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ABSTRACT

Background: **In 2018, of the 1.5 million people dying of Tuberculosis (TB), 11% were children. Tuberculosis preventive therapy (TPT) reduces the risk of contracting active TB by 60%. TPT of children below five years with household contact of bacteriologically diagnosed TB cases in Kenya was at 34% in 2018. The aim of this study was to determine uptake of TPT among eligible children under five years and to assess the knowledge, attitude and practice of health care workers (HCWs) regarding TPT in Mombasa County that has a high TB burden.**
Methods: **A mixed methods cross-sectional study (October 2020-January 2021) was carried out at selected health facilities in Mombasa County, Kenya. Quantitative data was collected using structured questionnaires. Consecutive sampling of bacteriologically confirmed TB index cases was used to acquire the sample size of 150 eligible under five-year children per index case. Thematic coding of qualitative data from in-depth interviews (IDI) was conducted to evaluate barriers of TPT uptake from the perspective of; patients', HCWs, and key informants in health facilities (n=20 for each).**
Results: **The uptake of TPT was 13.3%. The knowledge, attitude and practice among the health workers and index cases toward TPT was 60%, 80% and 68% respectively. The associated barriers to implementation of TPT included lack of awareness on TPT, cumbersome screening process, resistance by index cases, poor socio-economic status, interrupted supply of TPT drugs and resistance of caregivers/parents.**
Conclusion. **There is need to educate HCWs and the community on TPT importance and address the barriers.**

INTRODUCTION

Tuberculosis (TB) is an infection caused by *Mycobacterium tuberculosis* bacilli[1]. According to the World Health Organization (WHO) Global TB report 2019, 10 million people (IQR 9.0-11.1 million) got TB, equivalent to 1132 cases per 100 000 population. Of these, only 7 million were reported to have access to TB care[2]. Children under 5 years of age are at greatest risk of being infected by a smear positive sputum adult contact[3]. In 2016, the World Health Assembly endorsed WHO's End TB policy. Its purpose is to have a TB free world by 2035. It targets to reduce 90% of patients and 95% deaths from the disease all while protecting families from catastrophic costs that push them further into poverty[4].TB preventive therapy (TPT) refers to isoniazid medication to prevent progression of latent tuberculosis into active disease[5].

Worldwide, only 27% of children under 5 years, who were eligible, were started on TB preventive treatment. Evidence shows that it reduces TB related morbidity by 72% and mortality by 52%. According to WHO, in 2018, an estimate of 150,000 people had TB with 13% being children. In TB preventive treatment of children less than five years with contacts in the same household of bacteriologically diagnosed TB cases, coverage was at 34%[6].

As per the National Tuberculosis, Leprosy and Lung Disease (NTLD) Program, TB cases in Kenya is estimated at 426 cases per 100,000 with 156,000 incident cases in 2018. Approximately 36% of these new cases were not diagnosed, treated or notified. Countrywide, Mombasa ranks second in the number of TB cases and is among the top 10 counties with the highest TB related deaths. The notification is also low at 25% when compared to other counties like Machakos at 136% reflecting a poor roll out of Active Case Finding in health facilities in Mombasa[7].

Brent et al., conducted a study in Coast Provincial General Hospital (CPGH) and Kilifi County Hospital (KCH), Kenya. Estimated TB incidence was 53 cases/100,000 children/year locally and 95 cases/100,000 children/year nationally. The estimated Case Detection Rate (CDR) was 0.20– 0.35. Among children <5 years of age, 49% of cases were attributable to a known household contact with TB[8].

The possible side effects of TPT are hepatotoxicity and pyridoxine deficiency which are rare and well tolerated in children[9]. However, it is mandatory to give pyridoxine together with IPT to cater for this[9].

Some of the factors hindering TPT uptake include lack of awareness by HCW, risk perception among parents, cumbersome screening process, isoniazid stock-outs, inadequate knowledge among healthcare providers and poor programmatic monitoring with national leadership, non-compliance to existing guidelines, Isoniazid toxicity, isoniazid resistance concerns, transport and access to health facilities, attitude of healthcare workers and stigma[10–13].

The objective of this study was to determine proportion of children under 5years of age who were initiated on TB preventive therapy (TPT) and to assess the knowledge, practice and barriers/facilitators of TPT uptake from the perspective of caregivers and Healthcare workers in Mombasa County, Kenya.

METHODOLOGY

Study design: Cross sectional study utilizing qualitative and quantitative data (mixed-methods) collected between October 2020–January 2021.

Study setting and population: This study was undertaken in Mombasa County, which ranks second for all TB cases in the country with Paediatric TB cases ranked fourth. The study sites included: Coast General Teaching and Referral Hospital (CGTRH), Port Reitz

Sub-County Hospital, Likoni Sub-County Hospital and Ganjoni Dispensary. Study participants were included if there was documented pulmonary TB infection of adolescent (15yrs to <18yrs) and/or adult living in the same household with at least one child under five years of age, TB treatment ongoing for at least one month in the TB clinic of study facility, informed written consent for >18yrs and assent for 15-18yrs with consent from guardians. They were excluded if the exposed child had positive signs and symptoms of TB, was on treatment for active TB or if they had contraindication to TPT. Healthcare workers were included if they treated children under 5 years and provided written consent.

Sample size: For the quantitative arm of the study, Fisher's formula was applied to calculate sample size for a finite population[14]. The expected prevalence of IPT uptake for children under 5 years according to a study by Birungi et al., was 89%[12]. Sample size was estimated at 150 for the index TB case-child pairs. These were recruited by consecutive sampling.

Sample size for healthcare workers was estimated at 66 using Fisher's formula for finite population with a proportion estimate of 50% from a similar study carried out by Mwangi et al., in 2019[13]. For each health facility, doctors, nurses and clinical officers were selected using consecutive convenience sampling, proportionate to the number of workers in the cadre.

Data collection and analysis: Structured paper questionnaires with both open-ended and closed-ended questions were administered by the research team to adolescents/adults with bacteriologically confirmed PTB who had received at least 4 weeks of treatment and lived with at least one child under 5 years. The questionnaire also had a section targeting only the parents/primary caregivers of the child household contacts.

A self-administered questionnaire was given to healthcare workers to assess their knowledge, attitude and practices on IPT/TB Preventive Therapy as well as barriers to TPT uptake. Data was analyzed using SPSS.v27®. Descriptive statistics of adolescents/adult index cases was determined, and continuous variables were presented as medians with inter-quartile ranges. Categorical variables were presented as proportions with 95% confidence intervals. Associations between outcome variable and independent variables was determined by means of Chi-square test/Fisher's Exact test.

Bias: To avoid bias, the tools were pretested before implementation and research assistants were trained prior to data collection to understand the information that the tool is collecting.

Ethical approval was obtained from KNH and UON Ethics and Research Committee, County Government of Mombasa and administrative approval from each of the 4 participating facilities.

RESULTS

*Sociodemographic characteristics of index cases:*150 child household contacts were enrolled in the study. 51.3% were male while 48.7% were females. Median age was 2.2 years (IQR 2.4yrs). Likoni Sub County had the highest enrolment of 36% followed by Port-Reitz hospital with 33.3% while Coast General and Ganjoni each had enrolled 15.3%. Out of 150 under five-year-old children who were eligible for TPT, 13.3% (n=20) were on TPT while 86.7% (n=130) were not on TPT.

Number of household contacts per index case: From the 150 TB index cases enrolled, 130 TB index cases had one household contacts each, twelve TB index cases had two household contacts each, five TB index cases had three household contacts each and three TB index cases had four household contacts each.

Sociodemographic characteristics of healthcare workers: Out of 66 health workers interviewed, 35.5% were males while 64.5%

were females. In terms of cadre, clinical officer interns were the highest in number 33.3% while the least were medical officers and consultants 7.6%. Their median age was 27yrs (IQR 11yrs). (Table 1)

Table 1
Sociodemographic characteristics of Healthcare Workers

Characteristic (n=66)	Frequency	%
Sex		
Male	22	36
Female	40	64
Cadre		
Registered Clinical Nurse (RCN)	11	17
Clinical Officer Intern	22	33
Registered Clinical Officer	14	21
Medical Officer Intern	9	14
Medical Officer	5	8
Consultant Paediatrician	5	8
Health Facility		
Coast General Teaching and Referral Hospital (CGTRH)	32	49
Port Reitz Sub County Hospital	20	30
Likoni Sub County Hospital	10	15
Ganjoni Dispensary	4	6
Age Category		
20 – 29	37	56
30 – 39	16	25
40 – 59	13	19
Median Age = 27yrs (IQR 11yrs)		

HealthCare Workers Knowledge on TPT: Knowledge, attitude and practice questions were converted to percentage scores and classified into 3 levels using Bloom's cut-off point as; (Excellent: 80%-100% correct; Good: 60%-79% correct; Poor: ≤59% correct)[15]. 98.8% of the health workers interviewed agreed that TB can be prevented using medicine. Among the discussions, the HWs agreed to this and cited that the TPT is used to prevent TB as shown in Table 2.

Table 2

Knowledge of health workers on TB Preventive Therapy (TPT)

Knowledge		
	Correct answer(n)	**%**
Purpose of TPT		
TB can be prevented with medicine	65	99
Mean percentage		*99*
Drug Information on TPT		
Number of drugs that can be used to prevent TB in children under 5 years of age	64	97
Formulations of TB preventive drugs available	11	17
Fluids that are acceptable for dispersible drugs	35	55
TB preventive drugs dosage and frequency for children under 5yrs	11	17
Where to find TPT drug dose charts by weight	9	14
Dosage for a child weighing 5kg from the chart	38	58
Pyridoxine should be given with TPT	63	96
Pyridoxine is given to all children	39	59
Mean percentage		*52*
Guidelines and tools for TPT		
Children under 5 years of age who are eligible for TPT	25	41
How to screen/evaluate these children under 5 years for eligibility for TPT	30	45
Knowledge of adverse effects to counsel parents	36	54
Awareness of TB preventive drug dose charts by weight band	40	61
Awareness of any guidelines on prevention of TB	51	77
In Kenya, TPT is guided by WHO and MOH guidelines	47	71
Mean percentage		*58*
Child contact clinical evaluation		
Signs and symptoms to look for during follow up	39	59
Symptoms for referral/evaluation of household contacts of bacteriologically confirmed TB case	41	62
Mean percentage		*61*
Overall knowledge mean percentage		***60***

Majority (97%) were aware of the number of drugs that can be used to prevent TB in children under 5 years of age which were either INH or RH. In terms of eligibility 41% of the health workers had knowledge on children under 5 years who were eligible for TPT and this was also cited in the in-depth interviews.

HCWs were aware of how to screen or evaluate children under 5 years for eligibility for TPT and from the discussions they were comfortable due to the availability of screening tool such as chest x ray, GeneXpert, Sputum and symptom screening.

For drug dosage, 16.7% of the health workers stated that they had knowledge on TB preventive drugs dosage and frequency for children under 5 years, 60.6% were aware of TB preventive drug dose charts by weight band, 13.6% had knowledge on where to find TPT drug dose charts by weight band. 95.5% of the health workers had knowledge that pyridoxine should be given with TPT while 59.1% were aware that pyridoxine is given to all children.

Healthcare workers attitude towards TPT: Ninety three percent (93%) of the health workers agreed that all eligible children should receive TB preventive therapy drugs and 89.2% disagreed with the statement that it is preferable to wait until a child under 5 years contracts TB and then treat them rather than administer prophylaxis because it is effective, safe and reduces TB incidence and mortality.

64.1% felt that drug resistance is a major concern prescribing TPT. In terms of risks versus the benefits 62.5% disagreed that the risks of giving TB preventive therapy drugs outweigh the benefits (Table 3).

Table 3

Attitude of Healthcare workers towards TB Preventive Therapy (TPT)

Attitude	Positive n (%)	Neutral n (%)	Negative n (%)
Benefits and effectiveness of TPT			
TB preventive therapy drugs are effective	57 (86)	9 (14)	0
TPT reduces TB incidence and mortality	57 (91)	6 (9)	0
Mean percentage	**89**	**12**	**0**
Risks and fears on TPT drugs			
TB preventive therapy drugs are safe	53 (80)	10 (15)	3 (5)
Drug resistance is a major concern when prescribing TPT	41 (64)	7 (11)	16 (25)
The risks of giving TPT does not outweigh the benefits	40 (62)	3 (5)	21 (33)
Mean percentage	**69**	**10**	**21**
Provision of TPT			
All eligible children should receive TPT drugs	62 (94)	2 (3)	2 (3)
I comply with Kenyan guidelines on TPT in children under 5 years	56 (85)	9 (14)	1 (2)
It is not preferable to wait until a child under 5 years contracts TB and then treat them rather than administer prophylaxis	58 (89)	5 (8)	2 (3)
I am comfortable prescribing TPT drugs	46 (70)	13 (20)	7 (10)
Mean percentage	**85**	**11**	**4**
Overall attitude mean percentage	***80***	***11***	***9***

Implementation of TPT by Health Workers: Asked about the frequency of enquiring if index cases had a child household contact under five years 69.4% cited, yes, always, 70.3% always asked the index cases if their child household contacts under five years have symptoms suggestive of active TB and 60.9% of the health workers always advised index cases to bring their child household contacts under 5 years for assessment and evaluation. 87.9% always counselled them on adherence when prescribing TB preventive

drugs to child household contacts under 5 years and this prevents drug resistance which can be caused by the TPT drugs.

65.2% always monitored those children under 5 years on TB preventive therapy drugs for side effects during follow up clinics and 50.8% always engaged the community health workers in case a child under 5 years on TB preventive therapy drugs cannot come for the follow up clinics.

DISCUSSION

In this study the Tuberculosis Preventive Therapy (TPT) uptake was poor at 13.3% among eligible children under five years age in Mombasa County, despite Kenya having national guidelines. A similar study in Nairobi County of Kenya, among HIV infected children indicated that TPT uptake was at 53.2%[13]. This could be attributed to the target population of HIV infected children who are a special group and there is a lot of focus in terms of financial and social support and staffing by HIV programs. Their focus group was aged 1-15 years hence there was high probability of capturing large number of children on TPT as opposed to this study whose target group was under five years children with TB contact as a point of entry. In India TPT uptake was higher at 22%[11] and in Thailand it was found to be 19.3%[16]. In Rwanda, TPT uptake was much higher at 89% because of aggressive intervention by the Rwanda National TB Program to reduce the most important causes of mortality[12,17].

There was a knowledge gap among HCWs especially those not working in the TB clinic/program, and this was evidenced by the index cases since 18 out of the 20 index cases interviewed were not aware of TPT and had heard it for the first time during the time of the interview. Similar findings were reported in Rwanda where 50% of the parents/caregivers of child household contacts who were not initiated on TPT reported their lack of information about its usefulness. In India the index cases cited inadequate knowledge to help them make informed decision on whether to initiate TPT and inadequate knowledge among HCWs as a barrier to TPT implementation[11,12]. In contrast, South African HCWs had good knowledge in provision of TPT which was due to the formal training they received on TB and Isoniazid Preventive Therapy[18].

Transport cost was a limiting factor mentioned by the index cases as a challenge they experience when coming for TB services which means it can negatively affect the TPT services unlike in Rwanda where, there has been an improvement in the ease of access to healthcare centres therefore transport cost was not a limiting factor to TPT uptake. These findings reiterate what Mwangi et al.,[13] found out in Nairobi. HIV patients had an incentive to come to the clinic already and this was independent of TPT thus removing any additional travel and time burden related to acquiring TPT medication[19].

Birungi et al showed that parents/caregivers who found unfriendly healthcare providers at the PHCs were less likely to initiate their children on TPT than those who found them friendly. These findings were corroborated by Van Ginderdeuren et al., in South Africa[20]. Negative interactions and experience of people seeking treatment in government healthcare facilities can contribute to a reduction in subsequent medical visits and follow-ups and this could negatively affect adherence of TPT among the under-fives[10]. Social stigmatization when picking up the TPT drugs was cited by index cases as negatively affecting TPT uptake among children. This was observed in studies carried out in Ethiopia and Rwanda[12,21].

Garie et al, conducted a study in Southern Ethiopia, where the major reason for high interruption rate was families' refusal to have an otherwise healthy child treated for six months in a TB clinic which was similar to this study. The caregivers/parents didn't understand why a healthy child was being

started on TB medication[22]. This study found out that long duration of TPT (daily for 6 months) influenced non-compliance due to the pill burden which was similar to a study done in India and Kenya. In India, 75% did not complete TPT. Reducing the frequency or duration of drug intake may thus enhance initiation and completion of IPT[23]. Introduction of RH which has a short course of three months will probably result to better uptake and adherence of TPT. Relatively few health workers expressed concern that isoniazid INH was not effective enough (13.6%) and that it was a safe drug (80.3%). These findings complement the issues raised by Abdulrazaak et al, in which fear of generating drug resistance was a major barrier to TPT implementation[18]. However, they contrasted with those of Lester et al in South Africa who found out that the prescribers were unaware of benefits of TPT[24].

Drug stock out in this study was a major barrier to TPT adherence and treatment completion. This was reiterated by Singh et al in India[11] and Teklay et al in Ethiopia that the main barrier leading to sub-optimal implementation of IPT observed in this study was shortage of isoniazid[10]. It seems that lack of effective systems to manage drug supply is impeding implementation of the policy. Shortage of essential drugs, such as drugs used for TB prevention have been reported as a problem in health facilities of Mombasa County[25].

Chest x-ray was found to be a barrier in this study because of associated costs. A study done by Chai in Cameroon found reduced cost of screening as a facilitator of TPT uptake (unpublished thesis). Even though the specificity for chest x ray for TB diagnosis in children is low, it is of paramount importance to use chest x ray to exclude TB together with other signs and symptoms as stipulated in National and WHO guidelines. These gaps could indicate that health care providers should be equipped with the knowledge, skills, and tools to counsel parents or caregivers about the importance of screening children who are in contact with TB patients and about preventive treatment even for otherwise healthy children.

Having a policy/guideline for TPT, but lacking implementation, is common in many countries. A WHO study reported that only 28% of countries with a national policy for TPT had achieved nationwide implementation[2]. Fox et al.,[26] suggest that guidelines for practice may predispose physicians to consider changing their behaviour, but unless disincentives are removed, guidelines may be unlikely to effect, rapid change in actual practices.

CONCLUSION

TB preventive therapy uptake was poor among families with children under five years old exposed to index cases. One of the major reasons was poor knowledge regarding TPT among healthcare workers, understaffed public facilities with drug stock outs and poor access to diagnostic facilities aggravating the problem.

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