

Prevalence and Factors Associated With Initiation of Isoniazid Preventive Therapy among Children Aged Below Five Years in Kisumu County

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Abstract- Tuberculosis is a crucial global public health problem which ranks second to HIV/AIDS as cause of mortality and is the leading cause of morbidity and mortality among people living with HIV/AIDS. Kenya is burdened with an estimated TB prevalence of 266 per 100,000. 52.5% of cases and 5.2% TB associated mortality occur among children below 5 years. Kisumu County is a TB and HIV endemic zone with a prevalence of 208-306 per 100,000 and 19.3% respectively. Children below 5 years who are household contacts with sputum positive pulmonary tuberculosis persons should be initiated on Isoniazid Preventive Therapy (IPT). This practice remains low hampering the 'END TB' strategies in Kisumu County. This descriptive Cross-Sectional study determined prevalence and factors associated with IPT initiation among children below 5 years living in Kisumu County. Significance was set at $p < 0.05$ and analysis done using STATA. Prevalence was established as [70.2%; 95% C.I (63.0-76.6)] with highest uptake among females [72.6%; 95% C.I (67.7-80.7)] against [67.5%; 95 % C.I (56.3-76.9)] in males. Caregivers with Higher level of education [aPR=1.36; 95% C.I (1.04-1.78)] were more likely to initiate children on IPT compared to those with incomplete primary education. Respondents of younger age [aPR=1.48; 95% C.I (1.27-1.73)] were more likely to initiate children on IPT compared to those > 40 years. The study concluded that IPT uptake is still unexpectedly low and this may be a major driver of TB infection in young children. The study recommends that the Ministry of health should advocate for health promotion activities unlimited to sensitization. Further studies need to examine the correlates of adherence and predictors of missed opportunity to IPT initiation.

Index Terms- Prevalence, Isoniazid, Tuberculosis, cross-sectional, household.

I. INTRODUCTION

Tuberculosis (TB) is a universal public health problem, coming after HIV/AIDS as the greatest cause of mortality. *Mycobacterium tuberculosis* infection is also a leading cause of

morbidity and mortality among people living with HIV (PLHIV) worldwide [1] [2]. Overall, 83% of all TB cases in 2014 reportedly occurred in the 22 high burden countries. Of these countries, 9 are found in Africa: South Africa, Nigeria, Ethiopia and Kenya among others. In the year 2015, there were 10.4 million incident cases of TB globally of which 10% occurred in children. Prophylaxis with INH has been demonstrated to reduce remarkably the incidence of TB in children aged below five years who are household contacts of sputum positive Pulmonary Tuberculosis (PTB) persons and in people living with HIV/AIDS (PLHIV) through prevention of disease progression. Children are highly susceptible to TB infection, which mostly occurs following exposure from an infectious adult [3]. In Kenya, TB is the leading cause of morbidity and mortality among persons infected with HIV. Kenya is one of the 22 high TB burden countries in the world with a national prevalence of 266 (range 189-281) per 100,000 population, and an incidence of 81,518. Forty-five percent (36,817) were new sputum positive cases. Children contributed 8.5% (6,968) with county variations ranging from 4.6% in Murang'a to 17.8% in Turkana; 52.6% of the children being below the age of 5 years, and 47.4% between 5-14 years of age. Recognizing the high prevalence of TB in the country, especially in the wake of HIV epidemic, and in line with WHO policy on TB and HIV collaborative activities, The Kenyan Ministry of Health (MOH) recommends IPT for all children below five years who are in close contact with an infectious smear or culture positive PTB case. In Kenya uptake of IPT in children is still low with a national uptake of 5.5% among children aged below five years with a household contact of sputum positive PTB against an adult uptake of 33% [4]. This necessitates the need for IPT uptake to be met by the country as a whole, especially Kisumu County.

II. METHODOLOGY

Study design: The descriptive cross-sectional study was conducted in Kisumu East Sub County, Kisumu County

Table 1: Inclusion and Exclusion criteria

Inclusion criteria	Exclusion criteria
Sputum positive PTB persons with household contacts aged below five years enrolled for TB care within the selected TB clinics in Kisumu County.	Sputum positive PTB persons with household contacts aged below five years and are on transit to other counties
Ability to provide an informed consent.	Persons who are very sick and are unable to consent and respond the questionnaire
Persons aged 18 years and above.	

Sample size determination: Sample size used was 175, based on Cochran equation for proportion with estimates of IPT uptake in children at 6.0%. Disproportionate sampling technique was used to determine the number of smear positive TB persons with contacts aged below five years and Purposive sampling to select sputum positive PTB persons with at least one child below five years for each stratum.

Data collection: Data was collected from respondents during their clinic revisits. The questionnaires were administered at the end of patient clinical examination and dispensing of medications following successful consenting process.

Data Analysis: Data was keyed in Access, cleaned and validated for analysis. Fisher’s exact test was used to determine the association between categorical variables and initiation on IPT. Generalized linear model was used to model IPT initiation since the prevalence was greater (>10%), thus logistic regression with odds ratios was not appropriate measure of effect. Explanatory variables that were significant at bivariate analysis $P < 0.2$ were further incorporated in the final multivariable regression model using backward elimination and retaining predictors significant at $P < 0.05$. Potential confounding effect

was examined for each covariate by two-way interactions. Data analysis was done using STATA version 14.1.

Ethical considerations: Ethical approval was sought from Institutional Review Board of the University of Eastern Africa, Baraton (REC: UEAB/8/8/2017) and the JOOTRH (ERC.1B/VOL.1/398). A written informed consent was obtained from the participants before collecting data while privacy and confidentiality was ensured on all the information obtained.

III. RESULTS

Socio-Demographic Characteristics of respondents: The mean age of the respondents was 33.2 [SD± 11.2] with 102(27.4%) aged between 25-29 years. Out of 175, 95 (54.3%) were female and 51(29.6%) of the respondents had incomplete secondary education. One hundred and two (58.9%) of the respondents were in a monogamous marriage. Ninety-four (53.7%) of the respondents resided in urban settlement with 89(52.5%) of the respondents being unskilled in their occupation. (Table 2).

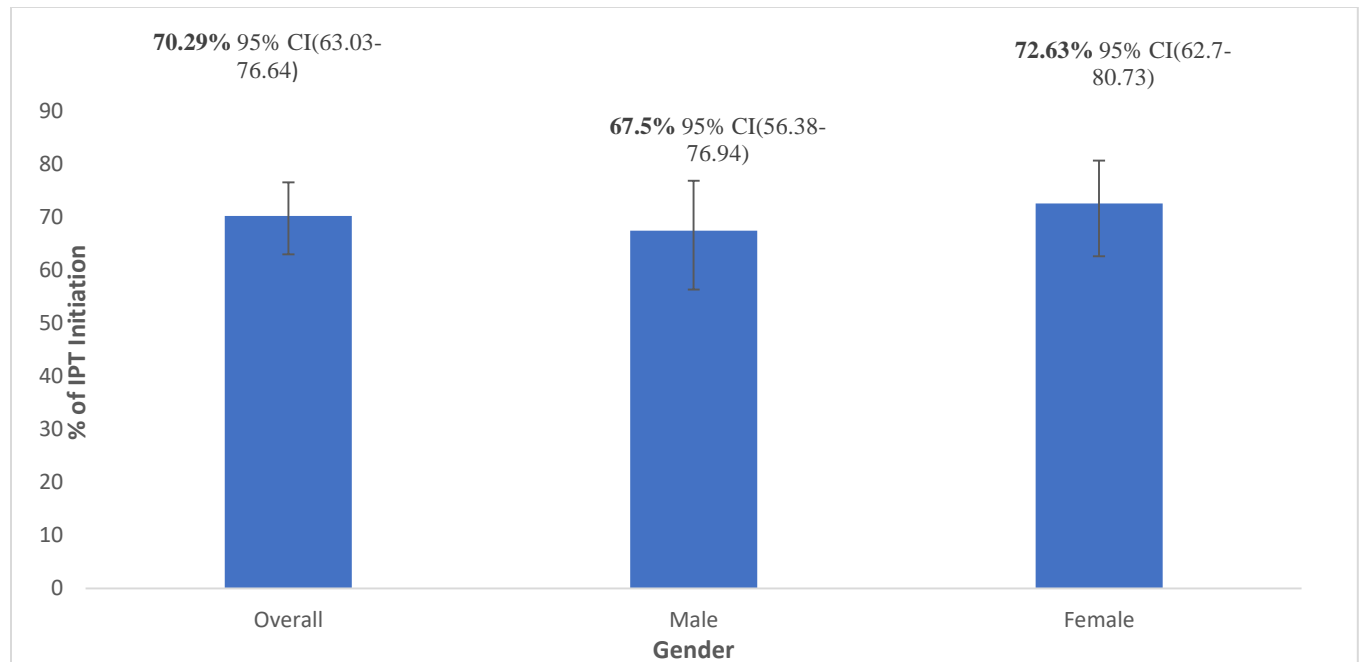
Table 2 Socio demographic Characteristics of the respondents

Characteristics (N=175)	Overall n(%)
Mean Age (33.2 ± 11.2)	
Sex	
Male	80(45.7)
Female	95(54.3)
Level of Education	
Primary incomplete	42(24.4)
Primary complete	29(16.8)
Secondary incomplete	51(29.6)
Above secondary	50(29.2)
Marital Status	
Married monogamy	102(58.9)
Married polygamy	23(13.3)
Divorced/Separated/Single	48(27.8)
Age group (Years)	
<25	30(17.1)
25-29	48(27.4)
30-34	41(23.4)
35-40	19(10.8)
>=40	37(21.1)

Residence	
Urban	94(53.7)
Peri-urban	33(18.8)
Rural	48(27.5)
Relationship to the child	
Parent	114(73.6)
Relative/caretaker	41(26.4)
Social economic Status	
Poorest	34(21.3)
Poorer	30(18.7)
Middle	33(20.6)
Richer	35(21.8)
Richest	28(17.5)
Number of persons in the household	
1-2	24(14.0)
3-5	106(62.0)
>5	41(24.0)
Average time of contact during the day	
<3 hours	26(15.7)
3-6 hours	71(43.0)
> 6 hours	68(41.2)
Sleep with the child in the same room	
Yes	107(61.1)
No	68(38.9)

The prevalence of IPT initiation: The overall prevalence of IPT initiation among children aged below 5 years was 70.3 % (n=123) with 69(72.6%) IPT initiation among female PTB contacts compared to 54(67.5%) among male PTB contacts (Figure 1).

Figure 1: The Prevalence of IPT initiation



Socio-demographic factors associated with initiation of IPT: Complete primary level of education, incomplete secondary level of education and above secondary (Crude PR=1.52; 95%CI 1.07-2.16; P=0.020); (Crude PR=1.49; 95%CI 1.30-1.71; P<0.001) and (Crude PR=1.56; 95%CI 1.21-2.01; P=0.001) respectively, were more likely to initiate their children on IPT as compared to those with incomplete primary level of education. Respondents whose age group was <25Yrs (Crude PR=1.43; 95%CI 1.02-1.99; P=0.038) were more likely to initiate their children on IPT compared to those of

>=40 Yrs age group. Moreover, respondents who resided in urban and pre-urban areas (Crude PR=1.89; 95%CI 1.49-2.40; P<0.001) and (Crude PR=1.66; 95%CI 1.35-2.05; P<0.001) respectively, were more likely to initiate their children on IPT compared to those who resided in rural areas. Notably, respondents who were skilled in their occupation (Crude PR=1.26; 95%CI 1.16-1.37; P<0.001) were more likely to initiate their children on IPT as compared to those of unskilled occupation (Table 3).

Table 3: Socio-demographic factors associated with initiation of IPT

Socio-demographic factors	Overall N(%)	Initiated n(%)	Not Initiated n(%)	Crude PR(95% CI)	P-value
Sex					
Male	80(45.7)	54(67.5)	26(32.5)	Ref	
Female	95(54.3)	69(72.6)	26(27.4)	1.08(0.98-1.18)	0.127
Level of Education					
Primary incomplete	42(24.4)	21(50.0)	21(50.0)	Ref	
Primary complete	29(16.8)	22(75.8)	7(24.1)	1.52(1.07-2.16)	0.02
Secondary incomplete	51(29.7)	38(74.5)	13(25.5)	1.49(1.30-1.71)	<0.001
Above secondary	50(29.1)	39(78.0)	11(22.0)	1.56(1.21-2.01)	0.001
Marital Status					
Married monogamy	102(58.9)	82(80.4)	20(19.6)	1.54(0.99-2.40)	0.053
Married polygamy	23(13.3)	15(65.2)	8(34.8)	1.25(0.76-2.05)	0.373
Divorced/Separated/Single	48(27.8)	25(52.1)	23(47.9)	Ref	
Age group (Years)					
<25Yrs	30(17.1)	22(73.3)	8(26.7)	1.43(1.02-1.99)	0.038

25-29Yrs	48(27.4)	39(81.2)	9(18.8)	1.58(0.99-2.51)	0.052
30-34 Yrs	41(23.4)	31(75.6)	10(24.4)	1.47(0.95-2.29)	0.086
35-40 Yrs	19(10.8)	12(63.2)	7(36.8)	1.23(0.68-2.21)	0.487
>=40 Yrs	37(21.1)	19(51.4)	18(48.6)	Ref	
Residence					
Urban	94(53.7)	78(82.9)	16(17.1)	1.89(1.49-2.40)	<0.001
Peri-urban	33(18.8)	24(72.7)	9(27.3)	1.66(1.35-2.05)	<0.001
Rural	48(27.5)	21(43.7)	27(56.3)	Ref	
Occupation					
Skilled	81(47.6)	63(77.7)	18(22.3)	1.26(1.16-1.37)	<0.001
Unskilled	89(52.4)	55(61.8)	34(38.2)	Ref	
Relationship to the child					
Parent	114(73.5)	91(79.8)	23(20.2)	1.13(0.93-1.37)	0.224
Relative/caretaker	41(26.5)	29(70.7)	12(29.3)	Ref	

PR- Prevalence ratio, CI- Confidence Interval

Socio-economic factors associated with initiation of IPT: Respondents whose social economic status were middle and richer (Crude PR=1.61; 95% CI 1.06-2.44; P=0.025) and (Crude PR=1.70; 95% CI 1.18-2.44; P=0.004) were more likely to initiate their children on IPT compared to those from the poorest social economic position. Respondents who had 3-5 and more than five persons in the household (Crude PR=2.35; 95% CI 1.21-4.56; P=0.012); (Crude PR=2.12; 95% CI 1.03-4.38; P=0.042) were more likely to initiate their children on IPT compared to those who had 1-2 number of persons in the household. Notably, respondents who sleep with their children in the same room (Crude PR=1.54; 95% CI 1.04-2.27; P=0.032) were more likely to initiate their children on IPT compared to those who did not sleep with the children in the same room (Table 4.3).

Table 4: Socio-economic factors associated with initiation of IPT

Household factors level	Overall N(%)	Initiated n(%)	Not Initiated n(%)	Crude PR (95% CI)	P-value
Social economic Status					
Poorest	34(21.2)	16(47.1)	18(52.9)	Ref	
Poorer	30(18.7)	20(66.7)	10(33.3)	1.42(0.83-2.42)	0.201
Middle	33(22.1)	25(75.8)	8(24.2)	1.61(1.06-2.44)	0.025
Richer	35(21.8)	28(80.0)	7(20.0)	1.70(1.18-2.44)	0.004
Richest	28(17.5)	24(85.7)	4(14.3)	1.82(0.93-3.55)	0.079
Number of persons in the household					
1-2	24(14.0)	8(33.3)	16(66.7)	Ref	
3-5	106(62.0)	83(78.3)	23(21.7)	2.35(1.21-4.56)	0.012
>5	41(24.0)	29(70.7)	12(29.3)	2.12(1.03-4.38)	0.042
Average time of contact during the day					
<3 hours	26(15.7)	14(53.5)	12(46.2)	Ref	
3-6 hours	71(43.0)	60(84.5)	11(15.5)	1.57(0.97-2.53)	0.065
> 6 hours	68(41.3)	49(72.1)	19(27.9)	1.34(0.92-1.95)	0.129
Sleep with the child in the same room					
Yes	107(61.1)	87(81.3)	20(18.7)	1.54(1.04-2.27)	0.032
No	68(38.9)	36(52.9)	32(47.1)	Ref	

Multivariate analysis of factors associated with initiation of Isoniazid Preventive Therapy: A multivariate prevalence revealed that respondents who had secondary incomplete level of

education (Adjusted PR=1.36; 95% CI 1.04-1.78; P=0.023), were more likely to initiate their children on IPT as compared to those with incomplete primary level of education level. Respondents

aged between 25-29 years (Adjusted PR=1.48; 95% CI 1.27-1.73; P<0.001) were more likely to initiate their children on IPT compared to those of aged 40 years and above. Those who resided in urban and pre-urban (Adjusted PR=1.56; 95%CI 1.16-2.09; P=0.003) and (Adjusted PR=1.60; 95%CI 1.06-2.42; P=0.024) respectively, were more likely to initiate their children on IPT compared to those who reside in rural areas. Respondents who had 3-5 people and more than five persons in the household (Adjusted PR=1.69; 95% CI 1.13-2.51; P=0.010) and (Adjusted

PR=2.19; 95% CI 1.42-3.37; P<0.001) were more likely to initiate their children on IPT compared to those with 1-2 persons in the household.

Moreover, respondents who had 3-6 hours and more than six hours' average time of contact during the day (Adjusted PR=1.63; 95% CI 1.14-2.33; P=0.007) and (Adjusted PR=1.50; 95% CI 1.09-2.06; P=0.012) were more likely to initiate their children on IPT compared to those who had less than three hours average time of contact during the day.

Table 5: Multivariate analysis of factors associated with initiation of Isoniazid Preventive Therapy.

	Overall N(%)	Initiated n(%)	Not Initiated n(%)	Adjusted PR (95% CI)	P-Value
Level of Education					
Primary incomplete	42(24.4)	21(50.0)	21(50.0)	Ref.	
Primary complete	29(16.8)	22(75.8)	7(24.1)	1.39(0.78-2.47)	0.259
Secondary incomplete	51(29.7)	38(74.5)	13(25.5)	1.36(1.04-1.78)	0.023
Above secondary	50(29.1)	39(78.0)	11(22.0)	1.37(0.86-2.18)	0.175
Marital Status					
Married monogamy	102(58.9)	82(80.4)	20(19.6)	1.27(0.90-1.79)	0.173
Married polygamy	23(13.3)		8(34.8)	1.30(0.88-1.94)	0.183
Divorced/Separated/Single	48(27.8)	25(52.1)	23(47.9)	Ref.	
Age group (Years)					
<25 Yrs	30(17.1)	22(73.3)	8(26.7)	1.21(0.90-1.62)	0.189
25-29 Yrs	48(27.4)	39(81.2)	9(18.8)	1.48(1.27-1.73)	<0.001
30-34 Yrs	41(23.4)	31(75.6)	10(24.4)	1.25(0.92-1.71)	0.138
35-40 Yrs	19(10.8)	12(63.2)	7(36.8)	1.13(0.65-1.95)	0.651
>=40 Yrs	37(21.1)	19(51.4)	18(48.6)	Ref.	
Residence					
Urban	94(53.7)	78(82.9)	16(17.1)	1.56(1.16-2.09)	0.003
Peri-urban	33(18.8)	24(72.7)	9(27.3)	1.60(1.06-2.42)	0.024
Rural	48(27.5)	21(43.7)	27(56.3)	Ref.	
Occupation					
Skilled	81(47.6)	63(77.7)	18(22.3)	1.05(0.84-1.30)	0.647
Unskilled	89(52.4)	55(61.8)	34(38.2)	Ref.	
Social economic Status					
Poorest	34(21.2)	16(47.1)	18(52.9)	Ref.	
Poorer	30(18.7)	20(66.7)	10(33.3)	0.87(0.52-1.45)	0.608
Middle	33(22.1)	25(75.8)	8(24.2)	0.75(0.50-1.12)	0.169
Richer	35(21.8)	28(80.0)	7(20.0)	0.76(0.46-1.27)	0.307
Richest	28(17.5)	24(85.7)	4(14.3)	0.86(0.47-1.59)	0.644
Number of persons in the household					
.1-2	24(14.0)	8(33.3)	16(66.7)	Ref.	
.3-5	106(62.0)	83(78.3)	23(21.7)	1.69(1.13-2.51)	0.010
>5	41(24.0)	29(70.7)	12(29.3)	2.19(1.42-3.37)	<0.001
Average time of contact during the day					
<3 hours	26(15.7)	14(53.5)	12(46.2)	Ref.	
3-6 hours	71(43.0)	60(84.5)	11(15.5)	1.63(1.14-2.33)	0.007
> 6 hours	68(41.3)	49(72.1)	19(27.9)	1.50(1.09-2.06)	0.012
Sleep With the child in the same room					
Yes	107(61.1)	87(81.3)	20(18.7)	1.26(1.05-1.50)	0.010
No	68(38.9)	36(52.9)	32(47.1)	Ref.	

IV. DISCUSSION

The prevalence of IPT initiation: This study established 70.2% prevalence rate of IPT initiation among children aged below 5 years. Females' contacts had the highest initiation rate 72.6% compared to 67.5% among males. A study in Ethiopia of 221 children eligible for IPT, 64.3% (142) received IPT, 80.3% (114) successfully completed six months of therapy. No child developed active TB while on IPT. Contact screening is recommended by the WHO despite the implementation challenges [5]. Children whose caregivers had a history of being on IPT had an increased likelihood of initiation according to a study in Nairobi [6]. It is estimated that around 10% of the world's tuberculosis (TB) cases occur in children 0–14 years of age [7]. WHO guidelines promote active screening and Isoniazid Preventive Therapy (IPT) for such children under 5 years, this established intervention is still not completely embraced in endemic countries [8]. Of the 184 children who were screened in a study of IPT Programme in South Africa, 59% ($n=108$) were documented as having started IPT, 2 started full TB treatment and for 40% ($n=74$) there was no documentation of further management or follow-up. The last represents missed opportunities for providing TB preventive therapy in a community where TB is rife [9].

A number of important initiatives have been facilitated by the childhood TB subgroup of the WHO Stop TB partnership aimed at greater emphasis on childhood TB by National TB programmes (NTP) that includes screening children living with an infectious case followed by the provision of preventive therapy (PT) for those cleared of TB disease [3]. However, these recommendations, including preventive therapy provision, are rarely fully implemented in high-burden countries. This is vital as a large proportion of childhood TB occurs in children younger than 5 years who would have been eligible for PT [10]. Literature review regarding barriers to implementation of PT found that there are a myriad of factors, including difficulties in screening, poor adherence, fear of increasing INH resistance and poor acceptability among primary caregivers and healthcare workers [8].

The benefits of PT have been recognized since the 1950s. Studies indicate that to attain TB eradication by 2050, preventive measures must be included in TB programmes [11]. Following infection, infants and young children (<5 years) are at the highest risk of progression to disease. Review of the pre-chemotherapy literature shows that 40–50% of infected infants (0–11 months), 10–20% of children aged 1 year and 10% of children aged 2–4 years progress to disease [12].

Household level factors associated with initiation of IPT: Studies in developed and developing countries show that the most effective means of case identification is at the household contact level [13, 14]. Studies have shown that risk of TB was associated with the number of people living together in the household also referred to as overcrowding [15–17]. Studies have shown that increased household size was found to be important factor in infection of TB and overcrowding has been documented as a risk factor for TB in a variety of settings [18, 19]. This study

is consistent with the fact that overcrowding is a risk factor for TB and revealed that respondents who had more than five persons in the household were more likely to initiate their children on IPT compared to those who had 1–2 persons in the household. Respondents who sleep with their children in the same room were more likely to initiate their children on IPT compared to those who did not sleep with their children in the same room. Studies have shown that children exposed to patients who are sputum positive and/or have extensive lung involvement are at high risk of infection. Children who sleep in close proximity to a source case and those whose source case is a female family member are also at increased risk, more than five times higher in some reports hence a higher likelihood of initiation to IPT [20–22].

Recommendation: This study recommends that the Ministry of Health and collaborates to advocate for health promotion activities such as sensitization among smear positive PTB persons with children aged below 5 years to help bolster IPT uptake in rural areas.

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