 is 91%, meaning that the distribution of data in this study is heterogeneous (random effect model).

b. Funnel Plot

Figure 5. The funnel plot shows publication bias, from the imbalance of the distance between the studies on the left and the right side of the funnel plot.

Asymmetrical shape of the funnel plot with the plot tendency to the right side. The

number of plots on the left is 3, the plots in the middle are 2 and 7 plots on the right side. The left side plot on the graph appears to have a standard error between 0.5 and 0 while the right side plot of the graph shows a standard error between 0 and 1. The publication bias in this study also occurs from an imbalance in the distance between the studies on the left and the right side of the funnel plot.

Table 1. Assessment of Research Quality

Scoring Item	Publication (Author, Year)														
	Muliyil et al., (1991)	Zodpey et al., (1998)	Kerr-Pontes et al., (2006)	Jariwala et al., (2013)	Efrizal et al., (2016)	Sari et al., (2019)	Harlim et al., (2019)	Lima et al., (2015)	Awaluddin (2004)	Feenstra et al., (2013)	Norlatifah et al., (2010)	Schmitt et al., (2010)	Murto et al., (2013)	Rodrigues et al., (2019)	Masrizal et al., (2020)
Relevance of goal and problem	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Relevance of methods and problems	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Sample adequacy	1	1	1	1	1	1	0	1	1	1	0	1	1	0	0
Validity sample	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cases and controls were comparable	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Criteria objective / unbiased	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1
Data search information	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
Revan and valid data analysis	0	1	1	1	1	1	0	1	0	1	1	0	1	0	0
The relevance of the effect size	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total	11	12	12	12	12	12	11	12	10	12	10	11	12	10	10

Note:
 Yes = 1
 No = 0

Table 2. Summary of sources of the effect of BCG immunization and contact history on leprosy risk

Author and Year	Country	Sample size		Intervention (I) and Comparator (C)	Outcome	Effect
		Case	Control			OR (95 % CI)
Muliyil et al., (1991)	India	397	669	I: BCG, No, contact C: Not BCG, Contact	Leprosy Risk	0.85 (0.59 to 1.10)
Zodpey et al., (1998)	India	76	172	I: BCG C: No BCG	Leprosy Risk	0.29 (0.21 to 0.41)
Kerr-Pontes et et al., (2006)	Brazil	226	875	I: BCG C: No BCG	Leprosy Risk	0.48 (0.33 to 0.70)
Jariwala et al., (2013)	India	76	152	I: BCG, No Contact C: No BCG, Contact	Leprosy Risk	0.30 (0.15 to 0.57)
Efrisal et al., (2016)	Indonesia	56	56	I: BCG C: No BCG	Leprosy Risk	4.13 (1.35 to 12.64)
Sari et al. (2019)	Indonesia	85	85	I: BCG, No Contact C: No BCG, Contact	Leprosy Risk	2.56 (1.24 to 5.29)
Harlim et al. (2019)	Indonesia	42	42	I: No Contact C: Contact	Leprosy Risk	9.19 (1.82 to 46.55)
Lima et al. (2015)	Brazil	185	136	I: No Contact C: Contact	Leprosy Risk	3.86 (2.21 to 6.75)
Awaluddin (2004)	Indonesia	80	80	I: No Contact C: Contact	Leprosy Risk	30.3 (3.90 to 233.90)
Feenstra et al. (2013)	Bangladesh	90	199	I : No Contact C: Contact	Leprosy Risk	1.09 (1.00 to 1.19)
Norlatifah et al. (2010)	Indonesia	31	62	I : No Contact C: Contact	Leprosy Risk	5.45 (1.89 to 15.69)
Schmitt et al. (2010)	Brazil	121	242	I : No Contact C: Contact	Leprosy Risk	8.33 (4.05 to 17.14)
Murto et al. (2013)	Brazil	340	340	I : No Contact C: Contact	Leprosy Risk	1.51 (1.0 to 2.28)
Rodrigues et al. (2019)	Brazil	40	164	I : No Contact C: Contact	Leprosy Risk	8.76 (3.41 to 22.50)
Masrizal et al. (2020)	Indonesia	32	32	I : No Contact C: Contact	Leprosy Risk	3.90 (0.9 to 16.7)

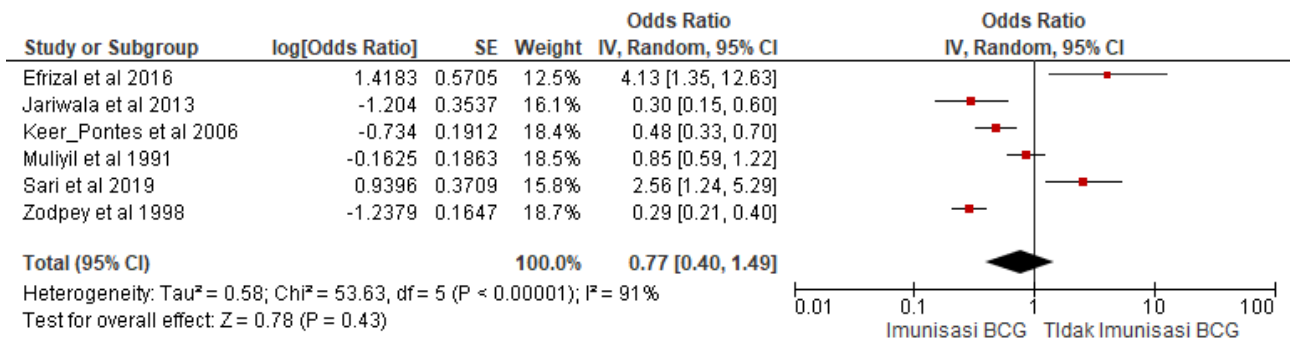


Figure 2. Forest plot of the effect of BCG immunization on leprosy risk

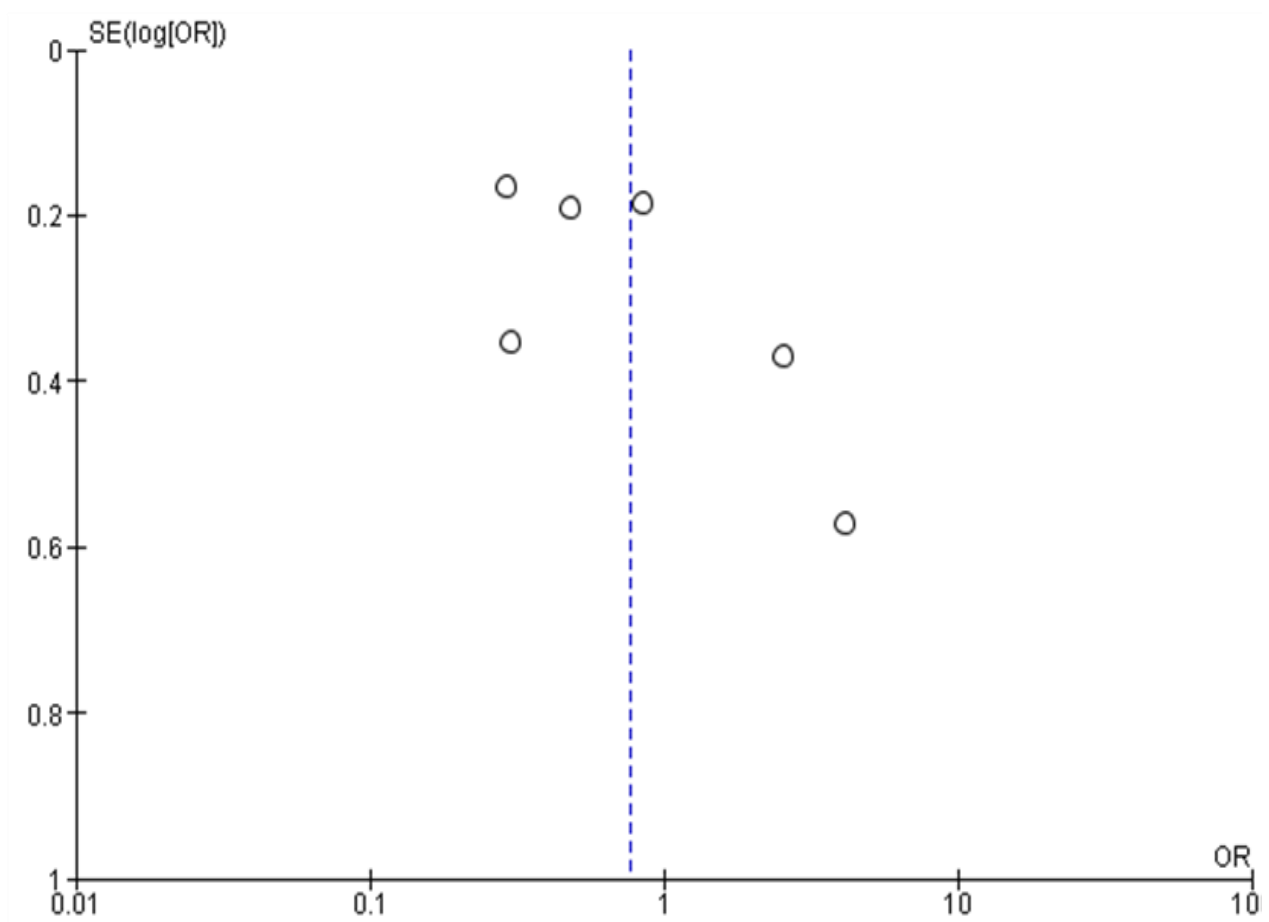


Figure 3. Funnel plot of the effect of BCG immunization on leprosy risk

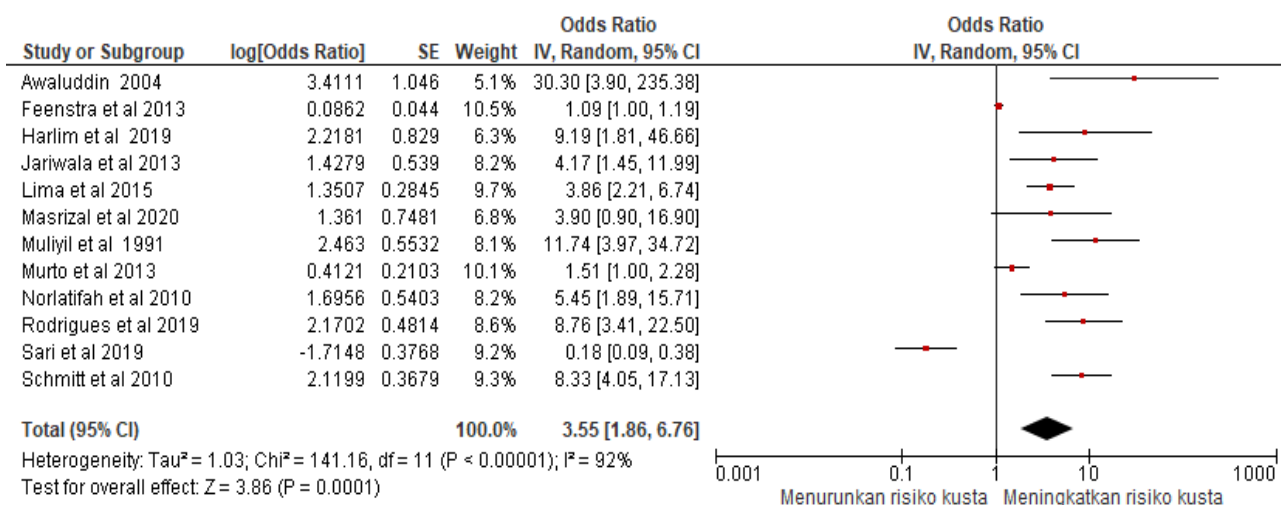


Figure 4. Forest plot of the effect of contact history on leprosy risk

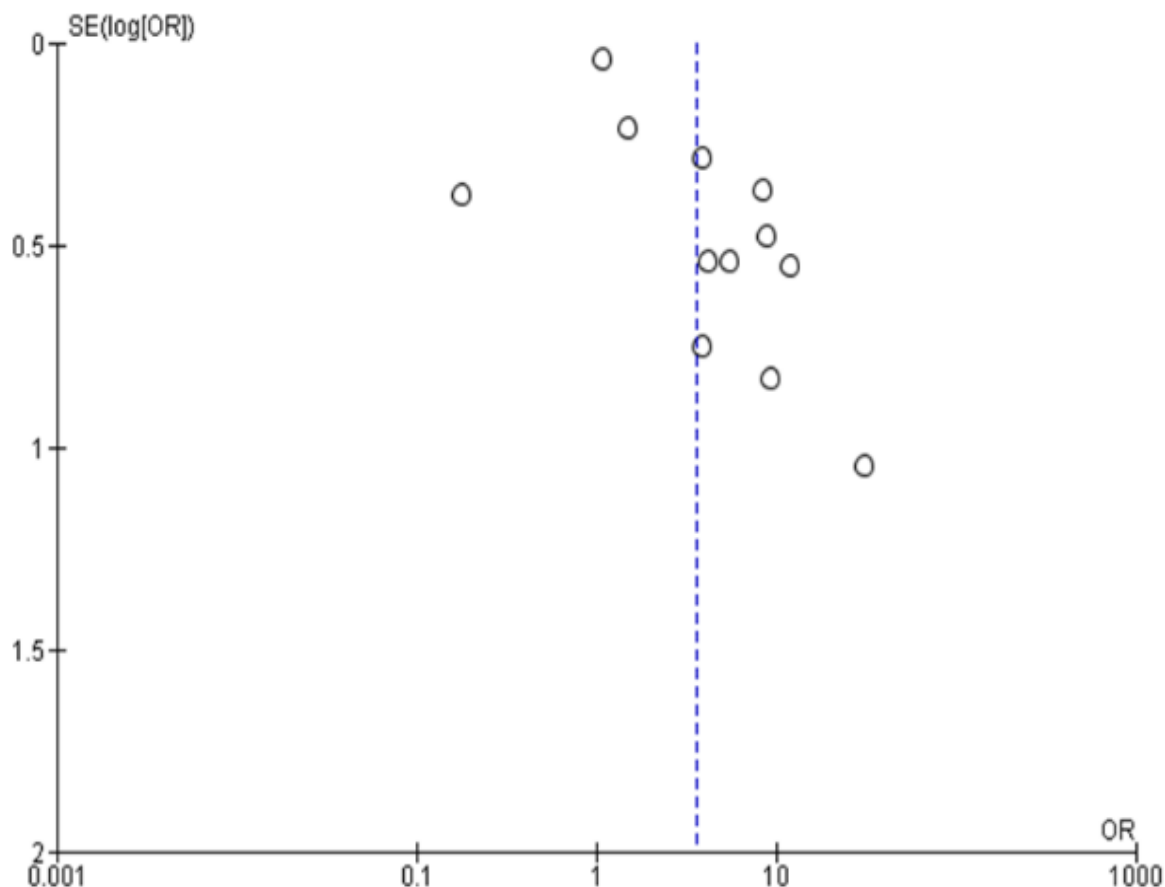


Figure 5. Funnel plot of the effect of contact history on leprosy risk

DISCUSSION

This research is a systematic study and meta-analysis of the risk factors for leprosy. The independent variables in this study were history of BCG immunization and

history of contact with patients.

Most of the primary studies only report the results of statistical analysis in the crude odds ratio (cOR), this shows that the results of these studies have not

controlled for confounding factors.

Confounding factor according to Murti (2018) is a mixture of estimated relationships between exposure and the disease under study, by other factors that are related, both to disease and exposure. According to the inclusion criteria, this study uses the results of primary studies that have controlled for confounding factors as shown by multivariate data analysis and the size of the relationship reported is in the form of Adjusted Odds Ratio (aOR).

Estimates of the combined relationship of the association of each risk factor with the incidence of leprosy were processed using the RevMan 5.3 application using the generic inverse-variance method. This method is used to analyze data in the form of: rate, time-to-event, hazard ratio, ordinal scale, adjusted estimate, difference of mean ratio of mean (Anulus, 2019). The results of the systematic review and meta-analysis of this study are presented in the form of a forest plot and a funnel plot.

A forest plot is a diagram that provides an overview of the information from each study examined in the meta-analysis, estimates of the overall results and the heterogeneity between study results. A funnel plot is a diagram in meta-analysis used to demonstrate possible publication bias. The funnel plot also shows the relationship between the Effect Size of the study and the sample size or Standard Error of the Effect Size of the various studies studied (Murti 2018).

1. The effect of BCG immunization on leprosy.

The results of the forest plot show that getting BCG immunization can reduce the risk of leprosy, namely 0.77 times compared to not getting BCG immunization, although it is statistically significant.

Sales et al., (2011) concluded that having a BCG scar showed a highly statistically significant protective effect for co-prevalent cases (OR = 0.28; 95% CI: 0.21 to 0.37) and incidence (OR = 0.45; 95% CI : 0.30 to 0.68). Contacts who received the BCG vaccine also showed significant protection against disease (OR = 0.44; 95% CI: 0.29 to 0.64).

According to Murti (2019), when someone pays for immunization, the costs incurred are marginal personal costs. The benefit of immunization is immunity to disease which is a marginal benefit. The positive impact of immunization is that the people around you indirectly benefit even though they do not pay.

BCG immunization does not provide a guarantee that a person can avoid leprosy infection. The results of this meta-analysis study provide evidence that there is an influence between BCG immunization and the risk of leprosy, namely as a protective factor against leprosy. BCG immunization reduces the risk of leprosy. Reducing the risk of leprosy can have an impact on reducing morbidity, disability, social stigma and mortality due to leprosy.

2. History of Contact with Leprosy

The effect of contact history with leprosy risk can be seen from the meta-analysis results. Forest plot shows that contact history with leprosy patients can increase the risk of leprosy by 3.55 times compared to not having contact with leprosy patients and it is statistically significant.

Bakker et al., (2004) concluded that household contacts of patients with multi-bacillary leprosy (MB) had an adjusted hazard ratio (aHR) of 4.6 (95% CI: 1.6 to 12.9) and household contacts were positive based on the results of the polymerase chain reaction (PCR) had an aHR of 9.36 (95% CI: 2.5 to 34.9) compared to no contact.

A history of household contact with a patient with leprosy increased leprosy (aOR= 1.48; 95% CI= 1.17 to 1.88), the risk increased for contacts aged ≥ 50 years (aOR= 3.11; 95% CI= 2.03 to 4.76) and boys have a higher risk than girls (aOR= 1.70; 95% CI= 1.20 to 2.42) (Teixeira et al., 2020).

Household contacts are the group with the highest risk, because of their closeness to persons affected by leprosy. The risk increases if the patient has a high bacillus content. However, these risk factors are often uncertain, even not well recorded in the leprosy monitoring program. This results in the maintenance of disease transmission chains and delays in diagnosis of leprosy reactions (Bakker et al. 2006; Goulart et al. 2008; Sales et al. 2011b).

According to Murti (2019), one of the reasons that health services for infectious diseases is important is because it has a positive externality of consumption. If cases of infectious diseases increase and are not treated, a large part of the population will become vulnerable to contracting the disease.

The importance of primary health services in controlling leprosy. The difficulty of primary health workers in recognizing community needs is a consequence of the weakness of the integrated health system health surveillance model. Leprosy is associated with information on signs and symptoms, although curable, its impact depends on early diagnosis and prolonged treatment (Figueiredo Vieira et al. 2020; Savassi et al., 2015).

Health education has a positive and statistically significant effect on healthy behavior ($b = 0.09$; $SE = 0.04$; $p = 0.018$) (Nasir et al., 2016). Rahmah et al., (2018) concluded that there is a relationship between personal hygiene and leprosy. The

risk of leprosy increased with worse personal hygiene ($b = -1.20$; 95% CI= -1.92 to -0.49; $p = 0.001$). Contact with sufferers cannot be avoided, but the risk of leprosy can be reduced through health education about leprosy, evidence-based health care, good personal hygiene and getting BCG immunization.

AUTHOR CONTRIBUTION

Priscilla Jessica Pihahey is the principal researcher who chooses topics, collects research data, formulates articles, and processes data. Bhisma Murti formulated the background, research data analysis. Yulia Lanti Retno Dewi helped formulate the framework and document review.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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REFERENCE

- Amiruddin MD (2019). Penyakit Kusta, Sebuah Pendekatan Klinis (Leprosy, A Clinical Approach) (1st ed.; A. Wijaya, Ed.).
- Anulus A, Murti B, Prasetya H (2019). Risk Factors of HIV among Male Military Personnels: A Meta Analysis. *J Health Promot and Behav*, 4(3): 178–188. doi: 10.26911/thejhp.2019.04.03.03.

- Aprizal LL, Soebono H (2017). Faktor risiko kejadian kusta di kabupaten Lamongan. *Berita Kedokteran Masyarakat (Risk factors for leprosy in Lamongan district. Community Medical News). J Community Med Public Health*, 33(9): 427–432.
- Awaluddin (2004). Beberapa faktor resiko kontak dengan penderita kusta dan lingkungan yang berpengaruh terhadap kejadian kusta di Kabupaten Brebes (Several risk factors for contact with leprosy sufferers and the environment that influence the incidence of leprosy in Brebes Regency). Tesis. Universitas Diponegoro. <http://eprints.undip.ac.id/14486/>.
- Bakker, Mirjam I, et al (2004). Population Survey to Determine Risk Factors for Mycobacterium Leprae Transmission and Infection. *J Epidemiol*. 33(6): 13-29-1336
- Bakker MI, Hatta M, Kwenang A, Van Mosseveld P, Faber WR, Klatser PR, Oskam L (2006). Risk factors for developing leprosy a population-based cohort study in Indonesia. *Lepr Rev*. 77(1):48-61.
- Efrizal, Lutfan L, Hardyanto S (2016). Faktor risiko dan pola distribusi kusta di Yogyakarta. *BKM Journal of Community Medicine and Public Health*. 32(10): 347-352.
- Feenstra SG, Nahar Q, Pahan D, Oskam L (2013). Social contact patterns and leprosy disease: A case-control study in Bangladesh. *Epidemiol Infect*. 141(3): 573–81. <https://doi.org/10.1017/S0950268812000969>.
- Figueiredo V, Nayara, et al (2020). Orientation of primary care in actions to control leprosy: Factors Relating to Professionals. *Gac Sanit*. 34(2): 120–26.
- Gomes RR, Antunes DE, dos Santos DF, Sabino EFP, Oliveira DB, Goulart IM. B. (2019). BCG vaccine and leprosy household contacts: Protective effect and probability to becoming sick during follow-up. *J Vaccine*, 37(43): 6510–6517. doi:10.1016/j.vaccine.2019.08.067
- Goulart IMB, Bernardes Souza DO, Marques CR, Pimenta VL, Gonçalves MA, Goulart LR. (2008). Risk and Protective Factors for Leprosy Development Determined by Epidemiological Surveillance of Household Contacts. *Clin Vaccine Immunol*. 15(1): 101–105. <https://doi.org/10.1128/CVI.00372-07>.
- Harlim A, Yulia HY, Suci AM (2019). Relation between Contact History and Bacille Calmette-Guerin (BCG) Vaccination Status with Leprosy Case in DR. Sitanala Hospital.” *IJRSR* 10(5). Diakses dari <http://www.recent-science.com/relation-between-contact-history-and-bacille-calmette-guerin-bcg-vaccination-status-leprosy-case-dr>.
- Jariwala DA, Pate BH, Godara NR, Kantharia SL (2013). Socio-demographic and environmental correlates of leprosy: A hospital based cases control study. *National Journal of Community Medicine*, 4(3), 369–376.
- Kerr-Pontes LRS, Barreto ML, Evangelista CMN, Rodrigues LC, Heukelbach J, Feldmeier H (2006). Socioeconomic, environmental and behavioural risk factors for leprosy in North-east Brazil: Results of a case-control study. *Int J Epidemiol*, 35(4), 994–1000. doi: 10.1093/ije/dy072.
- Lima LNGC, Frota CC, Mota RMS, Almeida RLF, Pontes MA de A, Gonçalves H de S, Rodrigues LC, Carl K, Kerr L (2015). Widespread nasal carriage of mycobacterium leprae among a

- healthy population in a hyperendemic region of northeastern Brazil. *Mem. Inst. Oswaldo Cruz*, 110(7), 898–905. <https://doi.org/10.1590/0074-02760-150178>.
- Masrizal M, Ananda PR, Ilham R (2020). Risk factors of leprosy and how its treatment is environmentally-friendly. *J. Phys.: Conf. Ser.*, 1469(1), 12113. Diakses dari <https://doi.org/10.1088/1742-6596/1469/1/012113>.
- Muharry A (2014). Faktor Risiko Kejadian Kusta (Risk Factors for Leprosy). *KESMAS*. 9(2). <https://doi.org/10.1-5294/kemas.v9i2.2846>.
- Muliyil J, Nelson KE, Diamond EL (1991). Effect of BCG on the risk of leprosy in an endemic area: A case control study. *J. Lepr* 59(2): 229–236.
- Murti B (2018). Prinsip dan Metode Riset Epidemiologi (Edisi V) (Principles and Methods of Epidemiological Research (Edition V). Program Pascasarjana, Universitas Sebelas Maret. Surakarta: Bintang Fajar Offset.
- Murti B (2019). Ekonomi Kesehatan (Health Economics) (Edisi ke II). Program Pascasarjana, Universitas - Sebelas Maret. Surakarta: Bintang Fajar Offset.
- Murto C, Chammartin F, Schwarz K, da Costa LMM, Kaplan C, Heukelbach J (2013). Patterns of migration and risks associated with leprosy among migrants in Maranhão, Brazil. *Plos Negl Trop Dis*, 7(9). <https://doi.org/10.1371/journal.pntd.0002422>.
- Nasir S, Murti B, Suryani N (2016). Path Analysis on the Association Between Predisposing, Enabling, and Reinforcing Factors, and House Sanitation in Bengkulu, Sumatera. *J Health Promot Behav*, 01(03), 190–200. <https://doi.org/10.26911/thejhp.2016.01.03.06>
- Norlatifah, Sutomo AH, Solikhah S (2010). Hubungan kondisi fisik rumah, sarana air bersih dan karakteristik masyarakat dengan kejadian kusta di kabupaten Tapin Kalimantan Selatan (The relationship between the physical condition of the house, clean water facilities and community characteristics with the incidence of leprosy in Tapin Regency, South Kalimantan). *Jurnal Kes Mas*. 4(3): 182–195. <https://doi.org/10.12928/kesmas.v4-i3.1016>.
- Pescarini JM, Strina A, Nery JS, Skalinski LM, Andrade KVF, Penna MLF, Penna GO (2018). Socioeconomic risk markers of leprosy in high-burden countries: A systematic review and meta-analysis. *Plos Negl Trop Dis*, 12(7):1–20. doi:10.1371/journal.pntd.0006622.
- Rahmah AH, Dharmawan R, Rahardjo SS (2018). Socioeconomic, environmental, and behavioral determinants of leprosy in Kediri, East Java. *J Epidemiol Public Health*, 03(02), 253–262. <https://doi.org/10.26911/jepublichealth.2018.03.02.05>
- Ratnawati R (2016). Faktor-faktor yang berhubungan dengan risiko kejadian morbus hansen (Factors associated with the risk of incidence of Hansen morbus). *2-TRIK*, 6(3): 103–109.
- Retnawati H, Apino E, Kartianom Djidu H, Anazifa RD (2018). Pengantar Meta Analisis (Introduction to Meta Analysis) (1st ed.; E. Apino, Ed.). Yogyakarta: Parama Publishing.
- Rodrigues TSV, Gomes LC, Cortela DCB, Silva EA, Silva CA L, Ferreira SMB (2019). Factors associated with leprosy in children contacts of notified adults in an endemic region of Midwest Brazil. *J Pediatr*. doi:10.1016/j.jped.2019.04.004.
- Sales AM, Ponce de Leon A, Düppre NC,

- Hacker MA, Nery JAC, Sarno EN, Penna MLF (2011a). Leprosy among patient contacts: A multilevel study of risk factors. *Plos Negl Trop Dis*, 5(3), 1–6. <https://doi.org/10.1371/journal.pntd.0001013>.
- Sari WM, Rokhmayanti (2019). Hubungan antara biological self dengan kejadian kusta di rumah sakit Sumberglagah Provinsi Jawa Timur Tahun 2019 (The relationship between biological self and the incidence of leprosy at the Sumberglagah hospital, East Java Province in 2019). Universitas Ahmad Dahlan Repository. <http://eprints.uad.ac.id/14958/>
- Santos VS, de Matos AMS, de Oliveira LSA, de Lemos LMD, Gurgel RQ, Reis FP Feitosa VLC (2015). Clinical variables associated with disability in leprosy cases in northeast Brazil. *J Infect Dev Ctries*, 9(3): 232–238. doi:10.3855/jidc.5341.
- Savassi KCM, Modena CM (2015). Hanseníase e a atenção primária: desafios educacionais e assistenciais na perspectiva de médicos residentes. *Hansen Int*, 40(2), 2–16.
- Schmitt JV, Dechandt IT, Dopke G, Ribas ML, Cerci FB, Viesi JMZ, Marchioro HZ, Zunino MMB, Miot HA (2010). Armadillo meat intake was not associated with leprosy in a case control study, Curitiba (Brazil). *Nona. Inst. Oswaldo Cruz*. 105(7): 857–862. <https://doi.org/10.1590/S0074-0276-2010000700003>.
- Sehgal A, Alcamo IE, Heymann DL (2006). *Deadly Diseases and Epidemics Leprosy* (1st ed.; I. E. Alcamo, Ed.). Chelsea House Publishers.
- Teixeira CSS, Pescarini JM, Alves FJO, Nery JS, Sanchez MN, Teles C, Ichihara MYT, et al. (2020). Incidence of and factors associated with leprosy among household contacts of patients with leprosy in Brazil. *JAMA Dermatology*, 156(6), 640–648. <https://doi.org/10.1001/jamadermatol.2020.0653>.
- Turankar RP, Lavania M, Singh M, Sengupta U, Siva SK, Jadhav RS (2016). Presence of viable Mycobacterium leprae in environmental specimens around houses of leprosy patients. *Indian J Med Microbiol* doi:10.4103/0255-0857.188322.
- WHO (2016). Global Leprosy Strategy 2016-2020: accelerating towards a leprosy-free world. In *Weekly Epidemiological record* (Vol. 1). doi:<https://policies.worldbank.org/sites/ppf3/-PPFDocuments/090224b0822f7384.pdf>.
- WHO (2019a). Global Health Observatory (GHO) Data Leprosy. Diakses dari https://www.who.int/gho/neglected_diseases/leprosy/en/
- WHO (2019b). Fact sheets Leprosy Diakses dari <https://www.who.int/en/newsroom/fact-sheets/detail/leprosy>
- Zodpey SP, Shrikhande SN, Salodkar AD, Maldhure BR, Kulkarni SW (1998). Effectiveness of Bacillus Calmette-Guerin (BCG) Vaccination in the Prevention of Leprosy; A Case-Finding Control Study in Nagpur, India. *Int J Lepr Other Mycobact Dis* 66(3), 309–315.
- Zuhdan E, Kabulrachman K, Hadisaputro S (2017). Faktor-Faktor yang Mempengaruhi Kejadian Kusta Pasca Kemoprofilaksis (Factors Affecting Post Chemoprophylactic Leprosy Incidence) (Studi pada Kontak Penderita Kusta di Kabupaten Sampang). *JEKK* 2(2): 89. <https://doi.org/10.14710/jekkk.v2i2.4001>.