



Systematic Review

**Contact Investigation and Preventive Therapy as Tuberculosis prevention in Children with Tuberculosis Household Contact: A Systematic Review**

**Apriana Rahmawati<sup>1</sup>, Budi Utomo<sup>2</sup>, Makhfudli Makhfudli<sup>1</sup>**

<sup>1</sup>Faculty of Nursing, Universitas Airlangga, Surabaya, Indonesia

<sup>2</sup>Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**ABSTRACT**

**Introduction:** he increasing tuberculosis cases in children showed management of Tuberculosis itself. There was a finding of TB case in children according to WHO TB report 2019 that not all childrens being well diagnosed, treated or reported each year. This systematic review aims to describes implementation of TB prevention often missed in children with adult TB household contacts.

**Methods:** is study uses based on PICO, which contains Participants are family who living household with adult TB, Interventions are CI followed by PT, no comparison, Outcomes are improving the implementation of CI and PT. Searching for article is using the Scopus, PubMed, and Science Direct and found 15 articles in final which limited to the last 3 years (2017-2020). Keywords used in searching are” Tuberculosis”, “Transmission”, and “Preventive Therapy”. The population included were respondents identified as family having child aged ≤ 15 years with TB Household Contacts. The study design varied in rigorousness form of quantitative and mixed studies.

**Results:** Household Contact (HHC) contribute to TB cases in children.

**Conclusion:** Contact Investigation (CI) and Preventive Therapy (PT) could be succesfull strategies to prevent TB transmission to children provided not only by Health Care Workers (HCWs) but also public concerned to community-based approach in order to encouraged family members of TB affected.

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**CONTACT**

Makhfudli Makhfudli

✉ [makhfudli@fkip.unair.ac.id](mailto:makhfudli@fkip.unair.ac.id)

📍 Faculty of Nursing, Universitas Airlangga, Surabaya, Indonesia

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**INTRODUCTION**

Tuberculosis continues to be a major global health threat which less than two thirds of cases are reported. Although the TB burden are infected in both adults and children, much of the attention on TB has been focused on adult TB. Only 46% of the estimated number of cases are reported by National TB Programs (NTPs) around the world, leaving a gap of over 580 000 children who are not diagnosed, treated and/or reported each year. TB can affect everyone, but one of specific population groups have a higher risk of acquiring TB infection and progressing to disease once infected are others in settings with a high risk of transmission of M. Tuberculosis (World Health Organization, 2018). The World Health Organization (WHO) recommendations

for investigating contacts of person with those settings endorse household contact investigation as the Active Case - Finding (ACF) strategy which enables early TB detection, including identification of latent TB infection, enabling preventive measures and prompt treatment initiation. Although TB programmes worldwide have adopted ACF, infrequent or inconsistent investigation of TB patient contacts remains a serious challenge .

Children represent about 10% of all TB cases. More than a million incident cases were estimated among children (aged <15 years) reflecting ongoing community transmission. The number of household contacts initiated on TB preventive treatment in 2018 was much smaller: 349 487 children aged under 5 years (a 20% increase from 292 182 in 2017), equivalent to 27% of the 1.3 million estimated to be

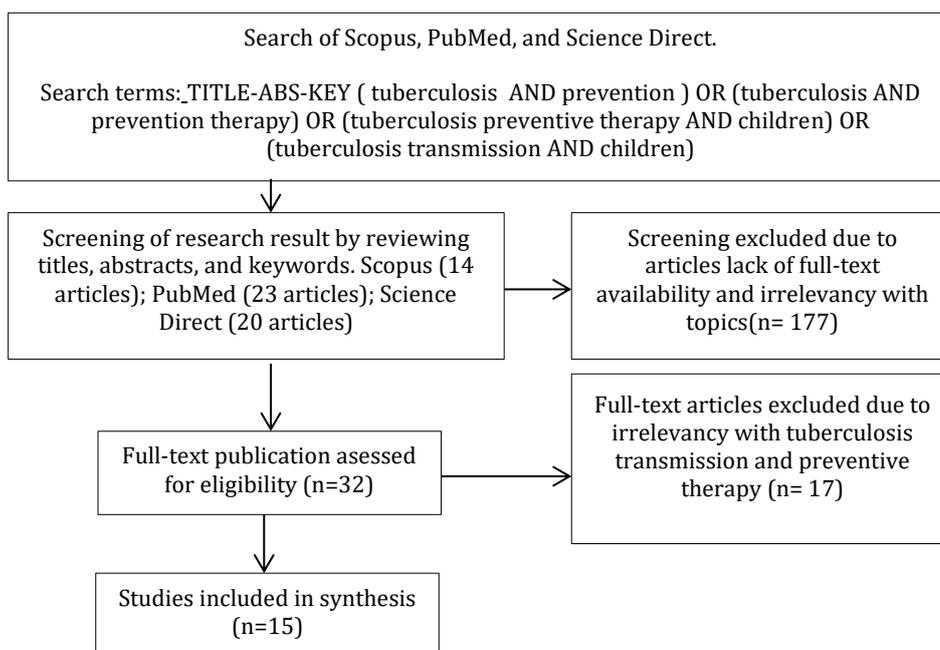


Figure 1 – Flow of articles selection

eligible, whereas household contact that untreated well can caused the increasing of tuberculosis cases in children (WHO, 2019). WHO said that the End TB Strategy milestones for 2020 and 2025 can only be achieved if TB diagnosis, treatment and prevention services are provided within the context of progress towards universal health coverage (UHC). due to a combination of underreporting of detected cases and under diagnosis (including people with TB do not access health care or are not diagnosed when they do) (WHO, 2015).

Childhood TB represents *Mycobacterium tuberculosis* (Mt) recent transmission and the failure of disease control in community. In this age group pulmonary TB is the most frequent presentation. Infants and young children are more likely to develop severe forms of TB (disseminated and meningitis) due to immature immunological response (Carvalho et al., 2018). The household contacts of TB patients (index case) are at the highest risk for TB infection. Around a quarter (25%) of household contacts have been infected at the time the index case was diagnosed (Wayan Gede Artawan Eka Putra et al., 2019). Household contacts (HHC) are highly susceptible to acquire TB infection from the index cases because of their close proximity. The goal of contact tracing and their screening for TB could lead to the detection of additional cases of TB, maximizing the impact of case detection and effective treatment (Begun, Newall, Marks, & Wood, 2013). Therefore, in high TB burden setting contact screening and preventive treatment in children less than 5 years of age need to be prioritized and implemented (Assefa, Klinkenberg, & Yosef, 2015).

The risk of exposure to MTb is a combination of epidemiological, environmental, sociocultural, and behavioural factors that reflect how children, adolescents, and adults interact within societies. Age-related and culture-related factors such as sleeping

practices, care-giving, play, religious practices, and school will influence how and where children interact with adults who might have tuberculosis and how much risk these interactions carry. Similarly, population density, household composition, crowding, transport systems, and ventilation, both at home and in health-care facilities, all contribute to the risk of exposure. Those are explaining that transmission of TB in children influenced by family role in household.. The aim of this review is to describe the implementation often missed and the obstacles of TB prevention in children with adult TB household contacts.

## MATERIALS AND METHODS

### Strategy for Study Selection

Arti To develop this review, a working group reviewed focuses on identification transmission factors of tuberculosis cases in children living with adult Tuberculosis, including procedure of contact screening in children, how children to be diagnosed, and family factor of infectious individual. A literature search for this systematic review is carried out in database such as Scopus, Pubmed, and Science Direct with result limited to the last three years from 2017-2020. The keywords used in literature search are tuberculosis, transmission, and preventive therapy.

### Type of Study

This systematic review was aimed to describes causing factors of TB transmission often missed in children with adult TB household contacts. Methods used to this systematic review was quantitative approach which have numerical data such as cross-sectional survey, either prospective or retrospective study.

Table 1. Summary Of Selected Studies

Author	Design	Sample	Variable	Results
(Bekken, G. K., Ritz, C., Selvam, S., Jesuraj, N., Hesselning, A. C., Doherty, T. M., Grewal, H.M. S., Vaz, M., and Jenum, S, 2020)	Cross-Sectional	525 Household Contacts	Tuberculin Skin Test, Quantiferon test result, Risk factors (age, gender, BCG-scar, diabetes, smokin, indoor pollution, crowding) Instrument : Tuberculosis Contact Score (TCS) and Relationship score Analysis : Chi-square test and ANOVA	Of 525 Household Contacts, 29 were MTb-culture positive and 96.6% of these asymptomatic.
(Birungi et al., 2019)	Quantitative – qualitative	270 contacts	Variable: characteristic of child, index cases, households and health facilities, IPT adherence Instrument: a questionnaire check list Analysis: Chi-square test	Of the 84 child contacts who started IPT, 74 (88%) had complete adherence and ten (12%) had incomplete adherence. There were no factors (individual characteristics of index cases, households and or health facility characteristics) found to be significantly associated with IPT adherence.
(Dorjee et al., 2019)	Cross-Sectional	617 participants	Clinical characteristics (age, sex, previous TB history, recent exposure, multiple TB exposure, exposure setting in school, cough-fever-night sweat, increased tiredness in last 2 weeks, weight loss in last 1 month) and risk of TB disease Instrument: Tuberculin Skin Testing Analysis: descriptive, univariate, and multivariable logistic regression)	Forty-six TB cases, including 1 with multidrug resistance, were found in schoolchildren, for a prevalence of 853 per 100 000. Extensively drug-resistant TB was diagnosed in 1 staff member. The majority of cases (66%) were subclinical. TBI was detected in 930 of 5234 (18%) schoolchildren and 334 of 634 (53%) staff who completed testing. Children in boarding schools had a higher prevalence of TBI than children in day schools (915/5020 [18%] vs 15/371 [4%]; $P < .01$ ). Preventive therapy was provided to 799 of 888 (90%) schoolchildren and 101 of 332 (30%) staff with TBI; 857 (95%) people successfully completed therapy.
(Datiko et al., 2017)	Prospective cohort	6161 Patient TB+	The number of children who completed 6-months IPT and the number who discontinued or were lost to follow-up, the number of children initiating IPT Instruments: semia-structured questionnaire Analysis univariate	Of 6161 PTB <sub>p</sub> cases identified by HEWs in the community, 5345 (87%) were visited, identifying 24 267 contacts, 7226 (29.8%) of whom were children aged ,15 years and 3102 (12.7%) were aged ,5 years; 2949 contacts had symptoms of TB and 1336 submitted sputum for examination. Ninety-two (6.9%) were PTB <sub>p</sub> and 169 had TB all forms. Of 3027 asymptomatic children, only 1761 were offered (and accepted) IPT due to INH shortage. Of these, 1615 (91.7%) completed the 6-month course. The most frequent reason for discontinuing IPT was INH shortage.

Author	Design	Sample	Variable	Results
(C. Emerson,1 B. Ng'eno,1 B. Ngowi,2 S. Pals,1 W. Kohi,3 M. Godwin,4 A. Date, 2019)	Quantitative – qualitative method	179 sputum smear-positive and 41 Health Care Workers (HCWs)	TB screening, HIV testing, and receiving IPT Instrument: A questionnaire study, in-depth interview with HCWs Analysis: using an Access database and analyzed	A total of 141 adult smear-positive TB patients reported 396 children living in households; detailed information on 346 (87.4%) was available. Only 37 (10.7%) children were clinically assessed for TB, 5 (13.5%) were diagnosed with TB, and 22 started on iso-niazid preventive therapy (IPT) (59.0%). Of the 320 children whose caregivers responded to whether their children had undergone human immunodeficiency virus (HIV) testing, 55 (17.2%) had been tested and one (1.8%) was HIV-positive. Forty-one HCWs described passive CCM without use of contact or IPT registers
(Van Ginderdeuren et al., 2019)	Quasy – experimental	Three clinics serving the Diepsloot community	Variables: average monthly number of new HIV diagnoses, IPT strategy, and TST placements Instrument: Survey questionnaire Analysis: Chi-square	Two clinics implemented TST-guided IPT for all clients receiving HIV care, one clinic decided against use of TST. According to routine register data, the proportion of clients initiating IPT increased substantially at the clinic not opting for TST (6% vs 36%), but minimally (34% vs 37% and 0.7% vs 3%) in the two other clinics.
(Kigozi, G., Heunis, J. C., Engelbrecht, M. C, 2019)	Cross-sectional	297 HHC	Variables: Characteristic of contacts, the yield of SHCI Analysis: Binary logistic regression	Of 259 contacts screened, just under half (47.1%) underwent TB clinical investigation, during which 17 (6.6%) new TB cases were diagnosed, which represents a prevalence rate of 6564 per 100,000 population. Fifteen contacts needed to be screened to detect one new TB case.
(Laghari et al., 2019)	Cross-Sectional	2397 Household Contacts	Characteristic of the HHC, environmental factors, active TB cases Instrument:a questionnaire consisting of patient characteristics Analysis: logistic regression	A total of 2397 family members at the median of 5 persons were recorded. Of these, 223 (9.3%) were screened on symptoms basis and 35 (15.7%) of these contacts were diagnosed with TB. Multivariate analysis revealed HHC with TB (OR = 15.288, 95% CI: 5.378–43.457), HHC with smoking (OR = 7.094, 95% CI: 2.128–23.648), and contact of > 18 h with TB individual (OR = 4.681, 95% CI: 1.198–18.294) as statistically significant risk factors of TB among the HHC.
(Marquez et al., 2020)	Cross-Sectional	3154 HHC	Prevalent TB infection, Proxies for household TB transmission Instrument: household survey in the SEARCH trial Analysis: unadjusted and adjusted odds ratios with generalized estimating equations (GEE)	Among children, having a household TB contact was strongly associated with TB infection (aOR 5.5, 95% CI: 1.7–16.9), but the strength of this association declined among adolescents and did not meet significance (aOR 2.3, 95% CI: 0.8–7.0).

Author	Design	Sample	Variable	Results
				The population attributable fraction of TB infection due to a household TB contact was 8% for children and 4% among adolescents. Mobile children and adolescents who travel outside of their community for school had a 1.7 (95% CI 1.0–2.9) fold higher odds of TB infection than those who attended school in the community.
(Okwara et al., 2017)	Cohort study	366 HHC	Variables: Contacts and index case characteristic, IPT failure Instrument: a structured questionnaire Analysis: Chi-square	At baseline, 428 contacts were screened, and 14(3.2%) had evidence of TB disease, hence excluded. Of 414 contacts put on IPT, 368 (88.8%) completed the 1 year follow-up. Operational challenges were reported by 258(70%) households, while 82(22%) reported side effects. Good compliance was documented in 89% (CI:80.2–96.2). By endpoint, 6(1.6%) contacts developed evidence of new TB disease and required definitive anti-tuberculosis therapy. The main factor associated with IPT failure was under-nutrition of contacts (p = 0.023).
(Wayan Gede Artawan Eka Putra et al., 2019)	Cross-Sectional	498 contacts	Variables: household contacts' sociodemographic characteristics, family relationship to index case, TB symptoms, participation in TB screening, evaluation (TB examination) Instrument: a structured questionnaire	124 TB patients being visited and identified 498 contacts, thus the ratio of contacts to cases is 4:1. All TB contacts were invited to participate in TB screening and evaluation program. A total of 100 (20.1%) contacts have attended at least one examination session and 41 contacts have completed all sessions. Ten TB cases were found among the contacts, of which four of them were adults (three bacteriologically confirmed and one clinically confirmed) and six were children (aged under 15 years).
(Mary R. Reichler <sup>1</sup> , Awal Khan <sup>1</sup> , Timothy R. Sterling <sup>2</sup> , Hui Zhao <sup>1</sup> , Joyce Moran <sup>3,4</sup> , James McAuley <sup>5,6</sup> , Patricia Bessler <sup>1</sup> , Bonita Mangura <sup>7</sup> , and Tuberculosis Epidemiologic Studies Consortium Task Order 2 Team Mary R. Reichler <sup>1</sup> , Awal Khan <sup>1</sup> , Timothy R. Sterling <sup>2</sup> , H., 2018)	Cross-Sectional	158 HHC	Variables: the timing of TB and TB rates Instrument: a structured questionnaire Analysis: Survival analysis (Proc life test)	Tuberculosis was diagnosed in 158 of 4490 contacts (4%) of 718 index patients with tuberculosis. Of tuberculosis cases among contacts, cumulative totals of 81 (51%), 119 (75%), 128 (81%), and 145 (92%) were diagnosed by 1, 3, 6, and 12 months, respectively, after the index patients' diagnosis. Tuberculosis rates among contacts were 2644, 115, 46, 69, and 25 cases per 100 000 persons, respectively, in the 5 consecutive years after the index patients' diagnosis. Of the tuberculosis cases among contacts, 121 (77%) were identified by contact investigation and 37 (23%) by tuberculosis registry cross-match

Author	Design	Sample	Variable	Results
(Martin-Sanchez et al., 2019)	Retrospective Cohort	3097 HHC	Variables: Characteristic of contacts, incident of TB (at 2 and 5 years) Instrument: Kaplan-Meier curves Analysis: the Log-Rank and Wilcoxon tests	953 contacts had LTBI, of which 14 developed TB. Their risk of developing TB after two and five years was 0.7% (CI: 0.3–1.6) and 1.8% (CI: 1.1–3.1) respectively. Contacts who had not been referred for LTBI treatment had a 1.0% (CI: 0.2– 4.0) risk at 5 years.
(Santos et al., 2020)	Retrospective study	72 patients	Variables: Treatment, Medical appointments, screening, and compliance Analysis: fisher exact and Mann-whitney test	A total of 72 patients were enrolled, 33 (45.8%) on chemoprophylaxis and 39 (54.2%) on latent tuberculosis infection (LTBI) treatment. The majority of patients were compliant (63.9%, n = 46).
(Wang, 2019)	Prospective-cohort	700 TB patients and 3417 HHC	Variables: HHC factors: Gender, age, previous TB history, HIV infection status, coexisting diabetes, socioeconomic status, employment status, and secondary education status TB patients factors: drug resistance status, alcohol and tobacco use, cough duration, hospitalization history, and side effect of treatment. Instrument: LASSO regression technique Analysis: Multivariate logistic regression	The incidence of TB disease among the contacts of index cases was 4.4% (149/3417). Ten variables (gender, age, TB history, diabetes, HIV, index patient's drug resistance, socioeconomic status, spoligotypes, and the index-contact share sleeping room status).

TB in their household mainly on Contact Investigation (CI) and Preventive Therapy (PT) implementation. All articles using English language were included. Articles would be excluded if the study did not use survey based research.

### Participants, Interventions, Comparators, and Outcomes (PICO)

The feasibility of the study was assessed using the PICO approach: Participants are children under 15 years and their parents who living household with adult TB, Interventions are CI followed by PT, no comparison, Outcomes are improving the implementation of CI and PT in order to reducing TB cases in children.

### RESULTS

Total articles collected were 17 articles. After reviewing the results, there are types of prevention

program influencing TB transmission to children, namely Contact Investigation (CI) and Preventive Therapy (IPT) implemented by Health Care Workers (HCW) affected by family factors of children exposed.

There are 7 articles that emphasized the implementation of preventive TB programs in children by HCWs in this review. The research conducted by Emerson et al (2019) in 10 Health Care Facilities (HCF) explained from 346 child contacts in household TB adult, only 37 (10.7%) children were clinically assessed. Five of them diagnosed with TB and received treatment, and 22 (59.5%) received IPT, and 10 (27.0%) of them received neither IPT nor TB treatment. The Health Care Workers (HCWs) interviewed was 41 HCWs, 25 (61%) clinicians (clinical officers and medical officers) and 16 (39%) nurses. They are all had worked an average of 6 years in the current TB clinic and 7 years in the field of TB. All HCWs reported they routinely ask adult TB patients about children with whom they are in

contact, yet none of those HCF applied a TB contact tracing or IPT register, they prefer to wait TB adult reported (C. Emerson,<sup>1</sup> B. Ng'eno,<sup>1</sup> B. Ngowi,<sup>2</sup> S. Pals,<sup>1</sup> W. Kohi,<sup>3</sup> M. Godwin,<sup>4</sup> A. Date, 2019). The low result of contacts investigated also found on study held by Kigozi et al (2019) that of 259 contacts screened, just less half (47.1%) underwent TB clinical investigation, during which 17 (6.6%) new TB cases were diagnosed.

Research conducted by Laghari et al (2019) also found that from 2397 Household Contacts (HHC), only 223 (9.3%) were screened on symptoms basis, and 35 (15%) of these contacts were diagnosed with TB. Research conducted by Putra et al (2019) also explained from 498 contacts identified, 100 (20.1%) out who attended at least one TB examination session at a Public Health Center (PHC). Twenty-two of them were children and 78 were adults. They who attended were completed anamnesis and physical examination. Those 3 articles pointed that the least number of contacts who screened caused by lack of HCWs so they were only provided a maximum five identified contacts to each HCWs, repercussion of the passive programs because screening depend only clinical symptoms being experienced by the contacts (Laghari et al., 2019).

Research conducted by Sanchez et al (2019) detected 565 TB cases with 3097 contacts, of whom 81 (2.6%) were found have co-prevalent TB, and 977 (31.6%) had Latent TB Infection (LTBI). Among the contacts with either co-prevalent TB or LTBI, the proportion of contacts that had co-prevalent TB in each age group was as follows: 60.7% in <5 years, 20.9% in 5–14 years; 6.9% in 15–39 years and 2.2% in >40 years. At the univariate level, TB risk was significantly higher in individuals who had not completed LTBI treatment. In the contacts who did not complete treatment, the risk of developing tuberculosis was 5% at 2 years, and 11.2% at 5 years. In contrast, the risk was close to 1% among contacts who had not been prescribed treatment and in those who had completed LTBI treatment. In addition to the cases that would have been prevented in the short term, secondary cases of these contacts would also have been prevented, as contact tracing makes it possible to break the infection. Due to their vulnerability, TB cases in <5 years age group probably appear even before the diagnosis of the index case. In our study population, a 60.7% of the contacts with either active TB or LTBI at the baseline contact tracing were co-prevalent TB cases in <5 years old, as compared to the 2.2% in >40 years old (Martin-Sanchez et al., 2019).

Children represent all contacts with TB cases also conceived by Reichler et al (2018), 718 TB patients with 4490 close contacts were identified, 158 contacts were diagnosed. Of the contacts with TB, 121 (77%) were identified during contact investigation (including 96 of 127 with a diagnosis after the index case), and 37 (23%) were identified by registry match; disease in 77 (49%) was confirmed by culture (67% of adults and 16% of children), and disease in

81 (51%) was diagnosed on the basis of clinical criteria. Of the contacts with tuberculosis, disease in 27 (17%), 4 (3%), and 127 (80%) was diagnosed before, on the same day as, and after, respectively, the index cases' diagnosis. Of the contacts with tuberculosis, cumulative totals of 81 (51%), 119 (75%), 128 (81%), and 145 (92%) had tuberculosis diagnosed by 1 month, 3 months, 6 months, and 12 months, respectively, after the index cases' diagnosis. They have shown that recently exposed close contacts have very high rates of tuberculosis, and that most cases occur soon after exposure and are already evident at the time of contact investigation (Mary R. Reichler<sup>1</sup>, Awal Khan<sup>1</sup>, Timothy R. Sterling<sup>2</sup>, Hui Zhao<sup>1</sup>, Joyce Moran<sup>3,4</sup>, James McAuley<sup>5,6</sup>, Patricia Bessler<sup>1</sup>, Bonita Mangura<sup>7</sup>, and Tuberculosis Epidemiologic Studies Consortium Task Order 2 Team Mary R. Reichler<sup>1</sup>, Awal Khan<sup>1</sup>, Timothy R. Sterling<sup>2</sup>, H, 2018). These findings emphasized the importance of performing contact investigations immediately after identifying index cases, as a public health measure for detecting new cases of active tuberculosis and taking steps to interrupt transmission. Research conducted by Dorjee et al (2019) and Bekken (2020) depicted that the window of HHC enrollment sooner following TB index cases identification could influence the number contacts tracing investigation, so the large case finding and implementation of preventive therapy by HCWs could reducing the increasing number TB cases of children (Dorjee et al., 2019).

Family of TB patients also hold important role for TB transmission regarding individual in contact with active TB patients are susceptible to TB, and household contacts are considered to be at higher risk due to their constant exposure to infected patients. Research undertook by Wang (2019) found that from 3417, 149 HHC developed TB disease. The median time for the first TB infection of HHC was 153 (52–264) days. That study incorporates 10 predictors such as contact's gender, age, previous TB history, diabetes, HIV infection status, index patient diabetes, index TB patient's drug resistance status, socioeconomic status, spoligotypes, and the index-contact share sleeping room status. From 10 predictors, researchers mentioned that main mode of TB transmission is contact with active TB due to their frequent exposure. As demonstrated from the previous study, the incidence of TB in HHC is higher in the case of drug-susceptible TB cases than in Multi Drug Susceptible-TB index cases, and the independent risk factors for TB transmission was the fact that contacts and TB patients share the sleeping room (Wang, 2019). Research held in Uganda and Brazil also revealed that household with more crowded condition (more than three people per room) caused increasing individual-level risk factors of infection from TB transmission in children. Prevalent TB infection was associated with other proxies of household transmission by having another child (5–15 years of age) in the house with TB infection (Marquez et al., 2020).

Delayed diagnosis due to unawareness of TB transmission in children from family is other factors that contribute to increasing TB cases in children. Study from Laghari et al (2019) that involved 2397 HHC were living with 443 index cases with a median number of 5 contacts, 1321 (55.1%) of those were adults and 1076 (44.9%) were children aged  $\leq 5$  years. The literacy in adult participants was very low as the researchers found that those participants having no formal education/ background. Two-hundred twenty-three (9.3%) of 2397 were screened based on symptoms, 119 (53.4%) were females, 143 (64.1%) were children  $\leq 14$ . Of 223 screened, 15.7% of them were diagnosed with TB. The low rates of contacts screened is a possibly repercussion of the passive nature of the program, which mainly depend on distinctive clinical symptoms being experienced by the contacts. Research conducted by Putra et al (2019) identified 498 contacts, and all were invited in TB screening and program, yet only 100 contacts have attended at least one examination session and 41 contacts have completed all sessions. As those of TB evaluation, 10 new additional new TB cases consisted of six childhood TB, three bacteriologically confirmed TB, and one clinically confirmed TB. Reported foremost reasons for this were unawareness in respect to the need for screening, illiteracy and fear stigma from society, also majority of caregivers did not know that contacts with prolonged cough be in need of screening (Wayan Gede Artawan Eka Putra et al., 2019).

Various preventive strategies have been adopted in endemic settings. Household Contacts' (HHC) tracing offers the best opportunity to identify children at risk and provide access to preventive therapy. World Health Organization (WHO) recommends 6 months isoniazid preventive therapy (IPT) for children under 5 years in close contact with infectious TB. Birungi et al (2019) evaluated adherence of IPT given as prevention of TB cases in children. Among 270 below 15 years-old child contacts, 84 (89%) started IPT and 74 (88%) of them completed six months of IPT, with ten (12%) of them who did not complete the treatment, whereas one (1.2%) of the 84 child contacts developed TB six months after completing the full 6-month of IPT. They were household-related factors affecting the incomplete adherence of parents/ caregivers. They were reported that poverty led to a lack of food, so they were prefer to gave priority to getting a job rather than going to PHC to collect medication (Birungi, Graham, Uwimana, Musabimana, & Van Wyk, 2019; Okwara, Oyore, Were, & Gwer, 2017).

Barriers to IPT implementation also discussed in study conducted by Santos et al (2020) and Ginderdeuren et al (2019). Santos et al (2020) enrolled 72 patients, 33 (45.8%) on chemoprophylax (CP) is in children under 6 years old TB exposure and 39 (54.2%) on LTBI strengthened with BCG vaccine according to standard in practice at that time. Isoniazid was the main drug used on CP with a median duration of 9 weeks and in 35 cases of LTBI for 9

months. There was compliance to screening, visits, and treatment in 63.9% (n=46) and non-compliance in 36.1% (n=26). The reasons for non-compliance are included social problems/ family dysfunction and medication problems, and doings for non-compliance are all parents/ caregivers were contacted by phone and encouraged to return to the appointments and take medication, and rescheduling a new appointments. By implementation of those strategies, a final compliance rate of 98.6% was achieved (n=71), and there were one case of loss of follow-up. Ginderdeuren et al (2019) also stated that the main barriers reported by HCWs were low family awareness of IPT, time needed counsel, burden to document IPT-related activities, and concerns regarding exclusion of active TB (Santos, Silva, Rangel, Barbosa, & Carvalho, 2020; Van Ginderdeuren, Bassett, Hanrahan, Mutunga, & Van Rie, 2019).

Though many study revealed about unawareness of infectious TB individual and the family, there are articles found in reverse. Datiko (2019) involved 3503 participants, and 2483 (96%) of them reported high level of awareness about TB, the majority had heard about TB, those participants also knew that TB could be cured and would go to PHC if they developed TB symptoms. Study from Rakhmawati (2019) revealed that 14 family caregivers participated as key informants, reflected their understanding of the risk of TB transmission from TB patients in the household to their children, and the importance of preventing TB transmission in the household (Datiko, Yassin, Theobald, & Cuevas, 2017; Rakhmawati, Nilmanat, & Hatthakit, 2019).

## DISCUSSION

This systematic review was aimed to identifying the articles around preventive strategies to TB transmission in children. As the point, an important role in TB child prevention is held by HCWs and family affected. Healthcare workers (HCWs) at TB clinics play a critical role in implementing strategies.

Identifying children in contact with adults with TB is one of the first strategies for implementing IPT and preventing TB in children, thereby interrupting further transmission of TB within the community (C. Emerson, 1 B. Ng'eno, 1 B. Ngowi, 2 S. Pals, 1 W. Kohi, 3 M. Godwin, 4 A. Date, 2019). Despite knowing the strategies, we need to know about the obstacles so implementation could be improved for the further. Several studies sound that HCWs only involved infected contacts were the cases in which contact tracing was successful, they do not have information on TB risk of contacts that could not be traced or identified. On the other hand, delays in TB diagnosis commonly occur in clinical practice. Atypical clinical presentations and clinician inexperience are partly responsible for delayed TB diagnosis [18]. Less attention may be given to HIV-negative TB patients. The finding of high prevalence of TB among household contacts of HIV-negative index cases

underscores the need for TB programmes to direct Active Case Finding (ACF) efforts, beyond children < 5 years and HIV-positive cases.

Community-based approach with collaboration of pediatricians with experience in tuberculosis, with closer contact with families and regular scheduled appointments was responsible for an increased awareness of the HCWs to TB preventive therapy importance, reducing this non-compliance determinant reported in other studies, and could train female Health Extension Workers (HEWs) to identify individuals with symptoms of TB and HHC affected (Datiko et al., 2017; Santos et al., 2020; Van Ginderdeuren et al., 2019).

The *Mycobacterium tuberculosis* can also influence the level of transmission in household contacts and in the community. As expected, an independent risk factor for TB transmission is the fact that contacts and TB patients share the same sleeping room. Therefore, accurate identification of active index TB cases and prediction of the risk of TB infection are essential to prevent transmission. Exposure to someone with active TB in the previous 2 years at school environment, suggesting that over several years the majority of the school population would be contact, and finding that the living facilities, including their ventilation and time spent in them, play important roles in TB transmission and acquisition (Dorjee et al., 2019; Wang, 2019). In addition, the degree of exposure with TB contacts was assessed by recording the closeness of patients to the individual with TB within the household (in terms of time spent with TB contact). Contact of > 18 h per day with TB individual was significantly connected with TB among HHC. Beside, there could be possibility that not all the symptomatic contacts could attend at the treatment centres. There might be some asymptomatic contacts that could have TB infection. For that reason, the entire HHC of TB patient regardless of symptoms should be screened in order to have the early finding of additional cases of TB and to reduce TB transmission (Laghari et al., 2019).

In TB endemic areas, duration and intensity of exposure might be a critical factor affecting IPT effectiveness. Factors were not independently associated with risk of IPT failure could suggest that they are surrogate indicators of the level of nutritional support from parents, indicated by closeness of the mother as the source of food or inability to get adequate nutrition on account of the numbers that need to be fed. Parents/caregivers own experience concerning TB disease or their experience of taking care of a relative with TB has been identified as one of the main factors facilitating IPT adherence. The fear to see their offspring suffering from TB, a disabling and killer disease, has been a primary factor motivating them to make sure that their children had complete IPT adherence (Birungi et al., 2019; Okwara et al., 2017).

## Limitation of Study

The following limitations are associated with the current study. First, the authors did not distinguished preventive therapy discussed in each study, even though preventive therapy has each of side effect influences adherence of the participants. Second, studies included all countries, whether it is categorized as low, middle, or high burden of TB cases. Third, authors did not discussed about other diseases could affecting the succes of the TB prevention program in children.

## CONCLUSION

Household Contact (HHC) contribute to TB cases in children. Contact Investigation (CI) and Preventive Therapy (PT) could be succesfull strategies to prevent TB transmission to children provided not only by Health Care Workers (HCWs) but also public concerned to community-based approach in order to encouraged family members of TB affected.

## CONFLICT OF INTEREST

No Conflicts of interest have been declared.

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