

Research Article

Factors Influencing the Practices and Adherence of Isoniazid Prophylactic Therapy Among Under 5 Years Children in Tb Referral Units, Peshawar

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Abstract

Importance: The under 5 years children of house hold contact with active tuberculosis cases is one of the main cause for the transmission of TB in pediatrics population, responsible for many complications and childhood mortality. **Objective:** To determine the factors influencing the practice and adherence of Isoniazid Prophylactic Therapy (IPT) among under 5 years children of house hold with cases of active pulmonary tuberculosis. **Design:** The study's design was cross sectional. **Setting:** This study was conducted in TB referral units of the National Tuberculosis Control Program in Peshawar City. **Participants:** The study participants included patients with sputum-positive pulmonary TB having at least one under-5 years' child in their household. Secondly, the doctors who were directly dealing with TB patients for diagnosis and treatments in referral units of the respective hospitals. **Results:** Most of the patients reported that doctors neither got some information about the under-5 years' children at their family nor to bring them for TB screening. Just 13.2% patients (36 out of 273) conceded that doctors mentioned them for prophylactic treatment with Isoniazid (INH) medication for their contact positive under-5years children. But only 4 of these 36 patients [(11.11%) 1.46%of the aggregate] completed the IPT course for their under-5 year children for 6 months duration. (Table 2) All the doctors claimed that they got information about the presence of under five years household contact in the family of TB patients. While the majority of the doctors/physicians (80%) had recognized that they neither requested the patients for screening from their family contact nor to give INH medication for their prophylaxis. This study showed that the practice of IPT was 13.2% and the adherence rate was just 11.11%, and the main factors for this poor result were poor healthcare system, lack of awareness, financial constraint and attitude of the patients. **Conclusion:** This study concludes that the extremely poor practice and adherence to isoniazid prophylactic therapy by doctors and patients in TB referral units in Peshawar city for under-5-year-old children of households with active tuberculosis patients was primarily caused by a lack of awareness, financial constraints, patient attitudes, and an inefficient healthcare system.

Keywords

House Hold, Contact Positive, Practice, Adherence

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1. Introduction

Tuberculosis is an old disease, having history of near 3 million years long. The Greek doctor Hippocrates called it with a name, "phthisis," or wasting sickness. [1] The word "tabes" for tuberculosis was used in Rome, [2] while in the ancient Hebrew (present Israel) it was known as "schachepheth". During the 1700s, TB was termed as "the white plague" because of the pallor of the patients. The current name (tuberculosis) was recommended by Johann Schonlein in 1834. [3] The ethological agent for this disease (*Mycobacterium tuberculosis*) was discovered by, Dr. Robert Koch in March 24, 1882. [4]

In 1948 when World Health Organization (WHO) came in to being, gave priority to TB because of the high burden of the disease throughout the world, combined with the realistic possibility of mass vaccination campaigns [5, 6]. As tuberculosis had turned into an illness of poor peoples — those proceeded with low access to health care services, overcrowding, lack of good sanitation, lack of education, and other social determinants of prosperity [7]. This likewise implied that TB got negligible consideration in the developed world until it reappeared in the late 1970s through 1990s [8]. A remarkable cases of tuberculosis found from this period in New York City, which has been associated to HIV infection. This resurgence took the ghost of TB back to the consideration of the world, and featured the significance of improved TB treatment and other TB control activities

According to world health organization the incidence rate of TB in 2015 was round about 10.4 million while its mortality was 1.8 million globally. Approximately 1.0 million cases which was almost equal to 10% of the total cases were evaluated in pediatrics population [9]. The largest incidence rate of tuberculosis (new cases of TB in 2018), 44% found in the South-East Asian region, followed by the African region (24%) and in the Western Pacific with 18%. Report also revealed that in 87% of new TB cases occurred in the 30 high TB burden countries. Two third of the total new cases reported in the India, China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh and South Africa. (WHO annual report 2018). The burden of pediatrics tuberculosis in high TB endemic zones is up to 10-20% [10]. Pediatrics population especially under the age of 5 year who are in contact to adults with active pulmonary TB (PTB) are more prone to acquire TB infection and disease progression because they are relatively immunocompromised [10-13].

In countries where Tuberculosis remained endemic the Isoniazid (INH) Preventive Therapy (IPT) among contact positive children and immunocompromised individuals has shown its efficacy to prevent new infections and inhibit progression from infection to TB disease and can reduce the incidence by around 40%-59% among Tuberculin Skin Test (TST)-positive individuals, therefore Isoniazid Prophylactic Therapy (IPT) is recommended to this vulnerable population

(14, 15). As cited above that the younger household contact positive and those who are absolute or relative immune-deficient are more susceptible to acquire TB infection, therefore World Health Organization (WHO) Stop TB Strategy states that those under-5 years children who have household contact (sputum smear positive TB patients) should be screened out to identify active TB infection, if found as infected will be treated as TB case otherwise should be started on daily Isoniazid Preventive Treatment (IPT) for 6 months duration. [16] but the practices and adherence of Isoniazid Preventive Treatment has been found very poor especially in high TB burden regions. Over all situation analysis shows that instead of that where isoniazid prophylactic treatment was the part of routine practice, only a minority of exposed children were started on prophylactic treatment, along with poor practice of IPT, it was also noted that the adherence rates tend to be less than 30% among those who did commence Isoniazid Preventive Treatment [17]. The reason for poor IPT in some of these high endemic zones was considered that the services of prophylactic therapy were limited to centralized hospitals and specialist clinics [18]. As the practice of Isoniazid Prophylactic Therapy is not fully exercised, and even if started the prophylactic therapy to the children exposed, the compliance and adherence has been found poor [19]. The effectiveness of Isoniazid Preventive Treatment is reliant upon 80% or more noteworthy to the adherence of the drug. A few studies from Indonesia, Ethiopia, Brazil and South Africa show low adherence to Isoniazid Preventive Therapy among under-5 year's children household contacts. Among these, the two research studies done in Indonesia reported that access, social support and regime, caregiver and health care related factors were hindrances to IPT adherence. Studies from Indonesia and Brazil additionally detailed that transportation and drug costs were related with deficient adherence [20]. In Pakistan some specialized centers routinely perform contact tracing, but not properly [21]. General practitioners (GP) and even specialists have a poor awareness of the WHO guidelines and do not adhere fully to the national treatment guidelines. Few initiatives were taken in Karachi Pakistan where team from Indus hospital started screening of under-5 years children from household of active contact, however even in a planned initiative only 32.6% completed treatment [16].

World Health Organization (WHO) has established guidelines and directed to National TB Control Programs (NTPs) of all the member countries (i) to screen out all under five years children who are with in household contact to active PTB patients and HIV-positive contacts of any age and (ii) to screen symptomatic child contacts 5–14 years for TB disease [22]. In the past 2 decades the incidence of Koch infection (tuberculosis) in pediatrics population are increasing and as the confirm diagnosis of tuberculosis in young children have many barriers,

therefore the management of those children who are contact positive to active TB case has key role in the prevention of TB infection, this is called as CCM (child contact management) program [23]. This is an important program for both preventive and curative purposes (Early diagnosis and treatment) [24]. The CCM program has been adopted by many WHO member countries but in the high burden regions (for TB) the implementation of this program faces many challenges, which causes the poor IPT practice and adherence rate. The aim of CCM program is to identify, screen out, and manage those children who are with in contact to active PTB cases. (Either to be treated as a case of TB or to be started on Isoniazid for prophylaxis). The steps of this program are resemble as for HIV case management cascade [23], i.e HIV Care Continuum Initiative in the United States [25]. According to a meta-analysis and systemic review done by Alsdurf and colleagues that HIV care steps should be applied for latent TB management for all ages to identify barriers and improve steps in the latent TB care cascade [26]. A Child Contact Management (CCM) is proposed for under-5 years children who have been presented to active TB patient in their household [27], but according to the WHO Just nine of 30 HBCs gave information for this new WHO Guideline. From the information accessible, only 7.1% of contacts started Isoniazid Preventive Therapy, which is far below the 90% target goal [23].

Study showed in developed and developing nations that the best methods for TB case detection are at the family unit contact level [28]. Screening takes into consideration for the identification of the individuals who are candidate for IPT and early recognition of active TB in family unit contacts of all ages. Potential screening apparatuses for tuberculosis diagnosis are: clinical examination, Sputum smear for Acid Fast Bacilli (AFB), tuberculin skin test (TST) or an interferon gamma release assay (IGRA), and chest X-rays [29]. These examinations have limitations in children: spitting up sputum for Acid Fast bacilli (AFB) examination in young children is very difficult task, in children TST or IGRA negative cannot rule out TB infection and vice versa (false negative and false positive) [30]. While chest X-rays in pediatrics patient having no clear finding of tuberculosis although infection is present. Screening of pediatrics population contacts in high-burden settings has been found poor. An absence of tuberculin and x-ray materials, absence of trained staff, the requirement for at least two appointment to complete screening, transport and time costs for the patients and their families and high healthcare worker (HCW) work load have been considered the main constrains for screening [31]. In Malawi, just 21% of adult sputum - positive cases with children in contact were educated about the need to screen their children, and just 9% of contact positive children of 365 adults who were positive for PTB were really screened for TB [32].

1.1. Adherence to Prophylactic Treatment

Poor adherence is an important barrier to Isoniazid Pre-

ventive Therapy programs, non-adherence may decrease treatment effectiveness by 50–80%. Recommendations for IPT duration are for 6 or 9 months, with large trials showing 6 months of treatment to be most beneficial when considering adherence rate. Factors associated with poor adherence include transportation costs, very young age (<1 year), living in large households, treatment duration, culture, knowledge and attitudes towards TB disease and IPT. [20].

1.2. Primary Caregiver Acceptability

The poor primary caregiver (PCGs) acceptability for TB preventive therapy of contact positive under-5 children is associated with lack of awareness about the IPT, cultural issues and poor health system. It has also been suggested that the importance of ongoing treatment of a healthy child is difficult to emphasize to PCGs for Isoniazid Preventive Therapy; one study found that 31% of PCGs did not believe their doctors when they were told that preventive treatment was necessary [33].

1.3. Rationale of the Study

TB and their consequences are currently most vital problems of public health worldwide. However, very little scientific investigation has been done in developing countries about the practices, adherence and the factors influencing the practice and adherence to Isoniazid Prophylactic Therapy among Contact –Positive under 5 years' Children. According to the knowledge of the author, limited research has been conducted in Pakistan on this topic among children.

This study would provide baseline data about the existence of practices, adherence and the factors Influencing the practice and adherence to Isoniazid Prophylactic Therapy among Contact –Positive Under 5 years' children and provide some guidelines to health authorities and public health department to take necessary steps regarding this issue to protect this vulnerable population from this serious problems.

1.4. Objective of the Study

To determine the factors influencing the practice and adherence of Isoniazid Prophylactic therapy among under 5 years children of house hold with cases of active pulmonary tuberculosis.

2. Methods

2.1. Overview and Data Collection

This cross sectional study was conducted in TB referral units in Peshawar city through Feb. 2019, after getting the approval from Institutional Review committee Khyber Institute of Child Health (KICH) and Advanced Studies & Research Board (AS&RB) of Khyber Medical University

(KMU). Sample size for the patient was calculated using WHO formula with 95% of confidence interval. A prior visit was done to all referral units in order to plan for the data collection. A team of two research assistance and principle investigator were involved in data collection. Consecutive sampling technique was used for data collection from 273 patients while for doctors (physician) the universal/census sampling technique was used.

The registered patients with active tuberculosis were identified and approach by the research team members. After taking informed consent, they were asked questions regarding presence of under-5 year's children at their house and about the status of Isoniazid Prophylactic treatment. Secondly whether their doctor have advised them to start Prophylactic treatment for their children. If they replied with Yes then, they were asked that whether they adhere to the prescribed protocol. If the patients reply with no, then they were further asked about factors leading to non-adherence of the regime.

Similarly, the doctors were asked about their practices. If they fail to advise these protocols, then they were asked about influencing factors leading to this failure.

Data for both patients and doctors were recorded on semi structured questionnaire. All data were kept confidential, only be used for the purpose of report writing and publication.

2.2. Data Analysis

The collected Data were analyzed using SPSS version 22. Results were subjected for appropriate statistical analysis. Descriptive statistics (mean, SD), were used to describe continuous data, categorical variables were presented in terms of proportions, percentages, frequency. The calculated Data were illustrated using Tables and graphs.

2.3. Results

As illustrated in [table 1](#) that among 273 patients, majority of the patient were in the age group of 30 to 40 years (65.2%) (Mean age of the patients in year 34.49 ± 6.81 SD) and most of the patients were male (77.3%) and married (83.9%). The frequency of illiterate patients was 53.8% and literate was 46.2%. Majority of the patients were middle class (50.2%) followed by lower middle class (49.8%). Majority of the patients (70%) had less than 3 children per household.

The percentage of doctors who were greater than 30 years of age was 70.0%. (mean age of the doctors in year 35.1 ± 6.33 SD) Majority of the doctors (80.0%) were male and were married (70.0%). According to graduation status, MBBS doctors were more in percentage (70.0%) than MD and 60.0% had not done post-graduation. All the doctors had done any special training for TB case management and 70.0% had attended workshops related to the training of TB case management. On the basis of experience as physician, half of the doctors had less than 6 years' experience and 80.0% doc-

tors had less than 6 years' experience at TB referral unit.

The majority of the patients (85.3%) reported that doctors did not ask them about the under-5 years children at their household and 85.72% patients also reported that doctors did not ask them to bring their children for TB screening while the remaining (14.28%) patients were asked by the doctors to bring their children for TB screening. 36 patients (13.2%) of the total participants admitted that doctors did request for prophylactic therapy with INH for their under 5 year children, however only 4 of these 36 participants (11.11%) completed the prophylactic treatment for their children. only 2 (0.73%) children were diagnosed as TB patients. 61.2% patients mentioned that they were not aware about the preventive treatment for their household contact while 35.89% had financial constraints. ([table 2](#))

All the doctors had positively responded to the question "Do you ask routinely about the presence of under 5-years child/children at the household of TB patients?" while most of the doctors had responded negatively to the questions such as "Have you advised the members of household for screening?", "Do you routinely provide NIH medicine to patients who have under-5 year children at their household?", and all (those 2 doctor who were practicing IPT) of the doctors had responded negatively to the question "Do the patients follow the instructions for screening and prophylaxes treatment?" According to possible reason for non-compliance, 2 out of 10 doctors reported that attitude of the patients was the possible reason for non-compliance. ([Table 3](#))

3. Discussion

The present study was a cross sectional study and was conducted in referral units of National Tuberculosis Control program in Peshawar City. The registered patients with active tuberculosis were identified and approached by the research team members. After taking informed consent, they were asked questions regarding the presence of under-5 year children at their house and about the status of Isoniazid Prophylactic treatment. Secondly whether their doctor have advised them to start Prophylactic treatment for their children. If they replied with Yes then, they were asked that whether they adhere to the prescribed protocol. If they patients reply with no, then they were further asked about factors leading to non-adherence of the regime.

Majority of the patients reported that doctors did not ask them about the under-5 years children at their household and 85.72% patients also reported that doctors did not ask them to bring their children for TB screening. Only 36 patients out of 273 (13.2%) admitted that Doctors requested them for prophylactic therapy with Isoniazid (INH) medicine for their under 5 years children contact positive. But only 4 of these 36 patients (11.11%) completed the course. The possible reasons that the child was not brought for screening and prophylaxis treatment, were lack of awareness and financial constraints. ([Table 2](#))

All the doctors had positively responded to the question “Do you ask routinely about the presence of under 5-years child/children at the household of TB patients?” while most of the doctors had responded negatively to the questions such as “Have you advised the members of household for screening?” and “Do you routinely provide INH medicine to patients who have under-5years children at their household?” and all doctors had responded negatively to the question “Do the patients follow the instructions for screening and prophylaxes treatment?” According to possible reason for non-compliance, 2 (Those who were practicing IPT) out of 10 doctors reported that attitude of the patients was the possible reason for non-compliance. (Table 3)

3.1. Those Studies Which Supported the Results of the Current Research Study

A hospital based study done in Malawi, which shows that only 7.7% of contact positive children to adult active pulmonary tuberculosis were brought for screening [34].

A large research study in Israel revealed the 28% of IPT practice and 16% of adherence rate among active PTB contact positive children [35].

In an Indonesia a study published which concluded that only 25.6% children completed the isoniazid prophylactic therapy for the duration of 4 months or more [36].

Table 1. Sociodemographic illustration of the patients and physicians.

| | | Count | Percentage |
|---|--------------|-------|------------|
| Age of the patient | <30 years | 50 | 18.3% |
| | 30-40 years | 178 | 65.2% |
| | >40 years | 45 | 16.5% |
| | Total | 273 | 100% |
| Gender of the patient | Male | 211 | 77.3% |
| | Female | 62 | 22.7% |
| | Total | 273 | 100% |
| Education status of the patient | Literate | 126 | 46.2% |
| | Illiterate | 147 | 53.8% |
| | Total | 273 | 100% |
| Socioeconomic status of the patients | Lower class | 136 | 49.8% |
| | Middle class | 137 | 50.2% |
| | Total | 273 | 100% |
| Marital status of the patient | Single | 26 | 9.5% |
| | Married | 229 | 83.9% |
| | Other | 18 | 6.6% |
| | Total | 273 | 100% |
| Number of children per household | <3 children | 71 | 26.0% |
| | children | 102 | 37.4% |
| | >4 children | 100 | 36.6% |
| | Total | 273 | 100% |
| Number of under 5 years children per house hold | <3children | 191 | 70.0% |
| | 3-4 children | 82 | 30.0% |
| | Total | 273 | 100% |
| Age of the Doctor | <30years | 3 | 30.0% |
| | >30years | 7 | 70.0% |
| | Total | 10 | 100% |

| | | Count | Percentage |
|---|----------|-------|------------|
| Gender of the doctor | Male | 8 | 80.0% |
| | Female | 2 | 20.0% |
| | Total | 10 | 100% |
| Marital status of the doctor | Single | 3 | 30.0% |
| | Married | 7 | 70.0% |
| | Others | 0 | 0.00% |
| | Total | 10 | 100% |
| Graduation status of the doctor | MBBS | 7 | 70.0% |
| | MD | 3 | 30.0% |
| | Total | 10 | 100% |
| Post-graduation | Yes | 4 | 40.0% |
| | No | 6 | 60.0% |
| | Total | 10 | 100% |
| Any special training for TB case management | Yes | 10 | 100% |
| | No | 0 | 0.00% |
| | Total | 10 | 100% |
| Type of training for TB case management | Workshop | 7 | 70.0% |
| | Diploma | 3 | 30.0% |
| | Degree | 0 | 0.00% |
| | Total | 10 | 100% |
| Experience (as physician) | <6 years | 5 | 50.0% |
| | >6 years | 5 | 50.0% |
| | Total | 10 | 100% |
| Experience working at TB referral unit | <6years | 8 | 80.0% |
| | >6years | 2 | 20.0% |
| | Total | 10 | 100% |

Table 2. Patient's response about the practice and adherence of IPT.

| | | Count | Percentage |
|--|-------|-------|------------|
| Have ever your doctor asked you about under-5 year children at your household? | Yes | 40 | 14.7% |
| | No | 233 | 85.3% |
| | Total | 273 | 100% |
| Did the doctor asked you to bring the child or children for TB screening? | Yes | 39 | 14.28% |
| | No | 234 | 85.72% |
| | Total | 273 | 100% |
| Did your child or children diagnosed as TB? | Yes | 02 | 0.73% |
| | No | 271 | 99.27% |

| | | Count | Percentage |
|--|---------------------------------------|-------|------------|
| Did you bring your children for prophylactic therapy | Total | 273 | 100% |
| | Yes | 36 | 13.2% |
| | No | 237 | 86.8% |
| Did you complete 6 months treatment with NIH? | Total | 273 | 100% |
| | Yes | 04 | 11.11% |
| | No | 32 | 88.89% |
| Why you did not bring your child for prophylactic therapy? | Total | 36 | 100% |
| | I was not aware nor advised by anyone | 167 | 61.18% |
| | Financial constraints | 98 | 35.89% |
| | Not applicable | 08 | 2.93% |
| | Total | 273 | 100% |

Table 3. Doctors, s response about the practice and adherence of IPT.

| | | Count | Percentage |
|---|------------------------|-------|------------|
| On average, how many patients you consult per day? | 30 | 5 | 50% |
| | 35 | 3 | 30% |
| | 40 | 2 | 20% |
| | Total | 10 | 100% |
| Do you ask routinely about the presence of under 5 year child at the household of TB | Yes | 10 | 100% |
| | No | 0.00 | 0.00% |
| | total | 10 | 100% |
| Have you advised the members of household for screening? | Yes | 2 | 20% |
| | No | 8 | 80% |
| | total | 10 | 100% |
| Even in case of non-compliance to screening, do you advise prophylaxes treatment for children? | Yes | 1 | 10% |
| | No | 9 | 90% |
| | Total | 10 | 100% |
| Do you routinely provide NIH medicine to patients who have under-5 years children at their household? | Yes | 2 | 20% |
| | No | 8 | 80% |
| | Total | 10 | 100% |
| Reason for not practicing the IPT? | No proper protocol | 6 | 60% |
| | Not applicable | 4 | 40% |
| | Total | 10 | 100% |
| Reason for poor adherence? | Attitude of care giver | 2 | 20% |
| | Not applicable | 8 | 80% |
| | Total | 10 | 100% |

3.2. Limitations of the Study

The three main limitations of the current study were:

- 1) Cross-sectional nature of the current study which can only determine the frequency and distribution of the outcome variable and cannot determine the causal relationship.
- 2) Non-probability sampling (consecutive sampling technique), due to which generalizability cannot be claimed for the results of the current study.
- 3) The current study was hospital based study and community based study will provide the true depiction of the current research problem.

3.3. Recommendations

Awareness campaigns for both the doctors in referral units of national TB program and for all the individuals in the community should be directed in order to promote the healthy practices among patients and doctors.

There should be proper health educational and promotional teams in the referral units of national TB program in order to provide all the information that is required for the benefits of the patient's health.

Proper monitoring precautions should be adopted for the doctors and patients, so that adherence of Isoniazid Prophylactic therapy among under 5 years children of house hold with active tuberculosis patients should be increased.

3.4. Recommendations for Future Research

Longitudinal studies should be conducted in order to get more in-depth information and true depiction of the problem.

Community based studies should be conducted to acquire more information of the patient's lifestyle and standard of living of the patients in order to seek the true picture of the problem and cope with the problem accordingly.

Qualitative research paradigm should be adopted to identify the in-depth and unique information about the problem in the community.

4. Conclusion

This study concludes that the extremely poor practice and adherence to isoniazid prophylactic therapy by doctors and patients in TB referral units in Peshawar city for under-5-year-old children of households with active tuberculosis patients was primarily caused by a lack of awareness, financial constraints, patient attitudes, and an inefficient healthcare system.

Conflicts of Interest

The authors declare no conflicts of interest.

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