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High Isoniazid Preventive Therapy Completion Rate among Household Contacts of Tuberculosis Patients in Duhok Province

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ABSTRACT

Background And Objective: Tuberculosis (TB) preventive therapy is a key intervention to achieve a world free of TB. We assessed the completion rate of isoniazid preventive therapy (IPT) among household contacts (HHCs) in Duhok province.

Methods: A cross-sectional study was conducted from April to September 2021 at the National TB Program Center (NTP). HHCs who were positive for the Tuberculin Skin Test (TST) and/or the Quantiferon TB-Gold Plus Assay (QFTPlus) with active TB cases were included in the study. A standard questionnaire was adopted for sociodemographic and clinical characteristics. The HHCs receiving INH therapy were advised to continue the treatment for 6 months under regular monthly follow-up.

Results: Of a total of 181, 134 (74.04%) were accepted and completed the treatment, whereas 47 (25.96%) declined IP. 41 (22.7%) of the LTBI-positive HHCs were among the 25–34 age group. The IPT completion rate in males (58.2%) was slightly higher when compared to females (42.4%) without a significant difference of p value 0.92 (OR 0.96, 95% CI 0.49–1.89). No differences were noticed among smokers, alcoholics, diabetics, or those on immunosuppressive treatment.

Conclusion: There was a high rate of LTBI completion with an excellent drug safety profile among the HHCs in Duhok province. Therefore, it is an essential component of the TB program to offer chemoprophylaxis to LTBI HHCs with regular follow-ups. Furthermore, there were no significant associations between age group, gender, smoking, alcohol consumption, DM, and immunosuppressive therapy, with the completion rate of IPT.

Keywords: *Tuberculosis, LTBI, Isoniazid, household contacts*

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INTRODUCTION

Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is the deadliest microorganism documented in human history. A recent World Health Organization (WHO) report estimated that the number of deaths was raised from 1.2 million in 2019 to 1.3 million in 2020, reversing years of global progression aimed to reduce deceased TB cases [1].

TB spread when individuals infected with TB expel the bacteria into the air. Infection with TB manifests as either a latent infection or disease. TB disease commonly affects the lungs resulting in pulmonary disease, but other sites are not exempt. While latent TB infection (LTBI) is known as a state of predominant immune response to stimulation by antigens of Mtb without evidence of clinically apparent active TB [2]. Approximately 2 billion people, equivalent to a quarter of the world's population, have LTBI. If left untreated, 5 – 10% of cases develop into TB disease, usually occurring within the first 5 years [3].

However, the likelihood of developing TB disease is higher among special populations such as close contacts, HIV people, diabetics, organ transplantation recipients, immunocompromised patients, chronic renal failure, smokers and alcohol consumers [4] Close contacts, particularly household contacts (HHCs), are at a paramount risk for LTBI because they share the same airspace with TB patients in a congregated setting for a prolonged period of time [5]. Accordingly, the WHO recommended TB preventive therapy as a key intervention to achieve a world free of TB. The popular regimen for treating LTBI is isoniazid (INH) and rifampicin (RMP), either separately or in combination [1, 3].

INH is commonly used for killing Mtb by inhibiting the synthesis of bacterial cell wall, hence used for the treatment and prophylaxis of TB. Since 1965, the American Thoracic Society (ATS) guidelines recommended the use of INH as a first line option, particularly in high risk individuals [6]. Six months of isoniazid preventive therapy (IPT) is strongly recommended for HIV- negative LTBI patients in a daily dosage of 300 mg to reduce the risk of TB reactivation [7]. The objective of this study was to evaluate the completion rate of IPT among 181 HHCs who tested positive for LTBI and had interactions with active TB

MATERIALS AND METHODS

Study Setting

The National TB Program Center (NTP) or Tuberculosis Respiratory Diseases Consultation Center (TRDCC) is a specialized healthcare institution for the treatment and monitoring of respiratory diseases including TB, which serve as a primary center in Duhok and its 6 districts. The facility has a pharmacy (mostly for anti-TB medications), an X-ray unit, and a laboratory. To manage TB cases, the center follows the DOTS program according to the WHO recommendation.

Study design, subject's enrollment

A cross sectional study was conducted for six months (from April to September 2021). In the current study we aimed to assess the IPT completion rate among 181 positive HHCs who had interactions interaction with active TB cases [8]. The diagnosis of LTBI was performed by Tuberculin Skin Test (TST) and/or Quantiferon TB-Gold plus assay (QFTPlus). All HHCs who tested positive for LTBI were offered IPT. To collect data on the sociodemographic and clinical traits of HHCs, a standard questionnaire was adopted.

Isoniazid preventive therapy regimen

The HHCs were instructed for a daily dose of 300 mg of INH for 6 months [9]. The HHCs receiving INH therapy were advised to continue the treatment for 6 months under regular monthly follow-up. Treatment was considered completed when the patients finished the 6 months of follow-up regimen.

Statistical analysis

Data were analyzed by using Statistical Package for the Social Sciences 27 (SPSS 27; IBM; USA), the findings of our study were described in

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frequencies and percentages. Chi square test or binary logistic regression was used for comparison characteristics to IPT treatment completion. P value of 0.05 was considered statistically significant.

RESULTS

Out of total 181 HHCs who tested positive for LTBI, 41 (22.7 %) belonged to the age group of 25-34 years, followed by 35 HHCs (19.3%) from the age group of 35-44 years. Considering gender, there were 105 (58 %) males among the LTBI positive HHCs. There were 49 (27.1 %) smokers and 13 (7.2%) alcoholics among the infected HHCs. Additionally, 4.4% of the LTBI positive HHCs reported having diabetes mellitus (DM). Moreover, 9 (5%) of the HHCs were taking immunosuppressive medication, including 5 patients with Rheumatoid arthritis, 2 kidney transplant recipients, and 2 patients with Crohn's disease. (Table 1).

Among the 181 positive HHCs, 134 (74.04%) accepted IPT, whereas 47 (25.96 %) declined the treatment (Figure 1). The HHCs who underwent a 6-month therapy of INH did not report significant side effects.

Higher acceptance rate was recorded among the age group of 25-34 years at 22.4 %, but there was no statistically significant association (P value 0.25 OR 2.72, 95 % CI 0.47-15.58). The IPT completion rate was higher in males (58.2 %) compared to females (42.4%), but the difference was not statistically significant (p value 0.92, OR 0.96 95 % CI 0.49- 1.89). Additional details are shown in table 2.

TABLE 1: Sociodemographic and clinical characteristics of the study population

Characteristics	Total (181) No. (%)
Age (year)	
1-4	6 (3.3)
5-14	20 (11)
15-24	33 (18.2)
25-34	41(22.7)
35-44	35 (19.3)
45-54	22 (12.2)
55-64	19 (10.5)
≥ 65	5 (2.8)
Gender	
Male	105 (58)
Female	76 (42)
Smoking	
Yes	49 (27.1)
No	132 (72.9)
Alcohol consumption	
Yes	13 (7.2)
No	168 (92.8)
DM	8 (4.4)
Yes	173 (95.6)
No	
Immunosuppressive therapy	
Yes	9 (5.0)
No	172 (95.0)

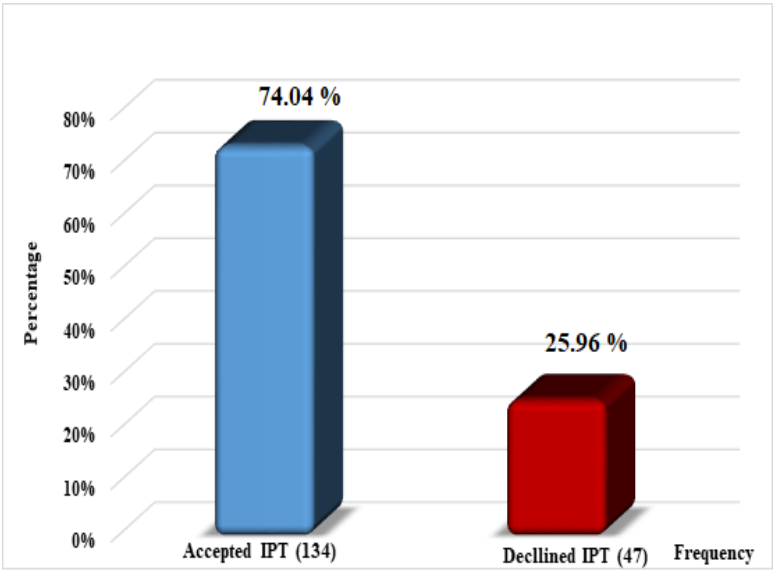

FIGURE 1: IPT completion rate of the total population (181)

TABLE 2: Univariate analysis of HHCs-level clinical and socio-demographic characteristics, by IPT completion status

Characteristics	IPT*		P- value	OR (95 % CI)
	Accepted No. (%)	Refused No. (%)		
Age (year)				
1-4	3 (2.2)	3 (6.4)	Reference	
5-14	15 (11.2)	5 (10.6)	0.25	3.00 (0.45-19.92)
15-24	25 (18.7)	8 (17.0)	0.21	3.12 (0.52-18.66)
25-34	30 (22.4)	11 (23.4)	0.25	2.72 (0.47-15.58)
35-44	27 (20.1)	8 (17.0)	0.18	3.37 (0.56-20.09)
45-54	17 (12.7)	5 (10.6)	0.20	3.40 (0.51-22.40)
55-64	14 (10.4)	5 (10.6)	0.28	2.80 (0.41-18.68)
≥ 65	3 (2.3)	2 (4.4)	0.74	1.50 (0.13-16.54)
Gender				
Male	78 (58.2)	27 (57.4)	0.92	0.96 (0.49-1.89)
Female	56 (41.8)	20 (42.6)		
Smoking				
Yes	35 (26.1)	14 (29.8)	0.62	1.20 (0.57-2.50)
No	99 (73.9)	33 (70.2)		
Alcohol consumption				
Yes	11 (8.2)	2 (4.3)	0.36	0.49 (0.10-2.32)
No	123 (91.8)	45 (95.7)		
Diabetes mellitus				
Yes	4 (3.0)	4 (8.5)	0.11	3.02 (0.72-12.61)
No	130 (97.0)	43 (91.5)		
Immunosuppressive therapy				
Yes	5 (3.7)	4 (8.5)	0.19	2.40 (0.61-9.34)
No	129 (96.3)	43 (91.5)		

*Count within treatment

DISCUSSION

In the present study, the IPT acceptance rate was higher (74.04%) than another study conducted on 400 healthcare workers (HCWs) from the same province [10]. The acceptance rate of INH was 63.3% in the later study. The lower refusal rate (25.96%) in our study is pertained to investigating general population; whereas, Almufty et al. [10] investigated the HCWs, as they are generally reluctant to prophylactic treatment. It has been evidenced that anti-TB chemoprophylaxis is low among HCWs than the general population [11, 12]. The acceptance rate in our study was also higher than studies from Turkey (66.3%) [13], and Brazil (53.5 %) [14]. Inversely, it was slightly lower than Singapore (81%) [15] and from a study investigating immigrant seeking asylum in Sweden (83%) [16]. The difference in the acceptance rate between these studies can be elaborated partly due to the differences in TB prevalence, the socioeconomic status, and health awareness in these countries.

The refusal rate (25.96%) in the current study could be attributed to the followings: first, lack of signs and symptoms among LTBI HHCs, hence misunderstanding latent TB; second, misconception about harmful effects of medication; third, patients with comorbid conditions on medications, especially elderly, could not bear additional long-term therapy; fourth, some families who lived in remote areas were unable to keep on track with monthly follow-ups.

In our study, the investigated variables including age group, gender, smoking, alcohol consumption, DM, and immunosuppressive therapy did not show significant influence on IPT completion rate. In contrast, Lavigne et al [17] stated that male gender (p value 0.01) and smoking (p value 0.04) were risk factors with LTBI treatment adherence. In fact, several studies [18-20] linked between smoking and TB infection, disease and related mortality anticipating that smokers tend to be less adherent to LTBI medication. Hence, increasing the risk of developing to active TB disease.

In general, our findings suggest that there may be other influential factors not considered in our study that contribute to IPT completion. Since the treatment completion rate is fairly high in our area and as Iraq is considered one of the seven highest TB burden countries in the Eastern Mediterranean Region [21], screening and treating close contact LTBIs is a fundamental strategy to control the disease.

The main limitation in this study was the small sample size. Another notable limitation was the lack of assessment of certain variables as education level, which might influence the IPT completion rate.

In conclusion, there was a high rate of LTBI completion with excellent drug safety profile among the HHCs in Duhok province. Therefore, it is an essential component of TB program to offer chemoprophylaxis to LTBI HHCs with regular follow-ups. Furthermore, there were no significant associations between age group, gender, smoking, alcohol consumption, DM, and immunosuppressive therapy, with the completion rate of IPT. Further larger studies are warranted to explore additional factors that could potentially influence the completion rate of IPT among household contacts

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

Author contributions

All authors have read and agreed to the published version of the manuscript. Fatima Nawaf Abdulkareem; writing-original draft preparation, Muayad Aghali Merza.; conceptualization, writing—review and editing, Ahmed Mohammed Salih.; review and editing, Abdulrahman Islam Rekani; review and editing.

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