IMPLEMENTATION FIDELITY OF TUBERCULOSIS PREVENTIVE THERAPY FOR UNDER FIVE CHILDREN EXPOSED TO SPUTUM SMEAR POSITIVE PULMONARY TUBERCULOSIS IN KASKI DISTRICT, NEPAL

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THESIS

Implementation Fidelity of Tuberculosis Preventive Therapy for Under 5 years Children Exposed to Sputum Smear Positive Pulmonary Tuberculosis in Kaski District of Nepal

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STATEMENT OF AUTHENTICITY

I hereby declare that this thesis is my own work and to my best knowledge it contains no material previously published or written by another person for the award of degree at Universitas Gadjah Mada or other institution, except where due acknowledgement is made in this thesis.

Yogyakarta, November 2019

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
AHW	Axillary Health worker
ANM	Axillary Nurse midwife
CI	Confidence Interval
CNR	Case Notification Rate
DOHS	Department of Health service
DOTS	Direct Observed Treatment Short Course
DPHO	District Public Health Office
DR	Drug Resistant
FGD	Focus Group Discussion
HCP	Health Care Provider
HMIS	Health Management Information System
HIV	Human Immunodeficiency Virus
IDI	In Depth Interview
INGO	International Non -Government Organization
LBTI	latent TB infection
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
NTC	National Tuberculosis Centre
NGO	Non-Government Organization
NHRC	Nepal Health Research Council
NSP-TB	National Strategic Plan for tuberculosis
OR	Odd Ratio
PBC	Pulmonary bacteriologically confirmed
PCD	Pulmonary clinically diagnosed
PI	Principal Investigator
RA	Research Assistant
RTC	Regional Tuberculosis Centre
SS+	Sputum Smear Positive
SOP	Standard Operating Procedure
SDG	Sustainable Development Goal

TB	Tuberculosis
TBPT	Tuberculosis Preventive Therapy
TDR	Tropical Disease Research
U5	Under Five
UVGI	Ultraviolet Germicidal Irradiation

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ABSTRACT

Background: In line with WHO recommendation, Nepal has started implementing Tuberculosis preventing therapy (TBPT). However, enrolment of children in preventive therapy is sub optimal. So this study measured implementation fidelity of programs in terms adherence and moderating factors influencing the implementation of TBPT program from parents/caretakers and providers perspective in Kaski district, Nepal, using implementation fidelity framework by carroll et. al.

Methods: We used a mixed-method explanatory sequential design study. Quantitative data was collected by retrospective review of secondary from April 2018 to May 2019 and established the level of adherence. Qualitative study was conducted to explore the moderators from both providers and parents/caretakers side. We undertook sixteen in-depth interviews with care givers and a focus group discussion which were analyzed thematically.

Results: The majority of the components of the TBPT program were found to be implemented with moderate level of fidelity. The proportion of under five years children initiate and complete full course of TBPT was 72.5% and 75.86% respectively. The proportion of index cases traced for household contact, timely contact tracing and timely initiation of therapy were 54.19%, 82.73% and 86.20% . The major moderating factors identified in implementation of TBPT from providers side were unregulated contact tracing, sub optimal service delivery, partnership and ownership, poor recording /reporting, knowledge and training, unstable financing and resource available. Likewise, poor dissemination of information, awareness, access, supports and drug characteristics were potential moderators identified from parents/ caretakers side.

Conclusion: TBPT program is being moderately implemented in Kaski districts. Addressing the key challenges identified; inconsistent contact tracing, sub optimal service delivery, partnership/ownership, unstable financing and knowledge of health worker results in more identification of children eligible for TBPT.

Keywords: Adherence, Implementation fidelity, Preventive Therapy, Nepal, Tuberculosis

CHAPTER I. INTRODUCTION

A. Background

Tuberculosis (TB) is the global public health problem with the leading cause of death and suffering worldwide. It is an infectious disease caused by *Mycobacterium tuberculosis,* which most often affects the lungs and other parts of the body. It transmits from one person to another through droplet infection such as coughing or sneezing. A decade of intensified effort to control TB, the incidence rate of TB is reduced by 2% per year. However, it should be reduced by 4-5 % yearly to reach the 2020 milestone of End TB strategy (WHO, 2018a). It is the leading cause of death worldwide with the highest-burden in South East Asia and the Western Pacific region with 62% of new cases followed by the African region, with 25% of new cases. In 2017, the percentage of new cases of tuberculosis was 87% in 30 high burden countries. Similarly eight countries: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa accounted for two-thirds of new TB cases (WHO, 2019a) .

Epidemiology of TB is closely related to the number of structural factors such as socioeconomic inequalities, poverty, malnutrition and weaknesses in health systems which is making prevention, care and control more complicated. It is more common in a special group of the population such as people living with HIV, children, prisoner, labor/migrant, pregnant women, etc (Sulis *et al.*, 2014). Worldwide, there were altogether 10 million reported cases of TB in 2018. Among them, one million were children, 59% were under five years of age and 2,33,000 (children with TB HIV) died from these diseases (WHO, 2019a). Children, less than 5 years of age contribute an estimated 10% - 20% burden of TB in endemic areas (Dodd *et al.*, 2014). It is also considered as a major contributor to morbidity and mortality of under five children (Graham *et al.*, 2014).

There is a gap in the exact identification of childhood TB cases. Globally, out of estimated childhood TB cases, overall 45% of cases are reported to national TB programs. Among them, 31% are under five years and 60% are 9- 14 years (WHO, 2018b). Underlying challenges in estimating the exact burden of childhood TB lack of proper diagnosis, well-defined case definition, and national TB program is giving

more emphasis only on adult sputum smear-positive (SS+) TB (Ritz and Curtis, 2014). So children dying from TB are also incorrectly classified as pneumonia, meningitis, human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) or malnutrition (Graham *et al.*, 2014). Childhood TB is mainly acquired from an infectious adult contact with a high rate of transmission in TB endemic areas and once infected are at greater risk of development to TB disease than adults (Marais *et al.*, 2004). Patient with SS+ cases has a high rate of transmission of diseases to their contact cases. Prevention is the best strategy in the reduction of childhood burden of TB.

The WHO strongly states the need for treatment of latent TB infection in people living with HIV and under 5 years of children who are in household contact with pulmonary bacteriologically confirmed (PBC) TB, as one of the strategies for prevention, care and control of TB (WHO, 2019a). WHO emphasized the need for contact tracing and preventive treatment among under 5 years of children who are household /close contacts of people with PBC tuberculosis. Contact tracing is an effective approach in early identification of eligible children and entry point for initiation of preventive treatment. Isoniazid prophylaxis for six months was a recommended drug regimen in countries with high and low burden settings for the treatment of LTBI (WHO, 2018c). Contact children without any active TB after an appropriate clinical evaluation are eligible to start preventive therapy. Isoniazid prophylaxis reduces the possibility of developing tuberculosis by 59% among children with the age of 15 years or younger (Ayieko *et al.*, 2014). Isoniazid preventive therapy prophylaxis should be given at least six months (10 mg/kg per day, range 7–15 mg/kg, maximum dose 300 mg/day) (WHO, 2014a). However, updated guidelines in the management of latent infection 2018, has replaced 6 months of isoniazid monotherapy to rifampicin plus isoniazid daily for 3 months as a substitute to as a preventive treatment for children and adolescents aged < 15 years in countries with a high TB incidence (WHO, 2018c).

It is estimated around one-third of the world's population (one billion) infected with latent TB infection (Houben and Dodd, 2016). Under-five years of children with exposure to adult pulmonary TB increased the risk of mortality by 70% in high burden setting and by eight folds when the mother had TB. There is an increased risk of

mortality among children if exposure belongs to index family than children who do not belong to the index family (Gomes *et al.*, 2010). Globally in 2017, over 75% (of 1.3 million eligible household contacts under 5 years of age) did not access preventive therapy (WHO, 2018b). Challenges in the initiation and completion of IPT among children are described in many studies. Lack of awareness among health workers, interruption of drug supply, HIV coinfection and underreporting and far distance to health facilities are some existing problems in different settings (Hall *et al.*, 2015, Triasih *et al.*, 2014).

In Nepal, TB is a major public health problem with seven leading causes of death. In 2018, there were altogether 32,474 registered cases of TB, among them 31,723 were incident cases (new and relapse). Out of all registered cases female were 11,889 (37%) and 20,585 (63%) male. Out of total incident cases PBC cases were 18,000 (57%) , pulmonary clinically diagnosed (PCD) were 4,411 (14%) and 9,312 (29%) were extrapulmonary incident TB cases. Nationally, all forms of case notification rate (CNR) is112/100,000population (NTC, 2019). Based on CNR, 22 out of 77 districts measured as a high burden, 29 districts as a medium burden and 26 districts as low burden (DOHS, 2017). Reported childhood TB was 5.5% in Nepal (NTC, 2019).WHO estimates 10% of childhood TB among notified cases which shows that there is a gap in the identification of childhood TB cases (NTC, 2017a).

In line with WHO recommendation, Nepal has also initiated implementing six months of IPT for children under five years of age who are in close contact with PBC TB, from the year 2017. IPT is recommended for immature children less than 5 years of age, a baby born to infected mother and immunocompromised (e.g. severely malnourished or HIV-infected, or on steroids/ immune-suppressive drugs), irrespective of their age. It is undergoing in 38 endemic districts where contact tracing is done (NTC, 2017b). Nepal also endorsed the new recommendation of rifampicin plus isoniazid daily for 3 months by replacing six months of isoniazid monotherapy from April 2019. IPT was replaced by the name Tuberculosis preventive Therapy (TBPT) in Nepal. However, an implementation strategy will remain as it is.

This program is undergoing under trilateral collaboration with the government of Nepal, Global fund and save the children international in 38 high burden districts with the involvement of sub-recipient (SR) organization. It has been implementing in Nepal by two approaches: SR and health facility. Through SR, mandatory contact

tracing of every smear positive tuberculosis and assessment of the household member including children for TB will be done (NTC, 2018). If any non-presumptive children are found he/she is eligible for preventive therapy. Then contact tracer will refer children eligible for therapy to the nearest Directly Observed Treatment Short-course (DOTS) taking consent with the parent of children. Through health facility (DOTS Center) health providers will ask newly diagnosis bacteriological confirmed pulmonary TB about them to bring several children living with them for ruling out TB. If children found not having TB, preventive therapy will be initiated (NTC, 2018).

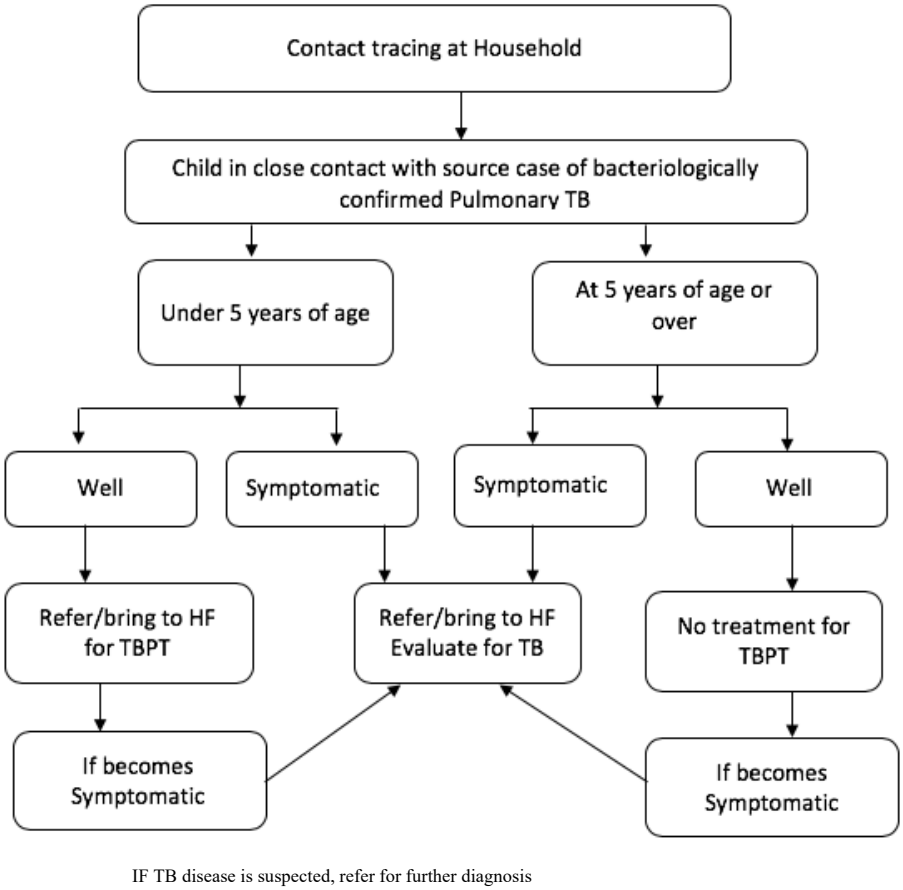

Figure 1: Childhood contact management approaches at community

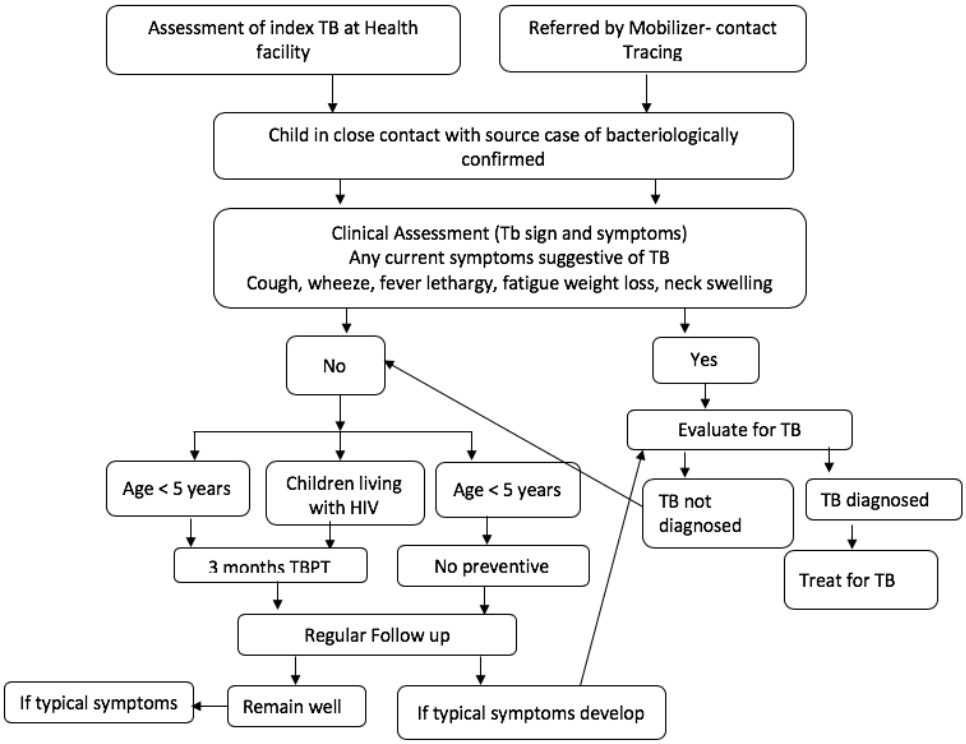

Figure 2: Childhood contact management approaches at a health

DOTS has been implemented since 2001 to promote proper adherence to the full course of drug therapy and to prevent TB. Till now 4344 DOTS center is providing TB diagnosis and treatment based on DOTS- TB control services. Among them, 4,204 are government health institutions and rest are been providing by different partner agencies of the National tuberculosis center . Tuberculosis preventive therapy has been providing through the DOTS center of 38 districts. In Kaski district there are altogether 65 DOTS center (DOHS, 2017).

National tuberculosis center has mentioned there is much need to be done for the prevention of TB among contact childhood and should improve initiation, completion for this risk group (NTC, 2017b). By the end of 2017, the total number of children enrolled in IPT were 745 children in 2017. Around half of the children eligible are not enrolled in preventive therapy (WHO, 2018d).

During the preliminary discussion with related stakeholders from SR organization, coverage of preventive treatment among exposed children is sub-optimal. It is difficult to enroll children in therapy. However, the rate of completion is satisfactory in a group who already initiate therapy. There are numbers of moderating

factors in adherence to preventive therapy among eligible children such as lack of education, family support, stigma, fear of side effects of the drug. Similarly, training, insufficient logistics supply, insufficient outreach services are the problem faced by the health care provider. However, reinforcement that is being provided to the patient (as transportation cost), contact tracer and health worker is remaining as an enabler in adherence to preventive therapy from both patient and provider side. Enrollment of children in preventive therapy is a challenging task that needs more counseling and more outreach activity. Considering this fact, it is important to study the implementation fidelity of the TBPT program from providers side and parents/caretakers of children and in Kaski district Nepal.

B. Relevance

Childhood TB was relatively neglected all over the world including Nepal. However, there has been an increasing concern about childhood TB in the last few years. WHO has developed Roadmap for Childhood TB in 2013 intending to achieve zero death due to TB in 2025. This emphasizes on contact tracing and provision of preventive therapy for childhood TB prevention. However contact tracing, IPT initiation and completion are not properly implemented in many countries (Belgaumkar *et al.*, 2018). According to the data reported from program implementation setting IPT initiation and completion rates were 21– 58% and 13% respectively (WHO, 2018e).

National childhood guideline in TB management has recommended preventive therapy among exposed children also in Nepal and started implementing it since 2017. There has not been any significant study conducted on the implementation fidelity of Tuberculosis preventive therapy in Nepal. In this perspective, this Implementation fidelity study provided information on what extent preventive program is being implemented.

This study measured adherence to TBPT through retrospective data analysis. Besides, explore the moderating factors associated with adherence to TBPT. Information obtained from this study would help the implementing bodies in addressing their problem and come up with necessary possible skills to deal with challenges.

C. Problem Statement

End TB strategy 2015, targeted to reduce incidence and number of TB death by 90% and 95% respectively by 2035, compared to 2015. It highlighted three major pillars to achieve target among them integrated, patient-centered care and prevention are one the major pillar of End TB strategy (WHO, 2015a). Therefore prevention of new Mycobacterium tuberculosis and their progression to active TB disease through the treatment of latent TB infection (LBTI) is a crucial aspect.

The national strategic plan for tuberculosis prevention and cure 2016 – 2021 in Nepal has an objective to increase childhood case notification to 10% by 2020. To achieve this objective Nepal has developed first Childhood Tuberculosis guidelines in 2016 which emphasize IPT for children in contact with TB for LBTI treatment and prevention of active TB. Implementation experience from different parts of the world shows that preventive therapy (antibiotic chemoprophylaxis) is an effective strategy and has underlying challenges. So this study assessed the adherence of TBPT from and identify moderating factors from provider side and parents/caretaker side.

D. Research Objective

General Objective:

To study implementation fidelity of Tuberculosis preventive therapy for under five children exposed to sputum smear-positive pulmonary Tuberculosis in Nepal

Specific Objectives:

1. To assess the adherence of TBPT program in terms of content and coverage
2. To explore the moderating factors in implementation of TBPT from providers side
3. To explore the moderating factors in initiation/not initiation and completion of TBPT from patients/caretakers side

D. Research Impact

This research attempted to identify adherence to preventive therapy among TB exposed children from parents/caretakers and provider side explore factors affecting implementation. This help in identifying gap and challenges in program implementation and suggest innovative ideas to mitigate them. Besides, these findings will be able to provide information on whether the implementation of the current guideline is effective or need revision.

E. Originality

Table 1. Originality of research

Author	Title	Objective and study design	Result
(Tadesse *et al.*, 2016)	Uptake of Isoniazid preventive Therapy among Under-five Children: TB Contact Investigation as an Entry Point	A cross-sectional study to assess the effectiveness of contact screening as an entry point for IPT implementation and treatment Study Design: Cross-sectional quantitative design	Of 221 children eligible for IPT, 64.3% (142) received IPT, 80.3% (114) of them completed six months of therapy.
(Belgaumkar *et al.*, 2018)	The barrier to screening and isoniazid preventive therapy for a contact of tuberculosis patients	To evaluate current status and barrier to screening and IPT provision among the contact of TB patients Study design: Cross-sectional quantitative	Nineteen 76% of HCP reported recommending child contact screening. Out of 28 children eligible children, only 8 (32%) reported ever prescribing IPT. Inadequate health care provider counseling, non-parents cases lack of postgraduate HCP counseling are some barriers.
(Gomes *et al.*, 2013)	Impact of isoniazid preventive therapy on mortality among children less than 5 years old following exposure to tuberculosis at home in Guinea-Bissau prospective cohort study	To compare mortality between exposed children on IPT and community control children, compare this relative mortality to the relative to the previously observed excess mortality Study design: Cohort Study	The mortality rate ratio comparing exposed children with and without IPT was 0.21 (0.0 to 1.1). The mortality among TB exposed children on IPT in 2005 -2008 was significantly lower than the mortality among TB-exposed children not on IPT in 1996- 1998
(Datiko *et al.*, 2017)	A community-based isoniazid preventive therapy for the prevention of childhood in Ethiopia	To assess the community-based approach to the provide IT at the level improves uptake and adherence in Ethiopia or not Study design: Prospective community-based cohort	Out of 3102 children under five years of contact with pulmonary tuberculosis 3204 were asymptomatic. Among them, 1761 were offered and accepted IPT due to the INH shortage. Of these, 1615 (91.7%) completed the 6-month course

(Indumathi *et al.*, 2014)	Evaluation of efficacy and adherence to INH preventive therapy in children at risk to develop active tuberculosis	To evaluate the efficacy of IPT in children who are exposed to adult pulmonary tuberculosis and in children with nephrotic syndrome having latent TB Study design: Prospective longitudinal study	Forty-three (86%) children completed six months of given INH treatment. Meantime of follow was 12.29 (13.13) months post-treatment. None of the participants who adhered to treatment developed active diseases. IPT is effective in preventing active diseases in both children in contact with infectious adults and those with nephrotic syndrome and latent infections.

CHAPTER II LITERATURE REVIEW

A. Literature Review

Tuberculosis Prevention Program

Prevention of new infection of Mycobacterium Tuberculosis and their progression to TB is a crucial aspect to achieve the target set in End TB Strategy for 2030 and 2035 and Sustainable Development Goals (SDGs) (WHO, 2018e). Preventive approaches for LTBI, prevention of transmission of M. tuberculosis through infection prevention and control and childhood vaccination with Bacille Calmette Guerin (BCG) vaccine (WHO, 2018c).

Treatment of Latent TB Infection

LTBI is a clinical condition without any evidence of active TB disease with the persistent immune response to M. Tuberculosis (WHO, 2018e). WHO updated guideline on the programmatic management of LTBI in 2018 strongly recommend in three priority group people living with HIV, under five years children with household contacts of bacteriologically confirmed pulmonary TB cases and clinically high risk groups, such as patients initiating anti-TNF treatment, receiving dialysis, organ/hematological transplantation and with silicosis (WHO, 2018c).

Treatment of Latent TB Infection among under five children

In 2017, an estimated 1.3 million of under 5 years children with household contact of bacteriologically confirmed pulmonary TB cases were eligible for treatment. There is an increase in the number of children who had started TB treatment by more than threefold from 87 242 in 2015 to 292 182 in 2017(WHO, 2018e). Latent TB infection can be identified using a tuberculin skin test or inferior gamma. Developed countries where frequent screening is possible, only children with a positive test result considered as infected an IPT will be initiated (WHO, 2015b). However, in countries with limited resources, all exposed children to pulmonary TB should start IPT irrespective of the test, once excluding active TB (Stephen M Graham, 2013). Children under the age of five years exposed to an adult with intrathoracic TB had a 66% higher mortality than unexposed children. Children exposed to tuberculosis who did not join in the isoniazid preventive therapy had 12-fold higher mortality (Gomes *et al.*, 2010).

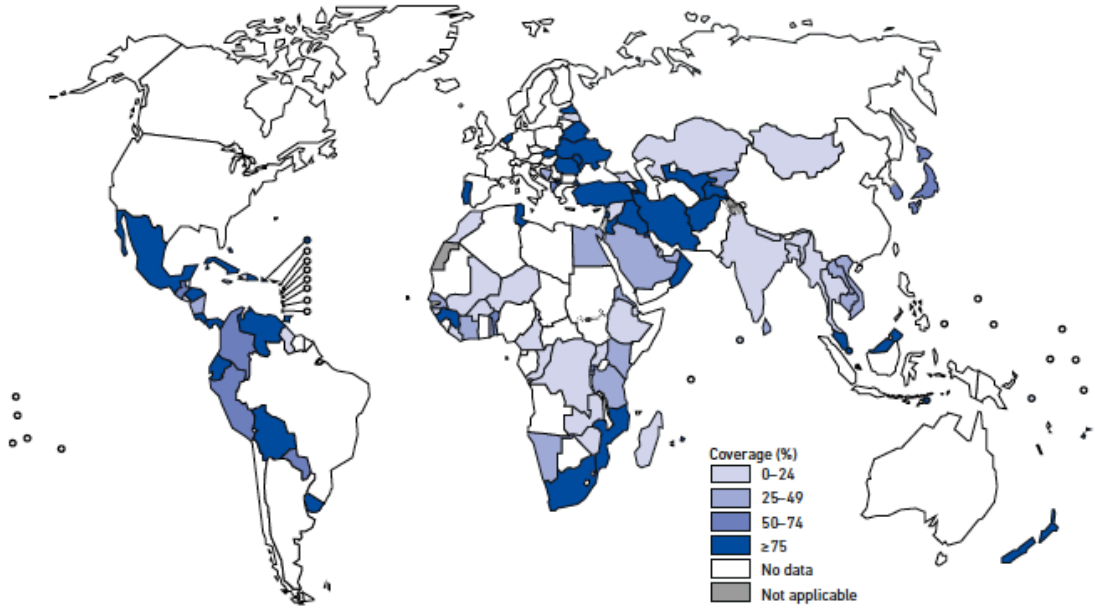

Figure 3: Coverage of TB preventive treatment among U_5 children (2017)

TB Infection Prevention and Control

TB infection prevention and control is one of the major components of the End TB Strategy. There is a high risk of TB transmission in health care and congregate settings which put health care workers at high risk of TB diseases, hospital-acquired infection and outbreak of drug-resistant (DR) TB in these settings (Gandhi *et al.*, 2012). So this requires the continuous assessment of TB infection prevention and control in all these setting and ensure that all measurements are taken appropriately. In this regards WHO has developed a policy for proper implementation of infection control by all stakeholders working in these settings (WHO, 2019b). In 2017, Out of the total of 9299 TB cases occurred among health workers from 65 countries, the majority of the case occurred in China (35%) and Brazil (11%) (WHO, 2018e).

In Nepal, TB infection control has been addressed by NSP-TB 2016/21 and several interventions are has been planned to achieve it. Recently, 17 DR treatment centers were provided with exhaust fan, Ultraviolet germicidal irradiation (UVGI), N95 mask and simple surgical mask as a part of infection control. Besides, all TB related training incorporate infection prevention sessions (NTC, 2017b).

TB vaccination

BCG is one of the effective vaccines to reduce the risk of infection with Mycobacterium tuberculosis and the risk of progression from infection to active TB disease. (NTC). In 2017, coverage of BCG vaccination was 90% in 120 countries among data available from 158 countries. Out of 30 High burden countries of TB coverage of BCG vaccine range from 53% in Nigeria to 90% in Bangladesh. Likewise, children immunized with the BCG vaccine was 87% in Nepal in 2016 (NTC)

Tuberculosis programmatic indicator for childhood preventive treatment

The proportion of under five years children who are household contacts of TB who completed contact investigation for TB, eligible for TB preventive treatment started treatment and who have completed a course of TB preventive treatment is the core programmatic indicator of IPT among children under five years of age (WHO, 2018c). LTBI among child contacts is among the top 10 core indicators for monitoring implementation of the End TB Strategy (WHO, 2014b).

Contact tracing

Young children are at increased risk of developing a severe form of tuberculosis such as (e.g. disseminated TB, TB meningitis) with 80% of death occurred in children under five years. Childhood TB is frequently being missed as the underlying cause or co-morbidity of children with different diseases (WHO, 2018b). Childhood case notification can be increased by a tuberculosis contact investigation. Contact investigation helps in early identification of active TB, which results in decreasing severity, reduce in the transmission of Mycobacterium tuberculosis to others and treatment of LTBI. Around 5-10 % of individuals with LBTI develop active throughout their lifetime and progression might reach 40% in younger children. (WHO, 2018c). A study on Uganda shows that contact tracing was able to identify a large proportion of culture-confirmed positive tuberculosis cases before the progression of diseases. Out of 761 contact children, the prevalence of tuberculosis was 10% among under 15 years' children. Cases were comparatively higher among under five years children than 5- 15 years children (61 cases [16.4%] vs 18 cases [4.6%]; $P < .001$) and 483 out of total 490 children started IPT did not develop the disease (Jaganath *et al.*, 2013). Contact screening is an important entry

point for the delivery of IPT to at-risk children. Out of 142 eligible children for therapy 114 children receive six months of IPT therapy. The research recommended it to be practiced as part of the routine program despite the implementation problem as part of childhood TB prevention strategy (Tadesse *et al.*, 2016).

Children eligible for preventive treatment

Children already treated with isoniazid preventive therapy cannot be protected from repeated TB infection. So children at risk should receive preventive therapy after each episode of TB exposure . Similarly, children with active TB should not give isoniazid preventive therapy. Asymptomatic children (playful and thriving, no cough or wheeze, no fever, no unusual fatigue or lethargy, no visible neck mass or gibbous) do not require additional tests to rule out active TB. These children can directly start preventive therapy of isoniazid. But, symptomatic children with (cough, wheeze, fever, lethargy, fatigue, weight loss, enlarged lymph node) should require TB examination such as Chest X-ray or persistent follow up for 1-2 weeks before enrolling in therapy (NTC, 2017a).

Adherence to preventive treatment (IPT)

Worldwide, many studies have been conducted based on acceptability, adherence, and feasibility of isoniazid preventive therapy among children exposed to pulmonary tuberculosis but till now this types of (implementation outcomes) studies has not been conducted in Nepal.

A Mixed-Method Study conducted in Bhopal, India showed that of 59 child contacts (<6 years) of 129 index patients, 51 were contacted. Out of them, 19 of 51 (37%) were screened for TB and one had TB. Only 11 of 50 (22%) children started IPT and 10 of 50 (20%) completed IPT. This shows that the proportion of children screened for TB and initiation of IPT is still low. However, the completion of IPT was good among those who initiate IPT (Singh *et al.*, 2017).

Another cross-sectional study conducted in Kigali, Rwanda to assess the uptake of IPT by eligible children. This study showed that among 270 children (under 15 years), who were household contacts of 136 index cases, 94 (35%) children were less than 5 years old and eligible for IPT; and 84 (89%, 95% CI 81–94) were initiated on IPT. The causes for not initiating IPT in the rest of 10 children were parents/caregivers' lack of information on the need for IPT, refusal to give IPT

to their children, and poor quality services offered at health centers (Birungi *et al.*, 2018).

A mixed-method study from Indonesia showed that out of 269 child contact involved in the cohort study, 99 were eligible for IPT. Among 99 eligible children, 13 (13.1%) refused the initial uptake, 36 (36.4%) did not complete 6 months of IPT and 50 (50.5%) complete 6 months of IPT. Those who take their medication form primary health care centers were more likely to have incomplete dose therapy than those who receive from the hospital (OR 2.9, 95%CI 1.1–7.8). This study shows that there is a need for improvement as only half of the patients completed the therapy (Triasih *et al.*, 2016).

A review of the retrospective record of review of infectious TB index patients aged ≥15 years in South Africa showed that out of a total of 261 registered child contact cases 184 (70.5%) were screened for TB, 2 initiated TB treatment and 108/184 (58.7%) started IPT. The rest of 74 (40.2%) children show no documentation of further enrollment in therapy Only 4 (3.7%) children completed the 24-week IPT course. Male patient and retreatment index patient had less liability to bring their children for screening ($\chi 2$=7.31; p=0.01; odds ratio (OR) 0.6; 95% CI 0.42 - 0.86) and $\chi 2$ =8.98; p=0.003; OR 0.41;95% CI 0.24 - 0.72) respectively (Black, F., Amien, F. and Shea, 2018). The dropout rate of children in each stage from case identification to completion of the full course of therapy is comparatively high. There suggested revising IPT guidelines with decreasing therapy duration which might increase adherence to IPT (Black, F., Amien, F. and Shea, 2018).

Barrier and Enabler in adherence to preventive treatment

Compliance remains an important barrier to effective chemoprophylaxis. IPT delivery to children remains an operational challenge in both low and high TB burden setting with limited resources. Common barrier in adherence IPT were lack of awareness, risk perception among parents, cumbersome screening process, isoniazid stock-outs, inadequate knowledge among healthcare providers and poor programmatic. Finding from the study recommend counselling of parents, training healthcare provider, simplifying screening procedure, ensuring regular supply of drug and development of IPT indicator strengthen and increase uptake of IPT (Singh *et al.*, 2017).

Lack of TB screening and IPT provision for child contacts were associated with an inadequate health care provider, counseling, a non-parent index case and a lack of postgraduate HCP qualification are some common challenges (Belgaumkar *et al.*, 2018). The uptake of IPT was significantly less likely when the index case was not the parent of the child contact. Contact may be located in diverse locations and far from the health facility (Hall *et al.*, 2015b; Birungi *et al.*, 2018). This suggests strategies to manage factors associated with IPT uptake which can facilitate timely TB screening and IPT for exposed children (Belgaumkar *et al.*, 2018; Birungi *et al.*, 2018).

Patients related factor in incomplete adherence to IPT were the length of IPT course, frequency and waiting time at the health facility, lack of social and family, stigma regarding TB. Whereas, belief about consequences, health information from health workers were some enablers that lead to a complete dose of therapy. No availability of syrup form of isoniazid (INH), Lack of confidence and knowledge of IPT, No guideline available and large flow of patients were the challenges reported from the provider side. There should be appropriate information about IPT and primary health care facility should be priorities to facilitate implementation with improved accessibility for caregivers to receive IPT at a primary health facility (Triasih *et al.*, 2016).

Another study conducted in Indonesia showed that respondents with good knowledge of TB disease transmission, the desire for the good health of children has good adherence with IPT and children from high economic status. However respondent with poor adherence mentioned that bitter taste of isoniazid, long waiting time at the health post, fear of staff, incorrect and insufficient information provided regarding IPT are some reasons behind poor adherence. The researcher recommended that dissemination of IPT provision increased awareness among caregivers increasing the availability of INH might increase adherence to IPT. (Rutherford *et al.*, 2012) .

Adherence to IPT among providers is influenced by contact tracing. Insufficient health manpower, lack of transport, poor reporting of TB cases and poor medical instar structure such as lack of diagnostic facility, insufficient logistics supply are the administrative factor for poor adherence. Besides, knowledge,

attitudes and practices, personal factors including lack of commitment and decreased motivation are provider individual factor. This suggests multiple factors that lead to poor adherence to IPT should balance accordingly (Tlale *et al.*, 2016).

Framework for Fidelity Implementation

Implementation fidelity is defined as the degree to which an intervention/program is implemented as it is proposed or as recommended in the approved protocol (Carroll *et al.*, 2007). It can be understand as whether intervention process is an effective realization of intervention as designed (Hasson, 2010) Five major dimension such as adherence to an intervention which can be influenced by other four variables such as quality of delivery, participant responsiveness, facilitation strategies, and program differentiation are been using in measuring fidelity (Hasson, 2010). Fidelity is evaluated through self-report, ratings, and direct observation and coding of audio and videotapes of actual encounters, or provider-client/patient interaction (Mihalic, 2002; Proctor *et al.*, 2010).

Adherence: Program adherence refers to the degree to which program components are delivered as prescribed by the model. Adherence data are typically reported as the proportion of program components that were delivered compared to the number prescribed (Associates, 2009). Adherence is further classified into content, frequency, duration and coverage (Carroll *et al.*, 2007).

Facilitation strategies: It optimized the level of fidelity achieved. It compromises the provision of manuals, guidelines, training, and monitoring and feedback for those delivering the intervention (Carroll *et al.*, 2007)

Quality of delivery: It measures if an intervention is delivered appropriately or not especially intervention techniques skills or approaches prescribed by the guideline, interest, readiness, and attitude (Carroll *et al.*, 2007). The quality of delivery may act as a moderator between an intervention and observed outcomes (Associates, 2009).

Program differentiation: Program differentiation can also refer to the process of identifying the critical components of a program that are essential for producing positive outcomes (Associates, 2009).

Participant responsiveness: It refers to the extent to which participant is involved in the program(Hasson, 2010). It is an important moderator in assessing implementation fidelity. An essential component of participant responsiveness include the level of interest/enthusiasm perceived belief, perceived usefulness of program, training, and support received (Carroll *et al.*, 2007)

B. Theoretical Framework

This study is based on the theoretical framework of the fidelity-outcome of implementation research. The Fidelity framework assesses the program dimensions as below;

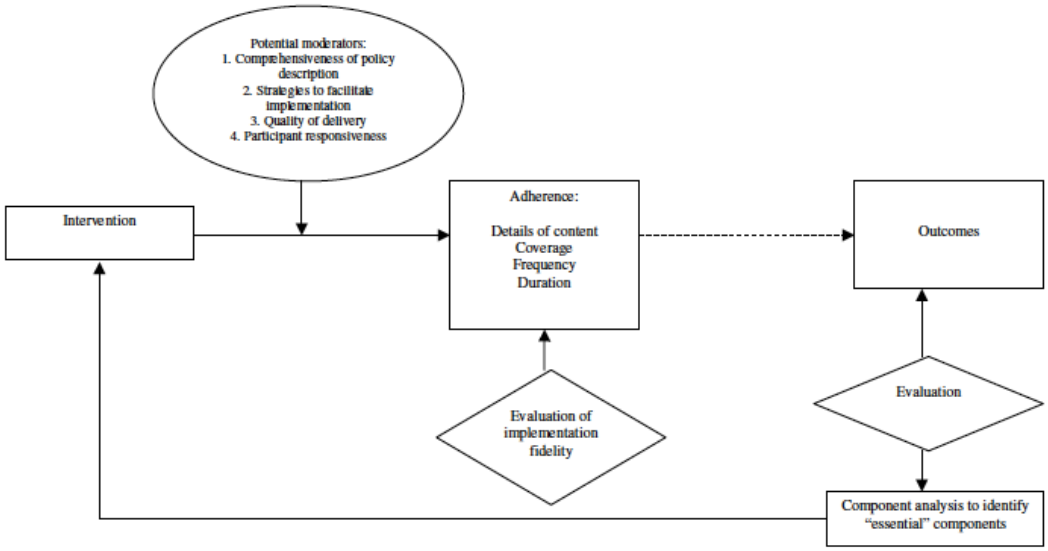

Figure 4: Implementation Fidelity framework (*Carrol* et.al *2007)*

C. Conceptual Framework

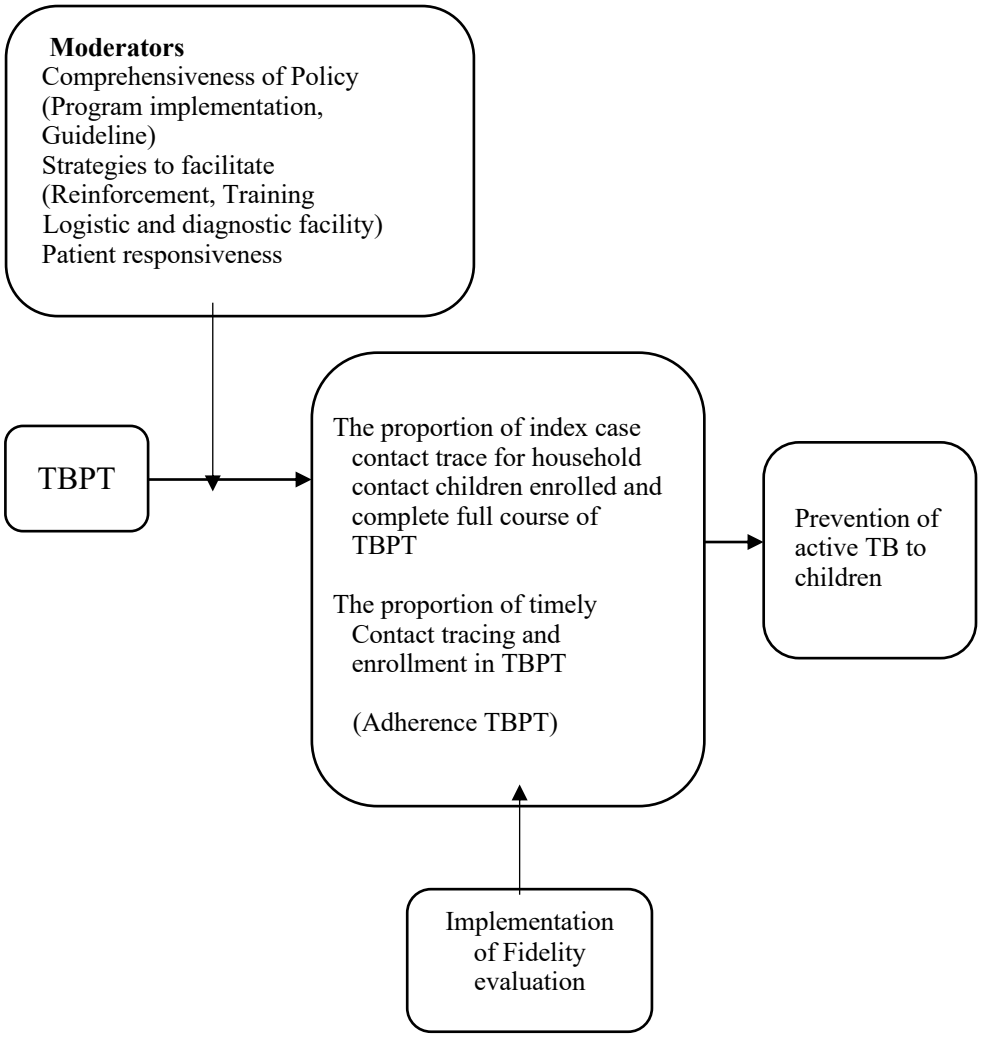

Figure 5: Conceptual Framework

D. Research Questions

1. What are the proportion of under five year children initiate and complete full course of TBPT?
2. What is the proportion of contact tracing, timely contact tracing and timely initiation of children in TBPT ?
3. What are the Moderating factors in implementation of TBPT from the providers side?
4. What are the moderating factors in initiation/not initiation and completion of TBPT from the patients/caretakers side?

CHAPTER III. RESEARCH METHODS

A. Research Type and Design

This study was mixed-method (explanatory sequential design), which involved a quantitative study followed by the qualitative study design.

Quantitative

Quantitative data was intended to analyze adherence of TBPT program through retrospective review of TB, contact tracing and TBPT register from April 2018 to May 2019 in Kaski district.

Qualitative

In the second phase, In-depth interviews (IDI) and focus group discussion (FGD) was conducted among parents/caretaker of contact children, service provider and contact tracer to explore the range of moderating factors that are responsible in adherence to preventive therapy in line with National childhood TB Management guideline.

B. Research Settings and Time

Nepal is a landlocked country with an area of 147181 square kilometers and a population of 26,494,405 (Central Bureau of Statistics 2011). It is divided into 77 administrative districts and seven provinces. Nepal has enormous geographical diversity ranging from an elevation of 194ft in the tropical plain to 29,029 ft in the mountain. From south to north transect, it is divided into three belts Terai (plain), hilly mountain and region. In terms of eco terrain region, the Terai belt reported more than half of TB cases (57%) followed by hilly (40%) and mountain (3%) region respectively (NTC, 2017b).

This study was conducted in the Kaski district of Nepal, as these districts well represent among medium TB burden districts from the hilly region of Nepal. Kaski district has medium notified bacteriologically confirmed PBC TB cases ie 242 including (New and Relapse) (DoHS, 2017. Kaski district is located in province 4 of Nepal with the population is 492,098 and an area of 2,017 square kilometers. The research was carried out from June to August 2019.

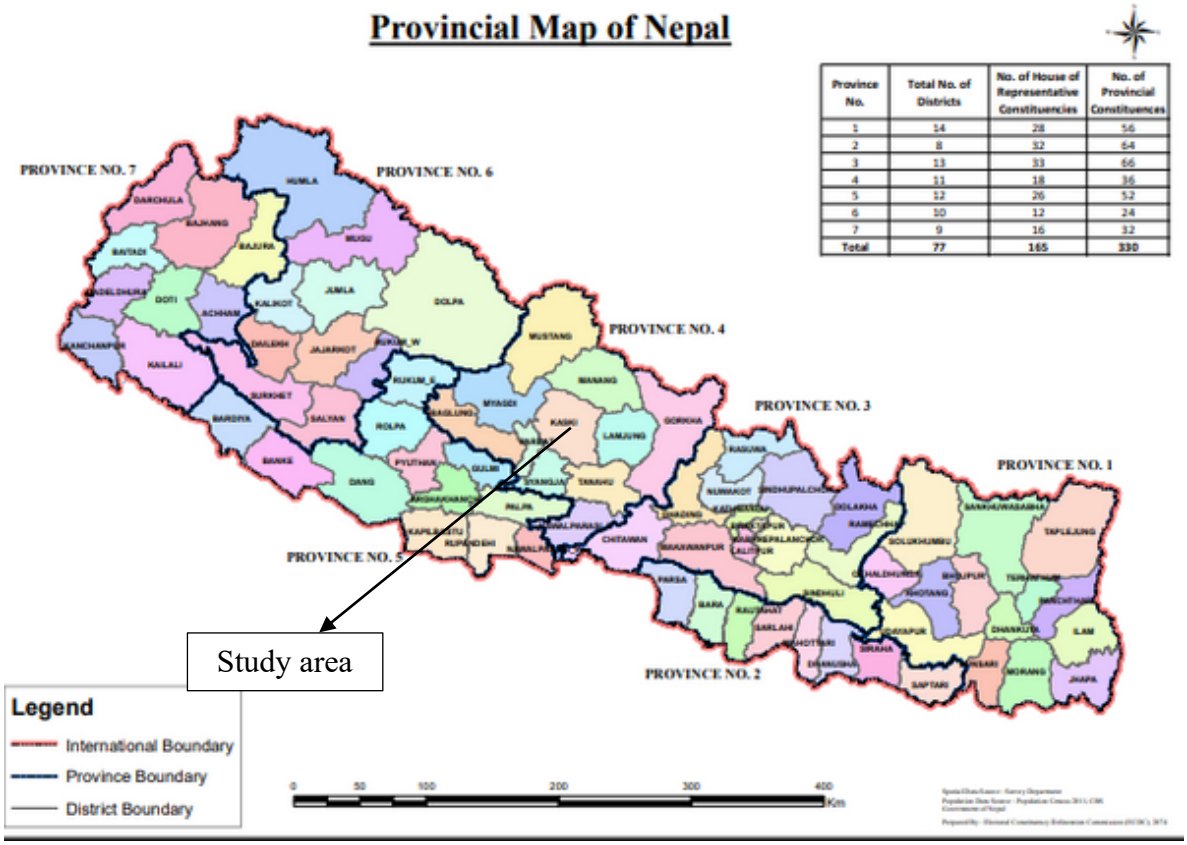

Figure 6: Study area (Kaski district of Nepal)

C. Research Subjects

1. Population

Quantitative

The unit of study for (TB, contact tracing and TBPT) register survey were all SS+ pulmonary TB patient, contact children and children initiate and not initiate in TBPT who were registered in Kaski district from April 2018 to May 2019.

Qualitative Study

The study unit for exploration of moderating factors was carried out among health care providers (HCP), contact tracers, parents/caretakers whose children initiated and not initiated therapy. Among initiated those who already completed full course of therapy and those in therapy were taken.

Inclusion Criteria:

- Six DOTS center providing preventive therapy for contact children

- Health care providers responsible for providing TBPT (Health assistant (HA)/ Axillary health worker (AHW) from DOTS center) , district-level TB focal person NGO representative was taken
- Contact tracer between the age of 18- 60

Exclusion criteria:

- Non-responsive study population
- Those parents/caretakers who cannot contact even after two attempts by the investigator were not included in the study
- Those who did not give informed consent to participate in the study

2. Sample Size

Quantitative:

TB, Contact tracing and TBPT register were surveyed. All registered TB cases, case index case trace for household contact, children contact with index cases, children initiate and not initiate therapy were extracted. Time of contact tracing and initiation of TBPT were also assessed.

Qualitative:

IDIs were taken among parents/caretakers, health care providers and one focus group discussion was taken among contact tracers from different health facilities to identify possible moderating factors. Qualitative data was conducted until saturation of information. The total number of sample size is involved is presented below:

Table 2: Sample size for IDI

Group of people	No of people
Parents/ caretaker of contact children who did not initiate their children in therapy	4
Parents/ caretaker of contact children whose children completed therapy	2
Parents/ caretaker of contact children whose children were under therapy	2
Health care providers (TB focal person, AHW/ANM)	6
District TB Focal person	1
NGO staff	1
Total	16

Table 3: Sample size for FGD

Group of People	Number of people	Round	Total number
Contact tracer	8	1	8

3. **Sampling Technique**

1. District sampling: One district with medium burden of TB was selected purposively.
2. Qualitative: Parents/ caretakers of children, health care providers and contact tracers were selected purposively for qualitative interview.

E. Identification of Research Variables

1. Adherence to tuberculosis preventive therapy (TBPT)
   (Proportion of index case traced, time timely traced)
   (Proportion of eligible children initiate, timely and complete the therapy)
2. Moderating factors in implementation of TBPT program
3. Moderating factors in initiation/not initiation and completion of TBPT
4. The implementation fidelity of this program. (Qualitative and quantitative)

F. Operational Definition of Variables

Table 4: Operational definition of research Variable

Type of Variables	Variable Name	Operational Definition	Measurement	
Quantitative Variable			Scale	Scoring
	Child contact	All the children less than 5 years of age who are in contact with smear-positive pulmonary TB case, who live within the household of the SS+ Pulmonary TB patient during his/her disease	Numeric	Percentage
	Adherence to TBPT program	Program or intervention content and coverage i.e., whether all the people who should be participating in or receiving the benefits of intervention do so.	Numeric	Perentage
	Timely	Within the intensive phase (2 months) after registration of TB cases in DOTS center	Numeric	Percentage
	Content and Coverage	Proportion of contact tracing of index cases, timely contact tracing Proportion of eligible children initiated , time of initiation, completed the full course of TBPT	Numeric	Percentage
	Provider adherence to guideline	To what extend provider are implementing the content of intervention Proportion of index cases screened, time of screening and eligible children timely initiate therapy	Narrative	Percentage
Qualitative variable				

	Moderating Barrier and enabler (fear/side effect, lack of family support, lack of logistic supply, training communication, guideline reinforcement)	A problem or situation that led problem in initiation/ completion and proper implement of therapy A situation or advantages that empower to initiate/complete and proper implementation of therapy	Narrative	Code
	Implementation fidelity Evaluation	Coverage of program by eligible children. The degree of intention program is delivered as intended.	Ordinal and narrative	Low implemented 0-50% Moderately implemented 51-79% Highly implemented 80-100%

G. Data Collection and Research Instrument

For the quantitative study, a secondary data collection checklist was designed and data were collected through tuberculosis preventive therapy register (TBPT), contact tracing register and TB master register from the district. Some data which were not available in the register were taken from the sub-recipient organization (NGO) providing technical assistant to this program. Data were retrieved on the programmatic indicator of TBPT such as initiation/not initiation and completion of full course of TBPT, contact tracing, time of contact tracing and enrollment in TBPT

Open structured questionnaire was developed to assess moderating factors in adhere to TBPT from parents/caretakers, health care providers, and contact tracers side. It assessed how well health care providers and contact tracers will rely on childhood TB management guidelines. The questionnaire was developed based on the algorithm of childhood contact case management at the health facility and community level and other components mention in the guideline. Thematic interview with open structured questionnaires were included. IDIs were conducted with health care providers and parents/ caretakers with/without their children enrolled in therapy. FGD was taken among eight contact tracers. To ensure the validity and reliability of information observation and triangulation was done. Qualitative data collection tool IDI and FGD guidelines were designed based on different literature review. Additional questions raised in the first few interviews were added later to the interview guide for future interviews. The interviews were recorded through the digital audio recorder.

H. Data Analysis

For quantitative data were double entered into Excel and double clean to minimize the error that could occur while retrieving information from different register. Then it was transformed into STATA 13 software for analysis. Descriptive analysis were done to establish frequencies and percentage. Level of adherence was calculate for individual components. The proportion of individual indicator which fall within the range of 0-50% were categorized as low implemented, 51-79 were categorized as moderately implemented and 80-100% were categorized as highly implemented (Nurjono *et al.*, 2019) .

For qualitative data, IDIs and FGD recording and handmade/fieldnote notes were transcribed. Then transcription will translate into the English language. Transcription and fieldnote will be cross-checked. Transcription was done on the same day of the interview to ensure the credibility and reliability of information gathered. Once the translation was done, appropriate code was developed for easy organizing and analysis of data. Generated codes were classified into meaningful categories. Synthesis of the category was done and themes were generated. For easy and fast understanding of qualitative information, data were presented in the form of a tree.

I. Research Ethics

Ethical approval was taken from the Ethical Review Board of the University of Gadjah Mada, Yogyakarta, Indonesia, and Nepal Health Research Council (NHRC). Permission was taken from, the National Tuberculosis Center (NTC). Informed consent was taken from each respondent before the interview. Children were not included in the study as information was gathered from parents/caretakers on behalf of children. Withdraw of respondents at any time from the study was acceptable. Anonymity and confidentiality of the individual participants were maintained.

J. Research Process

Research Preparation

Research preparation was started with writing proposals, proposal seminar and submitting the revised proposal at the ethical broad of Nepal Health research council and review board of Universitas Gadjah Mada. After getting ethical approval, administrative approval was taken from NTC and respective districts. Secondary data collection checklist and open structured questionnaire were designed for quantitative and qualitative data collection. Interview guides were shared among stakeholders and incorporated their feedbacks and suggestions.

Research Implementation

Study involved a quantitative study followed by the qualitative study design. Principal investigator (PI) was involved in collecting secondary data collection and IDI and FGD. Research assistants (RA) with public health and nursing backgrounds were involved in verifying of quantitative data collected and entered by PI . Besides, RA were involved in back translation (English to Nepali) to maintain the validity of quantitative data translation. The analysis was done by PI by discussion with supervisors.

Dissemination

After pre-data analysis, preliminary findings were disseminated among the district TB focal person, NGO level staff. However, the final report will be shared later to district public health offices, Save the Children International and NTC.

Stakeholder Response

NGO staff were not aware about how some of the indicator of program (enrolment in 3 and 4 months after TB registration) was running in grass root level. District focal person realize TBPT program is in shadow and they will definitely try to increase number of enrolment by overcoming challenges in future. However, district focal person added that provision of incentives and recruitment of NGO is from INGO and NTC side, so it should be taken into consideration from NTC/ INGO side.

K. Research Limitations

It relies on secondary data. So there was not sufficient information on children not initiated therapy. It has a limited sample size restrict establishing association between variable (i.e non enrolment with sociodemographic variable).

CHAPTER IV: RESULT AND DISCUSSION

A. Results

4.1 Quantitative part

Altogether, 310 SS+ pulmonary tuberculosis (index cases) were registered between April 1, 2018 to May 31, 2019 at Regional TB center in kaski district. Among them around one third 193 (62.17%) of the patients were male. The mean age ± standard deviation (SD) of registered patients was 41.99 ± 1.13 years with majority 168 (54.72%) from Janajati ethnic group. Detail description of sociodemographic and clinical characteristics of registered TB cases is shown in Table 5.

Table 5: Sociodemographic and Clinical profile of PBC cases registered in Kaski

Variables	Category	Number (n)	Percentage (%)
Total		310	100
Gender	Male	193	62.17
	Female	114	37.13
Age	0-14	8	2.61
	15-24	68	22.15
	25-34	53	17.26
	35-44	52	16.94
	45-54	38	12.38
	55-64	35	11.40
	>65	53	17.26
Ethnicity	Dalit	53	17.26
	Janajati	168	54.72
	Madeshi	3	0.98
	Muslim	2	0.65
	Brahmin/Chhetri	81	26.38
TB Category	New	243	79.15
	Relapse	46	14.98
	Treatment after lost to follow up	3	0.98
	Treatment after failure	3	0.98
	Previously treated history unknown	2	0.65
	Transfer In	10	3.26
HIV Status	Yes	8	2.61
	No	163	53.09
	Not documented	136	44.30

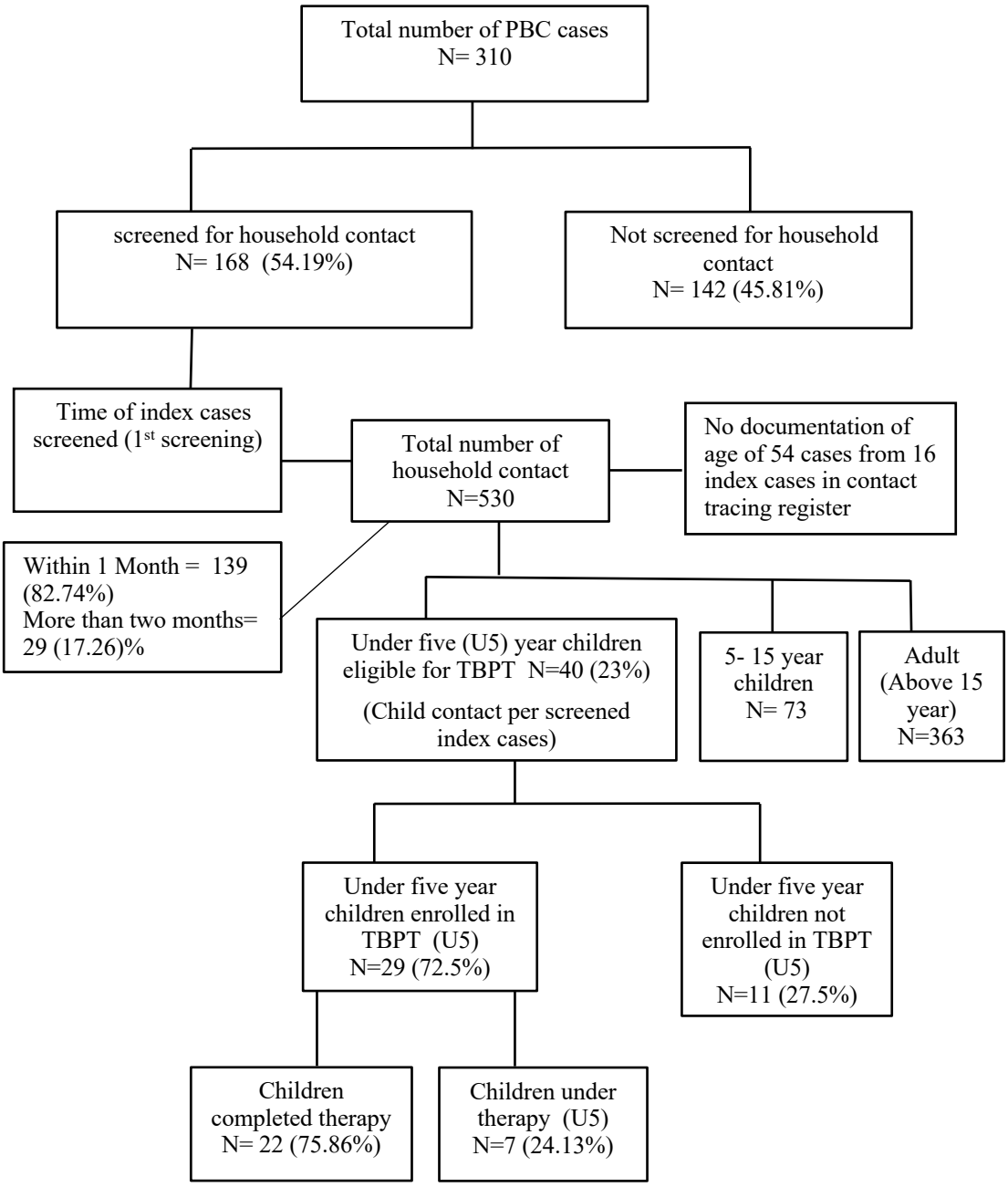

Figure 7: Flow chart of the program

Of the total PBC cases, 168 (54.19%)were screened for household contact and 147 (45.81%) not. Out of screened, most 139 (82.74 %) of the cases were contact traced within the intensive phase. There was no documentation of age in contact tracing register for 54 contact cases from 16 index. Of the children eligible for therapy only 29 (72.5%) children initiated therapy. Where 22 (76%) already completed course of therapy, 7 (24%) were under therapy and no any reported cases of withdrawal. Of children initiated therapy majority 20 (69%) were male. Only, 1(3.44%) child was HIV positive. Majority 25 (86.20%) of the children were initiated therapy within two months after registration of index cases whereas, initiation was recorded also in 3 and 4 months. The factor associated with not initiation in therapy is described qualitatively.

Table 6. Sociodemographic and clinical status of children initiate preventive therapy

Variables	Category	Number (29)	Percentages (%)
Gender	Female	9	31.03
	Male	20	69.96
Age	0-1	4	13.80
	1-2	12	41.37
	>2	13	44.88
Ethnicity	Dalit	9	31.03
	Janajati	10	34.50
	Madeshi	1	3.44
	Brahmin/Chhetri	9	31.03
HIV Status	Yes	1	3.44
	No	28	96.55
Relation with Index case	Father	8	27.59
	Mother	12	41.38
	Grandparent	7	24.14
	Other	2	6.90
Gap in Tb registration and enrolment in therapy	< Within two months	25	86.20
	>2months (3 and 4 months)	4	13.80
Education status of parents	< secondary level	13	44.82
	>secondary level	16	55.18

There were no reported information on children not initiated therapy. However, out of four IDIs done with parents/caretakers of children not initiated therapy showed that all of the parents were literate. All of them are HIV negative and belong to Janajati ethnic group. Among them, relation of index case with one child is grandparent and the rests are their own parents.

Table 7. Implementation fidelity of TBPT components

Content	Proportion (%)	Implementation Fidelity
Eligible children initiated TBPT	72.50%	Moderate
Completion of TBPT	75.86%	Moderate
Timely initiation of TBPT	86.20%	High
Contact tracing for household contact	54.19%	Moderately
Timely of contact screening	82.73%	High

Qualitative Part

After review of secondary data, we conducted in-depth interviews among 16 respondents including parents/caretakers of children, health care provider, TB focal person and NGO level staff. Health care providers were taken from six health facility (Regional TB center, District Hospital, 2 Health post, 1 urban health facility and urban DOTS center) community which has been providing TBPT services during the period of one year. One, FGD was organized among 8 contact tracers (female community health volunteers/cadres) working under respective health facility. Majority of the interviewee is less than 40 years with dominance of female participants.

Table 8. Socio-demographic characteristics of the respondents

Character	Categories	In depth Interview (n=16)	FGD (n=1)	Total
Gender	Male	5	0	5
	Female	11	8	19
Total		16	8	24
Age	<40	13	4	17
	>40	3	4	7
Education	Elementary	1	1	2
	Secondary/Technical health training	5	5	10
	Intermediate level	6	2	8
	Bachelor and above	4	0	4
Participants	Health care provider	6	0	6
	TLO (District Level)	1	0	1
	Program officer (NGO level)	1	0	1
	Parents/caretaker (Initiated children)	4	0	4
	Parents/caretaker (Not Initiated children)	4	0	4
	Contact tracers	0	8	8

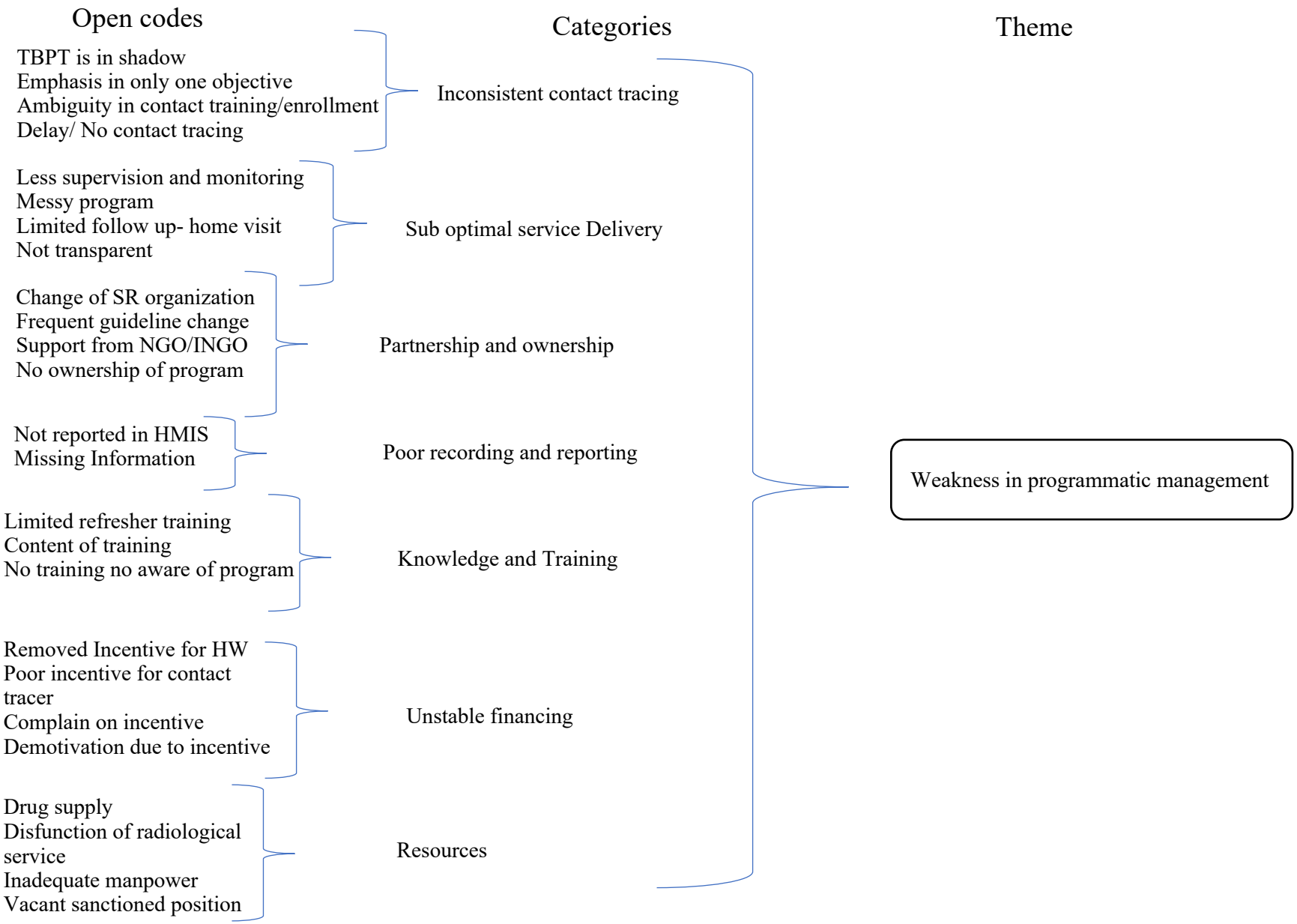

Figure 8: Moderating factors in Implementation of TBPT

2. Moderating factors experienced by Health care providers in Implementation of TBPT

A. Inconsistent Contact tracing and TBPT Enrolment

Study showed that, most of the index cases which were traced within the intensive phase were from RTC. An urban health centre, district hospital, urban DOTS and others health facility from rural areas centre were doing delay /no contact tracing of cases.

> *"Usually I have reached them within six months and sometimes even after completion of the therapy." (Contact tracer, 38 years, Female,)*

Health care provider in RTC is doing contact tracing of the cases from private DOTS centre because they were not given authority to provide this services. So RTC is taking responsibility of contact tracing and enrolment of eligible cases from private centre. Observation of the register showed that children from other health facility were enrolled in TBPT from RTC's initiation because respective health facility did not disseminate the information properly.

Except RTC, all the health facilities with a higher number of PBC cases were facing problems in tracing all of the cases. One of the health care provider from RTC also acknowledge this fact and added it is quite easy for identification and enrolment of eligible cases in RTC.

> *"I only look at TB programs and therefore more close to them. At other health centres, they have to look at different programs. The staff for TB is also less there. They don't give so much emphasis to TB which is why finding children is difficult for them*." (Health care provider, 42 Years, female)

Health care workers and contact tracers illustrated that contact tracing was difficult if index cases are from a different family. Two health care provider and all of the contact tracers has mentioned that movement of people as a barrier in reaching people for contact tracing. People staying in rent were more likely to move which affects contact tracing. Stakeholder also emphasized that the possibility of children enrolling in therapy is high if index cases are from the same family.

"Sometimes, the index case is not from the same family, the case stays on rent where he comes into close contact with the children, in such cases most of the children are left behind unenrolled." (District program officer, NGO level, 30 years Female)

"It is not difficult to trace people sharing kitchen but two or three families are living in rent in the same house, it is tough in such cases" (Contact tracer, 36 years, female)

District level TB focal person emphasized that prevention programs, despite having effective implementation policies has not been conducted satisfactorily. Two objectives of contact tracing (TB case identification and initiation of preventive chemotherapy if the child is healthy) has not been well understood by all. But, everyone even NTC is more concerned with TB case identification than prevention programs.

"We identified more than 250 pulmonary positive cases in a year. And moreover, if we screen them well, we can find 110-150 patients who need to be treated with TBPT, but we have given it to only 30-40 patients so far. The follow up in those patients is poor." (District TB focal person,56 years, Male)

"*These days NTC has been mostly focused on active case finding which might have put the preventive chemotherapy program in the shade." (District TB focal person,56 years, Male)*

B. Poor Service delivery

Contact tracers and health care providers mentioned that there is no proper supervision for this program from the district and national level. Supervision team just come to health facilities they have never visited the field with them.

"The current program is a mess. No supervision. We become more aware when there is supervision but when nobody comes we become carefree". (Health care provider, 44 years, female)

To ensure that the child is taking medicine, health care providers/contact tracers should do follow up visits after the child initiated the therapy. It was twice when drug duration was six months and now is once, as course changed into 3 months . And, based on the latest guideline, as it changed into 3 months of therapy. Most of the health care are aware of this but except from two health post none of them were doing home/follow up visit. This has been confirmed by the majority of parents, who stated neither health care

providers nor contact tracers did follow up home visit. However, they argued that health care providers asked whether children were given medicine or not.

> *Nobody has yet come to see if the child is taking medicines. They have never come. They keep asking when I go for receiving medicines in the health center but they don't visit us at home. (Aunt of a child, 18 years, female)*

Some health workers agreed that they had no time and enough manpower for the home visit and some did not feel the importance. However, they also reported they often asked parents when they come to DOTS.

> *"They have readily accepted the medicine, Therefore we have not visited them we don't think it is so important."(Health care provider, 36 years, Female)*

C. Partnership and ownership of the program

TBPT program is running in collaboration with NTC, Save the children (INGO) and SR (NGO) organization. Different SR organizations are responsible for providing technical support to the program under the INGO. The study found that collaboration with external development organizations acts as an enabler for proper implementation of the program.

> *"Coordination is obvious. The SR program is for technically strengthening the government. They have supported us well." (District TB focal person 56 Years, Male)*

In Kaski district, SR organization HERD had started working at first and then JANTRA took it over later. Contact tracers in FGD and TB focal person mentioned that frequent change of SR organization and guideline as a problem in the smooth running of program and patient are also affected. One of the contact tracers stated that because of gap in program, the people were deprived of its benefits.

> *"It was different with HERD. I worked for 5-6 months then. And then it disappeared. And then JANTRA came asking us to do contact tracing. Then, asked us to stop it in the middle and again restarted it after some time. It has affected timely contact tracing and enrolment in TBPT. (FGD respondents, contact tracer)*

> *"HERD had started it at first and then JANTRA took it over later. There was some gap in contact tracing between this period like for 3-4 months." (Health care provider, 44 years, Female)*

However, staff working in NGO has denied this and mentioned that HERD beforehand circulated messages and informed all the responsible health workers to continue the program but health workers didn't take ownership of the program. NGO staff further added some health facilities stopped contact tracing results in delay/no in contact tracing and delay in initiation.

> *"Sometimes they feel like it is not their program and stop working especially when some changes happen in guideline and supporting organization."* *(District program officer NGO level staff, 30 years, Female)*

D. Training and knowledge

One health care provider and selected contact tracers from each health facility were given a one-day orientation. While one contact tracer who was newly recruited didn't receive any training. The major content of orientation was contract tracing and screening, TBPT, home visit, recording and reporting, sputum courier, a dose of therapy, side effect. However, contact tracers and health workers argued that all contents were not discussed in detail and more emphasized on TB case identification than TBPT.

> *"Not much time is given for TBPT discussion. We just touched the topics. It would be better if there was a training regarding contact tracing IPT with full process and norms."(* Health care provider, 25 years, female)

All of the health care providers mentioned that training increased their understanding but since only one staff was trained from each health facility they were having difficulties in performing activities and others do not want to take the risk in their absence. One health care provider stated that one-day orientation which they received is from NGO and there still many health care providers who didn't receive training. She further added time discussed in TB modular training was also not enough. District TB focal persons also acknowledge that the district was not been able to conduct refresher training for many years and some health care provider in rural areas were unaware of the program.

> *"We have around 150 of them who have not received any training. We could not conduct refresher training for 5-7 years. The system of health staff is messed up" (District TB focal person, 58 years, Male)*

E. Poor recording and reporting

According to the guideline, after contact tracing each PBC cases contact tracers should record the information in contact tracing mobilizer register. Health care providers should then copy the same information again in the health facility contact tracing register and if there are any children eligible for IPT they should report again in the IPT register. This practice is done in most of the health facilities but information were missing. However, two health care providers mentioned that contact tracers use to miss some of the information in recording format.

> *"Contact tracer used to go for visits but used to miss some information in the form like age of the child, other family members, no signature. They only did half of the work. So we have a problem in maintaining health facility register"*
> *(Health care provider, 44 Years, Female)*

Observation of health facility contact tracing register has shown that in some health facilities there was no documentation of age. Similarly, there was no backup copy of the contact tracing mobilizer register in any health facility. Health care providers argued that NGO level staff carry contact tracing mobilizer register with them. It was found that there were not specific recording and reporting formats for contact tracing and TBPT in Health Management Information System (HMIS). The current format they were using was designed by NGOs. So health care providers report to NGOs. NGO level staff (Program officer) has mentioned that they have their online reporting software by which they report to INGO and through INGO it goes to NTC and they give a monthly report to District TB focal person. But observation has found that they were not doing the electronic entry of all cases they were manually generating a result and reporting through software.

"We don't have HMIS section for contact tracing and TBPT. We have been given a recording format by JANTRA for contact screening and TBPT. We have no idea how they've managed reporting at the national level. Other indicators of TB are recorded in HMIS."(Health care provider,36 years female)

F. Unstable financing

Recent revision in the guideline has deducted incentives for health workers for contact tracing which demotivate them to work.

"NGO used to give money for contract tracing but they slashed down I feel really bad about it. I have decided not to do contact tracing anymore."
(Health care provider, 42 years, Female)

G. Resources

This study found out that there was no problem in maintaining stock of medicine at the health facility. Health care providers maintained stock at the health facility according to the number of patients they have. When therapy was isoniazid only, NGO used to supply the drug. But now they received from Regional TB centre every month or quarter according to the need. There had not been such a situation where children had to skip medicine due to the shortage of medicine. Likewise, parents/caretakers of children also added that they did not face medicine in medicine supply. One of health care provider from RTC has mentioned that sometime disfunction of X-ray services in RTC was remaining as problem. This resulted parents in not seeking of X-ray services, as X- ray fee in private place is expensive

"There is no problem with medicine. JANTRA used to provide before as regimen changed RTC is providing"(Health care provider, 25 years, female)

Health care providers in Urban health centre and urban mentioned that there were limited sanctioned position of staff. But in RTC despite of sanctioned position of doctor there was no regular availability of doctor and paramedic have to operate service on behalf of doctor as sanction position of doctor is usually vacant.

"We don't have trained doctors in RTC, we have doctors for short term(on contract), they stay for 4- months and then leave this place. It's been nearly six months that not a single doctor is available, a paramedic has been looking after the place." (Health care provider, 42 Years, female)

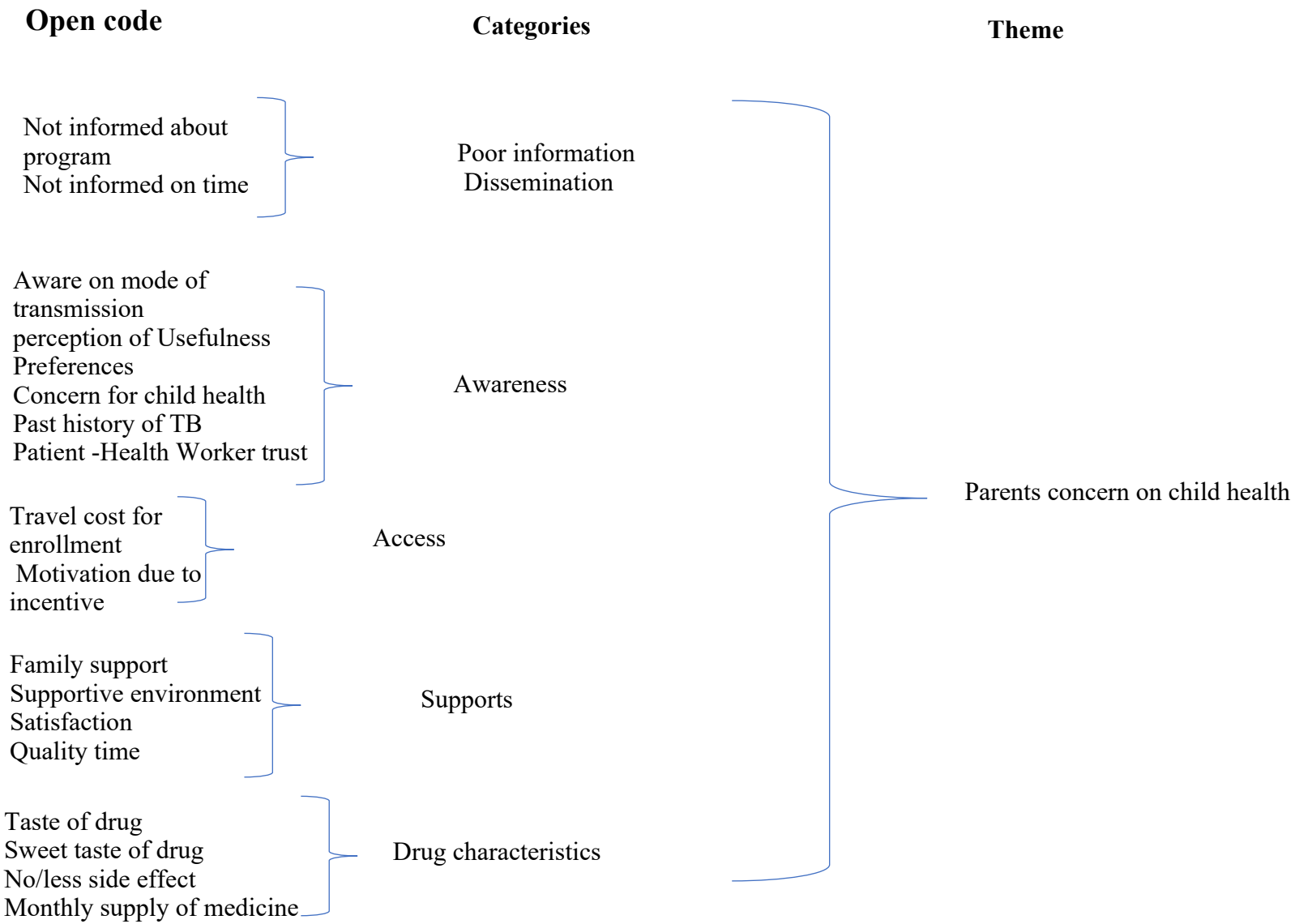

Figure 9: Moderating factors in initiation/not initiation and completion of TBPT

3. Moderating factors experienced by Parents/caretaker in Initiation/ not Initiation and completion of TBPT

A. Poor information Dissemination

All of the parents/caretakers whose children did not initiated in therapy have stated that neither HCP nor contact tracer counseled them about TBPT. They argued that HCP only focused on nutritional, psychosocial and drug adverse effects counseling. Furthermore, one parent stated that they didn't have a problem in enrollment if they could have informed on time. One of the respondents mentioned that their child was deprived of the important services that the child should have taken.

> *"Contact tracer counselled on the mode of transmission and inquired about other problems. She did not mention TBPT and I have no idea about giving medicines to the children." Mothers of a child, 24 years, Female)*

> *"If the doctor had told me to provide medicines to a child, there would have not any problem in doing" (Father of a child, 36 years, Male,)*

One health worker at RTC and district TB focal person agree to the fact that sometimes they don't have trained medical doctors so they can't convey information, whereas other health care provider denied it.

B. Awareness

The parents' understanding of the mode of transmission, prevention strategy and history of TB on family were enabling factors in initiation of therapy. The study found that these days patients are so much concern about their child's health. All of the health care providers added that irrespective of their good or poor knowledge, parents enroll their children if they were counseled properly.

> *"When I was a child, my daddy had TB, it got transmitted to my mother there was not such a program before like today so I got it now but I think that this TBPT will prevent direct transmission of TB to my nephew." (Aunt of a child, 18 years Female)*

> *The parents used to be quite reluctant before. After counselling, they understood the importance of the medication and accepted it. (Health care provider, 42 years Female)*

Perception of usefulness

Most of the parents/caretaker had perceived that TBPT is a good concept and prevent their children from having TB in the future. However one of the parents whose child was in therapy stated it is not sure that it prevents transmission. Health care providers have also taken the concept of TBPT as nice. They had observed improvement in the health status of children after the therapy. Contact tracers in FGd have also mentioned this program is good.

> *I don't know much about that. It is all about one's fate. If she stays healthy, it won't transmit to her. I don't think it will prevent the transmission at once.(Aunt of Patient, 30 years, Female)*

> *"I observed children gaining weight and looking healthier than before. The medicines have worked effectively which has made the parents very happy." (Health care provider, 33 years, Male)*

C. Access

All of the parents/caretakers and health worker has taken the provision of travel cost for children as a motivating factor for parents to enroll their children in therapy.

> *"It encourages. We should at least thank the government. I think it's better to have something than nothing." (Aunt of a child, 30 years, Female)*

Half of the respondents did not report distance to a health facility as a problem, whereas half (receiving form RTC and urban health center) perceived distance to a health facility as a problem. But in spite of long health distance, their children enroll in therapy. Likewise, insufficient human resources were also perceived as a barrier to the proper implementation of the program.

> "*It is quite far, I have to walk to Ranipauwa and then from there I have to get a bus. I have a problem to walk carrying the child." (Female, Mothers of child 23 years, Female)*

D. Support

The majority of the parents get support from their family, whereas one parent did not shared to share with the head of the family that their child was under

medication. Besides, participants experienced the role of a family member as a principal factor in the initiation of therapy. They further added that family support and suggestions matter a lot in enrollment.

Most of the respondents with their children in therapy were satisfied by the health care provider behavior. They mentioned that they were treated well and given enough time to clear their doubts. They felt that they were given more concern and frequently advise on the side effects of the drug and medicine will prevent transmission to their children. One respondent showed dissatisfaction with no regular availability of medical doctor but whenever the doctor was there they used to quality time and information. Respondents whose children were not enrolled in therapy were also happy with TB services available there but were not happy that they were not informed about this program.

> *"Behaviour of the health workers here is perfect. I was assured that no reactions would occur and if they did I was asked to come to the centre. She keeps on asking about my child." (Mother of the child, 25 years, Female)*

> *"They counselled me well but there are no doctors here now, which I think is wrong" (Father of the child, 36 years, Male)*

E. Drug Characteristic

All parents of children mentioned that the taste of the medicine and absence of side effects was considered as a crucial factor for the completion of a full course of therapy which is also confirmed by all of the health care providers.

> *“The medicine is just like the cotton candy, it melts in the mouth as soon as the child takes it. It tastes like a sweet chocolate”(Health worker, Female, 36years)*

> *"The medicines used to dissolve once put into the mouth. She liked its taste."(Mothers of a child who completed therapy, 23 years Female)*

There was not far reported the adverse reaction of drugs which act as an enabler in drug administration and completion, however, one child got minor allergy with the drug. All of the respondents mentioned that monthly availability of drug for children is making easier in continuation of therapy .

"At first I was quite a skeptic about giving drugs to the child, I thought the tablets would cause allergic reactions to the small child. Nothing like that happened to the child therefore, I am really happy." (Mothers of a child who completed therapy, 25 years Female)

Confirmation of the finding with preliminary discussion done with stakeholder

Results generated from our study is somehow similar with preliminary discussion with NGO level stakeholder where identification of eligible children is an challenging and once identified completion of therapy was not identified as problem. However, lack of education, poor family support was not identified as problem in our setting which is different than preliminary information which we gathered. New moderating factors we identified from our study were unstable financing, no/delay contacting, poor dissemination and change of NGO e.t.c

B. Discussion

This is the first study in implementation of Tuberculosis preventive therapy for under five years children exposed to pulmonary bacteriologically confirmed tuberculosis in Nepal. It involved review of secondary data which revealed that TBPT program. Review of secondary data revealed that majority 3 out of 5 components of the TBPT program were found to be implemented with moderate level of fidelity. The proportion of eligible children initiate and complete full course of therapy were in therapy 72.50% and 75.86% respectively with moderate level of implementation. The proportion of index cases traced for household contact, timely contact tracing and timely initiation of therapy were 54.19%, 82.73% and 86.20% which signifies moderate and high level of implementation. Under the qualitative part, two major theme were identified weakness in programmatic management and parents concern on child health. The major moderating factors identified associated with implementation of TBPT from providers side were unregulated contact tracing, sub optimal service delivery, partnership and ownership, poor recording /reporting, knowledge and training, unstable financing and resource available. Likewise, poor dissemination of information, awareness, access, supports and drug characteristics were potential the moderators identified from parents/ caretakers side.

Adherence of TBPT services

Our study showed that 72.5% of eligible children initiated therapy. Majority of them already completed it and some were still in therapy with no reported cases of withdrawment. In contrast, one study in India showed only 22% of eligible children were enrolled in therapy and 2% did not completed therapy (Singh *et al.*, 2017). Other study from Ethiopia illustrated that out of 221 eligible children more than three fifth 64.3% received preventive therapy, out of them 80.3% completed and 19.7% did not complete full course of treatment (Tadesse *et al.*, 2016). Completion of IPT was identified as major challenge in most of the study. Completion rate in our study was 75.86% which is higher than study done in pune, India and timor le state (Belgaumkar *et al.*, 2018 and (Hall *et al.*, 2015). Withdrawment was not reported as a problem in our study this is because all of the responsible parents/caretakers were literate. Besides, Government of Nepal is providing medicine free of cost medicine , travel cost for children enrolling in therapy. Furthermore, in study area parents were more concern on their children health.

Moderating factors in implementation of TBPT program

WHO has emphasized on two major dimension of contact screening first- to identify all contact cases of different ages group which are not diagnosed with TB among contact of an index case, second is to enroll all cases into preventive therapy for contacts without TB disease who are susceptible of having disease following recent infection (WHO, 2014a). Contact tracing is identified as feasible entry point for IPT initiation and completion by overcoming underlying factors associated with it However, in our study most of the health care providers and contact tracers were found to be ignoring this issue and focusing only one objective which is consisted to the finding from India where inadequate screening facilities was the programmatic challenges they has been facing (Singh *et al.*, 2017). Home based contact screening had to led significant improvement in contact tracing and IPT enrolment (Rekha *et al.*, 2013). However, our study found despite of health facility and community level contact screening strategies, enrolment is not satisfactory. This emphasized the issue how well contact tracing has been done.

Contact tracing is a crucial component for proper implementation and timely initiation of TBPT. According to the guideline, contact screening should be done twice (one in intensive phase one in the treatment phase) for each cases registered in given year. However, our study identified that delay/no contact screening as the barriers experienced by parents/caretakers whose children were not enroll in therapy. This is because of frequent change of guideline and working modality which demotivate health worker to take ownership to the program. This is consisted with study in India, where paramedical health workers were not identifying and refer eligible children for TB screening and IPT in accordance with national guidelines was not being followed (Belgaumkar *et al.*, 2018). Systematic review has highlighted socio-structural factor such as movement of TB patients has been identified as hinderance to parents/caretaker who wants to complete IPT to their children (Fox *et al.*, n.d.). This was experienced in our study by health care provider and contact tracer during contact tracing of the PBC cases. The RTC, located in study area is medical hub for seeking TB care, of western Nepal. People from different area come here and temporarily stay in rent for seeking health services. The fear of suffering and stigmatized from house owner and community has been a primary factor why TB patients don’t want to

cooperate in contact tracing resulting in no/delay in contact tracing. This is consisted with study conducted in Rawanda (Birungi *et al.*, 2019).

On the basis of implementation fidelity framework by Carroll, guideline availability and dissemination are included as one of the main fidelity components for enabling the program (Carroll *et al.*, 2007). Furthermore, the national guideline on childhood TB management provides detail procedure on how the services should be operated by health care providers, NGO level and district level. If program implemented as specified in the guideline it will be more effective and produce a higher level of adherence. Therefore, no availability of national guideline at health facility level has affected implementation of the program.

TBPT has guideline has emphasized on follow of home visit by health care provider to ensure that children are taking medicines but home visit was not going well. This is due to lack of sufficient human resources, health care provider perception that parents are aware and accepting medicine. Our study found poor supervision from district level to health facility and community level. However, supervision is considered to be an integral component of a TB control program as it contributes positively to the provision of quality TB services (USAID 2013b).

We found major gaps in maintenance of register, with missing of needed information (age, time of contact tracing). This is because of negligence as there is no HMIS for these indicator and contact tracers (volunteer) are doing recording at community level.

Inadequate knowledge among all health care providers regarding TBT was responsible for no/delay in dissemination of information. This is consisted with study in Indonesia where health workers were having difficulties to educate care givers about the rationale and need for IPT when the child is asymptomatic (Triasih *et al.*, 2016).

Moderating factors in initiation/ not initiation and completion of medicine

Sweet taste of drug was identified as key enablers in initiation and completion of full course of therapy which is completely different with study done in Indonesia where parents were having problem in drug administration due to the bitter taste. (Triasih *et al.*, 2016). Since government of Nepal is providing medicine free of cost,

purchasing cost was not reported as problem which is somehow similar with study in Indonesia where medication was included in the registration fee at primary health care (Triasih *et al.*, 2016). So purchasing was not reported as problem. In Timor-Leste, difficult terrain as main barrier for IPT, which has not been reported in our study however long distance to health facility was identified as problem.

Study found that side effect has great impact in parents/caretakers psychology. All of the parents were continuing therapy to their children, as no severe sign and symptoms were observed in children which is similar to in Indonesia (Rutherford *et al.*, 2012) where absence of sign and symptoms was identified as facilitator and only one children experienced side effect. Side effect of drug was also considered as important factor, in South Africa the adjusted odds of IPT completion was higher among who did not experienced side effect (Maharaj *et al.*, 2017). In contrast, in Guinea Bissau, despite of low adverse effect of drug there was problem in completion of IPT due to migration and travelling (Gomes *et al.*, 2011). In Indonesia, poor adherence is associated due to lack of family and social support (Triasih *et al.*, 2016). In contrast in our study, lack of family support is not a problem. Our study showed that non enrolment is associated to relationship with index cases this has been reported in most of the study (Birungi *et al.*, 2019).

Parents/caregiver understanding on TB diseases, belief on TBPT, their experience, suffering and past history of TB among immediate family were identified as enabling factor in initiation and completion of TBPT to their children. The insecurity of parents/caretakers that their children might get TB, was encouraging them in enrolment. This is consistent with studies in Indonesia and Rowanda where parents/caretakers with good understanding and experiences were identified as having good adherence (Triasih *et al.*, 2016 and Birungi *et al.*, 2019).

Study in Rawanda showed that the friendly, supportive health provider and information procedure have been identified as facilitators of IPT adherence (Birungi *et al.*, 2019). In our study, parents/caretakers whose children were enroll in therapy argued friendly environment and support from health worker as an enabling factor for initiation. In contrast, parents without children enrollment argued that they information were not disseminate properly. Patient's Satisfaction towards the program delivery mechanism is key for its effective implementation. Satisfaction toward the

program was influenced by health care provider behaviour, quality of time spend during counselling (USAID, 2013) which is implied in our study where respondents showed dissatisfaction in terms of availability of doctor. One study done in Nepal found that poor quality of communication between health professionals and patients was significantly associated with non-adherence to TB treatment (Mishra *et al.*, 2006) which is consisted to our study where children were deprived of services due poor communication of health care provider.

Government of Nepal has been giving travel cost to the children enrolled in therapy for motivation. Such practice is rarely seen in other countries. This could be the reason travel cost was not reported as problem in Nepal. In contrast one study (Rutherford *et al.*, 2012) has reported the travel cost is expensive than cost of medicine.

Our finding highlighted the challenges that weakness in programmatic management, basically in terms of ownership of the program, incentive and dissemination of information, which posed in implementation of the TBPT program in our setting. Our study provide insight to the implementer in other setting that NGO and INGO support should be there but government ownership is most important. Therefore, for stakeholder it is necessary to address this issue and achieve highest possible level of implementation.

Strengths our study is, it is mixed method (Sequential Explanatory) design. It provide quantitative evidence supported by qualitative results with several programmatic implications. Respondents were chosen purposively but it is expected to generalize within in district, as it tried to include different respondents from different health facility. But this study has some limitation. It is based on secondary data from TB register, contact tracing and IPT register. There were limited information with missing of information in register. Interview was taken among parents/caretaker whose children already completed medication, this might relates to recall bias. However, to address this issue, children in therapy were also taken.

CHAPTER V: CONCLUSION AND RECOMMENDATIONS

A. Conclusion

1. The majority of the TBPT program components were found to be implemented with moderate level of implementation fidelity.
2. The proportion of eligible children who initiated therapy were 72.5% and among initiated 75.86% completed full course of therapy. This signifies with moderate level of implementation.
3. The proportion of index cases traced for household contact, timely contact tracing and timely initiation of therapy were 54.19%, 82.73% and 86.20% which signifies moderate and high level of implementation.
4. Moderating factors identified associated with implementation of TBPT from providers side were unregulated contact tracing, suboptimal service delivery, partnership and ownership, recording-reporting, knowledge and training, unstable financing and resources .
5. Poor dissemination of information, awareness, access, supports and drug characteristics were the potential moderating factors identified from the parents/ caretakers side.

B. Recommendations

Government level Stakeholder

1. Effective sensitization program (i.e. training, orientation, and onsite coaching) should be enhanced by government level targeting all health facilities. This could increase government employee ownership to the program and importance of the TBPT program.

2. Government initiated supervision should be intensified to field and NGO level focusing on TBPT related indicators to ensure how the program is being implemented.

Health Care provider

1. Contact tracing of individual PBC cases should be done for more identification of eligible cases.
2. Health care providers and contact tracers should ensure proper/timely dissemination of required information.

NGO level Stakeholder

1. The issue of incentive sustainability should be addressed while updating the guidelines by cost evaluation of program.
2. TBPT related indicators should include in HMIS as soon as possible.

Researcher

1. Due to limited time we could not assess out how many eligible children were left behind enrollment from untraced PBC cases. So, further research could be done in this area.
2. Effectiveness of TBPT in prevention of childhood TB has not been studied our setting. So this could be assessed.

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APPENDIX

I. Information Sheet

Introduction

Before we start let me Introduce myself. I am Ashmita Ghimire. I am currently pursuing master degree in Public Health at Universitas Gadjah Mada. Right now, I am doing my research on TB prevention Program with Title entitle "Implementation fidelity of Isoniazid preventive Therapy for under 5 years children exposed to sputum smear positive pulmonary Tuberculosis in Kaski distrrict, Nepal.

This research relates to the implementation of tuberculosis preventive therapy (TBPT) for under 5 years process. It will review secondary data and will involve the parents/caretaker of under five years children exposed to sputum smear positive pulmonary Tuberculosis, health care provider, contact tracer and district to respondent open ended questionnaire.

Purpose

Tuberculosis preventive therapy for under 5 years children exposed to TB is a part on Tuberculosis prevention program of National tuberculosis center (NTC). The results from this study is expected to find moderators in adherence to Tuberculosis preventive therapy for under 5 years children. Therefore, information generated from here can be helpful to plan better preventive treatment services.

Sponsorship of services

This study is granted by World Health Organization (WHO) special master program in Implementation research of Tropical diseases.

Selection of Participants

This research expects the review of recorded from April 2018 to may 2019 registered in Kaski district. In addition parents/caretaker of under 5 years children who exposed to TB, health care provider, contact tracer and district level focal person will be included. Because your participation will become an outstanding contribution to the improvement in tuberculosis preventive therapy program for under 5 years. We want to interview about TB contact screening and enrolment process in tuberculosis preventive therapy for under 5 years. We would to ask you to join this research as the participant because you are health worker/ contact tracer/ district focal TB program/ parents caretaker of under five years children with whom this program is related.

Voluntary Participation

Participation in this research is completely voluntary and there is no compulsion. You are also entitled to choose whether or not to participate in this research. Your decision not to join this research will totally acceptable. If you are not interested in responding to the questions, you may quit the interview at any time.

Duration

We will ask you to participate in an in-depth interview which will take around 30-45 minutes of your time.

Risk and Discomfort

There is no risk as this survey solely to assess the Implementation fidelity of Isoniazid preventive Therapy for under 5 years children exposed to sputum smear positive pulmonary Tuberculosis in Kaski distrrict, Nepal. You do not have to answer any question or take part in the in-depth interview if you do not want.

Benefits

There will be no immediate and direct benefit to you, but your participation is likely to help us find out more about how well the fidelity of Tuberculosis preventive therapy TB contact for under 5 years in kaski district.

Confidentiality

We maintain the confidentiality of your information. The information that we collect from the study will not be distributed to anyone other than the research team. Your identity is also concealed in this study. If you are willing to participate in this study, you will be asked to give verbal consent witnessed by a witness that you choose and you trust to assist you. If you are asked for time to rethink, we provide the information sheet to be studied first.

Right to Refuse or Withdraw

There is no compulsion. You are also entitled to choose whether or not to participate in this research and during the research process, you also have the right to withdraw any time

Who to Contact

If there is something unclear with this research, you have the opportunity to ask me as a researcher by calling at number +977 9846330886 [Ashmita Ghimire] or email ashmi.gr8@gmail.com. You can also inquire about this research in the Research

Ethics Committee of Medical and Health Faculty of Medicine (Telp.9017225 from UGM) or 0274-7134955 from outside of UGM, or email: mhrec_fmugm@ugm.ac.id

II. Willingness approval

APPROVAL OF PARTICIPATION IN RESEARCH

I have been looking at this information, all explanations have been presented to me and all my questions have been answered by researchers. I concern to be respondents in this study, and I understand that if I need an explanation, I can ask Ashmita Ghimire as a researcher.

By signing this form, I agree to participate in this study:

Date

Name :

Sign of participant:

Name:

Witness signature

Secondary data collection checklist

Data extraction from TB register									
District:									
Fiscal Year:									
SN	TB Patients characteristics							TB characteristics	
	Name	Date of registration	Age	Sex	Ethnicity Code	HIV status	Documentation of ph number	Type	Treatment
1									
2									
3									
4									
5									
6									

Data Collection Sheet

Data extraction from Contact tracing register									Data extraction from TBPT register						
Fiscal Year															
District															
S.N	Name	Contact traced Status	Date of contact tracing	Total number of contact	Documentation of age of contact person	Total Number of under 5 years children	Total number of 5-15 years children	Adults Above 15 years	TBPT enrollment status	Date of enrollment	Age	Sex	Relation with index case	Education of parents	Therapy status
1															
2															
3															
4															

Questionnaire for Indepth Interview among Health care provider

1. How do you counsel SS+ patient? What are the information
   (probe : Household contact, under five years contact, TBPT)
2. Do you always ask SS+ patients if they have under five children in their home? Do you ask by yourself or hand over to contact tracer to visit home and trace?
3. What are you going to do if the SS+ patients refer that there are children five years living with them?
   (Refer to HF for further treatment, screen for TB)
4. What thing do you consider while screening for TB?
   (TB screening questionnaire, 4 sign and symptoms)
5. What will you if they don't have TB?
   (Enroll in TBPT)
6. What is your understanding on TBPT
   (Advantage, disadvantage, treatment procedure)
7. How do you counsel before enrolling in therapy?
   (side effect, Dose, duration, sign and symptoms of negative reaction)
8. For how long do you give medicine?
9. How do you find TBPT guideline?
   ((prob: clarity, simple, complex, rolling out eligible cases)
10. How do you ensure that children are taking medicine which you have given?
    (probe : homevisit, how often)
11. Is it easy/difficult to do home visit? Why easy/ why difficult?
    (probe: insufficient manpower, overload, insufficient time)
12. Do you give necessary information to contact tracer for contact tracing? With in how much time contact tracer visit patient home?
13. Do you properly make report data which contact tracer bring from community? What are barrier in recording and reporting?
14. Have you ever take training regarding this program? Do you think training is important? How long was the discussion session? Do you think that was enough?
15. How many health worker and contact are involve in this program. Is that enough? Do you think contact tracer are loyal to the program?

16. How is the collaboration between contact tracer, DPHO and SR staff?
17. What is your particular feelings and emotion about this program IPT?
18. What are the distracting factor in providing IPT services?
    (pro: overload tiredness, drug supply, diagnostic facility,)
19. Are you getting your incentives regularly? Do you think, these kind of reward encourage you for better performances?
    (probe sufficient, not sufficient)
20. Government is giving travel cost for children enrol in therapy? Do you think this encourage them to enrol in therapy. Is it important for patient. Or they enroll because they are aware?
21. According to you, what should be improved from the provision of IPT for under 5 years program in this PHC?
22. Do you want add something more?

Indepth Interview Questionnaire for Parents/caretaker whose children are not enroll in TBPT

1. Have you ever heard about IPT? IF yes, by whom ? What is your understanding about IPT?
   (probe: worthwhile, strength, weakness)
2. Did contact tracer, health provider counsel you about IPT? What did they say?
   (Probe: drug regimen, duration, where to get, how to take)
3. How often they visit your home?
4. Why didn't you start IPT to your children?
   (pro: distance to health facility, child don't like taste of medicine, relation with index cases ,fear of side effect)
5. What do you think about travel cost that government has been providing for children enrolling in IPT?
6. What is your family/husband perception about IPT? (pro support)
7. Have you ever communicate with parents/caretaker who do not enroll their children in IPT ? What are their suggestion?
8. Will you enroll in therapy if medicine is given community. What is your preference ?
9. Do you have anything to add?

Indepth Interview Questionnaire for Parents/caretaker whose children completed /under therapy

Questions

1. Have you ever heard about IPT? IF yes, by whom ? What is your understanding about IPT? (probe: worthwhile, strength, weakness)
2. How is you experience when bringing your children to the services?
3. Why you start and complete IPT to your children?
4. What do you think about travel cost that government has been providing for children enrolling in IPT? Does it motivated you to take services
5. What is your family/husband perception about IPT?
6. Have you ever communicate with parents/caretaker who do not enroll their children in IPT ? What are their suggestion?
7. Did contact tracer, health provider counsel you about IPT? How often they visit your home?
8. Are you satisfy with their service? (Probe: Counselling, follow up)
9. What would you suggest to improve quality of service?
10. Do you have any additional comment about IPT?

Focus Group discussion Guideline with contact tracer

1. What is your understanding about contact tracing? Do you contact screen all SS+ patient?
2. How do address issue of privacy and confidentiality during contact screening?
3. How fast do you do contact screening once SS+ case is registered in Health facility?
   (problem, particular experience, early and late date)
4. Have you ever heard about tuberculosis preventive therapy? What is your understanding?
   (Probe: Pros and cons, treatment regimen)
5. Have you ever enroll or refer under five years children for TBPT from your own effort?

6. Do you have any eligible children for preventive therapy but not enroll in therapy in your community ?
   (Probe: delay in contact tracing, lack of message dissemination)
7. Have you had any training for this program? Do you think training is important?
8. How is the support from health care provider ?
9. (probe: regularly providing detail of SS+ pulmonary Tb cases)
10. How do you find guidelines and SOPs regarding IPT?
11. (prob: clarity, rolling out eligible cases)
12. What are the distracting factor in IPT services?
13. (probe: convincing parents,)
14. Are you getting your incentives regularly? Do you think, these kind of reward encourage you for better performances?
15. What is your particular feelings and emotion about IPT?
16. What are the additional challenges/ you are facing?

Government of Nepal

Nepal Health Research Council (NHRC)

Estd. 1991

Ref. No.: 2996

16 May 2019

Ms. Ashmita Ghimire
Principal Investigator
Universitas Gadjah Mada
Indonesia

Ref. **Approval of thesis proposal** entitled **Implementation fidelity of tuberculosis preventive therapy for under 5 years children exposed to sputum smear positive pulmonary tuberculosis in Kaski district of Nepal**

Dear Ms. Ghimire,

It is my pleasure to inform you that the above-mentioned proposal submitted on **16 April 2019** (**Reg. no. 224/2019**) has been approved by Nepal Health Research Council (NHRC) National Ethical Guidelines for Health Research in Nepal, Standard Operating Procedures Section 'C' point no. 5.3 through Expedited Review Procedures.

As per NHRC rules and regulations, the investigator has to strictly follow the protocol stipulated in the proposal. Any change in objective(s), problem statement, research question or hypothesis, methodology, implementation procedure, data management and budget that may be necessary in course of the implementation of the research proposal can only be made so and implemented after prior approval from this council. Thus, it is compulsory to submit the detail of such changes intended or desired with justification prior to actual change in the protocol. Expiration date of this proposal is **January 2020.**

If the researcher requires transfer of the bio samples to other countries, the investigator should apply to the NHRC for the permission. The researchers will not be allowed to ship any raw/crude human biomaterial outside the country; only extracted and amplified samples can be taken to labs outside of Nepal for further study, as per the protocol submitted and approved by the NHRC. The remaining samples of the lab should be destroyed as per standard operating procedure, the process documented, and the NHRC informed.

Further, the researchers are directed to strictly abide by the National Ethical Guidelines published by NHRC during the implementation of their research proposal and **submit progress report in between and full or summary report upon completion.**

As per your thesis proposal, the total research budget is **$ 4,500** and accordingly the processing fee amounts to **$ 100.** It is acknowledged that the above-mentioned processing fee has been received at NHRC.

If you have any questions, please contact the Ethical Review M & E Section at NHRC.

Thanking you,

Prof. Dr. Anjani Kumar Jha
Executive Chairperson

Tel: +977 1 4254220, Fax: +977 1 4262469, Ramshah Path, PO Box: 7626, Kathmandu, Nepal
Website: http://www.nhrc.gov.np, E-mail: nhrc@nhrc.gov.np

MEDICAL AND HEALTH RESEARCH ETHICS COMMITTEE (MHREC)
FACULTY OF MEDICINE, PUBLIC HEALTH AND NURSING
UNIVERSITAS GADJAH MADA – DR. SARDJITO GENERAL HOSPITAL

ETHICS COMMITTEE APPROVAL

Ref. No. : KE/FK/0963 /EC/2019

Title of the Research Protocol	:	Implementation Fidelity of Tuberculosis Preventive Therapy for Under 5 Years Children Exposed to Sputum Smear Positive Pulmonary Tuberculosis in Kaski District, Nepal
Document(s) Approved and version	:	1. Study Protocol version 02 2019 2. Information for Subjects version 02 2019 3. Informed consent form version 02 2019
Principle Investigator	:	Ashmita Ghimire
Participating Investigator(s)	:	1. Prof. dr. Adi Utarini, M.Sc., MPH., Ph.D. 2. dr. Yodi Mahendradhata, M.Sc., Ph.D.
Date of Approval	:	16 AUG 2019 (Valid for one year beginning from the date of approval)
Institution(s)/place(s) of research	:	Kaski District, Nepal

The Medical and Health Research Ethics Committee (MHREC) states that the document above meets the ethical principle outlined in the International and National Guidelines on ethical standards and procedures for researches with human beings.

The Medical and Health Research Ethics Committee (MHREC) has the right to monitor the research activities at any time.

The investigator(s) is/are obliged to submit:
□ Progress report as a continuing review (state its due time)
□ Report of any serious adverse events (SAE)
☒ Final report upon the completion of the study

Prof. dr. Madarina Julia, Sp.A(K)., MPH., Ph.D.
Panel's chairperson

dr. Shinta Prawitasari, M.Kes., Sp.OG(K).
Panel's secretary

Recognized by Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP)
14-Aug-19