Passive case finding: Diagnostic approaches, cost and delay in TB management in Dar es Salaam and Pwani regions, Tanzania.

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Abstract

Background and objectives

TB case detection in Tanzania is mainly through passive case finding, however, it has remained below the WHO and national target of 70%. Several studies have investigated different strategies to increase TB case finding and how to reduce TB diagnostic and treatment delay. A study conducted in Brazil showed that the probability of having TB did not depend on cough duration. Moreover, interventions aimed at integrating passive TB case finding in other clinics like antenatal clinics have proven to be acceptable and have also been recommended in Malawi and South Africa. Active case finding for TB revealed a significant number of undiagnosed TB cases among women attending PMTCT clinics in South Africa. Still, delay in diagnosis and treatment is a challenge, and case detection remains low, especially among women. Therefore, this thesis is based on studies that were conducted to determine the following:

i) the proportion of smear positive TB among patients with cough attending OPD, FP and MCH clinics in Dar es Salaam, regardless of the duration of cough (paper I and II)

ii) the extent of, and factors responsible for delay in TB case detection in Pwani region (paper III)

iii) the cost associated with TB healthcare seeking for the current passive case finding strategy in Dar es Salaam (paper IV).

Study design and Setting

We conducted a cross sectional hospital based study in Dar es Salaam and Pwani region between 2007 and 2008. The two regions are adjacent to each other and are located along the coastal area of Tanzania, and share cultural values. Dar es Salaam and Pwani have a total population of 2,497,940 and 889,154 respectively.

Study participants and data analysis

Study participants for detection of pulmonary tuberculosis among patients with cough attending OPD (paper I) involved patients aged 5 years and above. Study participants for paper II were women aged 15 years and above attending MCH and FP clinics with a cough. We actively asked for a cough, all study participants from FP and MCH clinics. All participants included in paper I and II were screened for TB by sputum microscopy, regardless of the duration of cough. Study participants for paper III were smear positive TB patients diagnosed to have TB within three months prior to the commencement of the study. The study for paper IV involved patients aged 15 years and above and who have just been diagnosed to have TB. We trained all research assistants. Questionnaires were pre tested. The outcome variables included: diagnosis of smear positive TB, magnitude of TB diagnostic delay and risk factors associated with delay as well as patients and households cost before TB diagnosis. We explored possible associations between cough duration and smear results, clinic of diagnosis, place of first presentation and number of visits made prior to diagnosis. The main methods for analysis were cross tabulation and bivariate logistic regression. We applied the following statistical tests to determine estimated proportions and risk factors: odds ratios, means and medians, Pearson Chi- square, Wald statistic and 95% CI.

Results

The study involved 3,372 patients: 2274 patients with cough attending OPD; 749 women with cough attending FP and MCH clinics; 226 smear positive pulmonary tuberculosis patients from DOTS clinics and 123 TB patients who have just been diagnosed to have TB.

The probability of being smear positive does not depend on cough duration. Out of 2274 patients with cough, regardless of the duration, and attending OPD, 2214 (97.4%) remembered their cough duration. One thousand nine hundred and seventy three patients (89.1%) coughed for two weeks or more compared to 241 (10.9%)

patients who coughed for less than 2 weeks. Of those who coughed for two weeks or more, 250 (12.7%) had smear positive PTB, and of those who had coughed for less than two weeks, 21 (8.7%) had smear positive PTB. There was no statistically significant difference in the proportion of smear positive tuberculosis among the two comparison groups (Pearson Chi-Square 3.2; p = 0.074).

The proportion of smear positive TB patients among women with cough attending FP and MCH clinics was 3.8%. Out of 749 women with cough, regardless of duration, attending FP and MCH clinics, 529 (70.6%) were from MCH clinics. Six hundred and sixteen (82.2%) patients had coughed for less than two weeks compared to 133 (17.8%), who had coughed for two or more weeks. Among 616 TB suspects, 14 (2.3%) were smear positive TB patients, and of the 133 who had coughed for two or more weeks, 13 (9.8%) were smear positive TB patients. Risk factors associated with smear positive results included attended more than one visit to any facility prior to diagnosis (OR = 6.8; 95%CI 2.57–18.0) and having HIV/AIDS (OR = 4.4; 95%CI 1.65–11.96). Long duration of cough was not a risk factor for being smear positive (OR = 1.6; 95%CI 0.59–4.49).

Out of 226 patients enrolled for studying delays in TB detection in Pwani region, results were available for 206. The majority (66.5%) of the patients were males. Mean age for males and females was 37.3 and 33.7 years, respectively. Mean (SD) total delay before initiation of treatment was 125.5 (98.5) days (median 90 days). Out of 206 patients, 79 (38.4%) delayed to seek TB healthcare. Health facility delay was observed among 121 (58.7%) patients. Risk factors for patients' delay was poor knowledge that chest pain may be a TB symptom (OR= 2.9; 95%CI 1.20- 7.03) and the belief that TB is always associated with HIV/AIDS (OR=2.7; 95%CI 1.39-5.23). Patients who presented with chest pain were (OR= 0.2; 95%CI 0.10-0.61) less likely to delay compared to those with no chest pain.

One hundred and twenty three TB patients were enrolled for studying patient and household costs for TB diagnosis. The majority (53.7%) were males. The mean age for male and female patients was 34.8 and 37.0 (14.8) years, respectively. Before TB

diagnosis, overall, TB patients lost 46% of their mean monthly income. At individual level, poor patients had relatively higher mean loss of income (15 USD, 52%) of mean monthly income compared to less poor patients (45 USD equivalent to 46%) of mean monthly income. Thirty eight (39.2%) patients stopped working due to TB illness with an average of 77 days off. Before diagnosis, overall, tuberculosis caused on average 25 patients lost work days. Among patients who stopped working, 17 (47.7%) were head and the main bread earner for their households whereas, 5 (55.6%) were poor compared to 12 (41.4%) less poor. At the household level, overall household mean monthly income dropped by 28%. Poor households had relatively higher loss of monthly income compared to less poor. In-direct cost contributed to almost two thirds of the total cost. While poor households spent 150% of their mean monthly income, less poor spent 43%.

Conclusions

- Detection of smear positive PTB among patients who coughed for less than two weeks, was as high as for those who coughed for two weeks or more.
- Almost four percent of women with cough attending MCH and FP were smear positive TB patients.
- There is a considerable delay in TB diagnosis and treatment in Pwani, mainly due to patients' delay.
- The economic burden of TB health care seeking is high, especially for the poorest households.

List of publications

Paper I

Ngadaya, E.S., Mfinanga, G.S., Eliud R Wandwalo and Odd Morkve. **Detection of Pulmonary Tuberculosis among Patients with cough attending Outpatient departments in Dar Es Salaam, Tanzania: Does duration of cough Matter?** BMC Health Services Research 2009, 9:112doi:10.1186/1472-6963-9-112.

Paper II

Ngadaya, E.S., Mfinanga, G.S.,Wandwalo, E.R. & Morkve, O. **Pulmonary tuberculosis among women with cough attending clinics for family planning and maternal and child health in Dar Es Salaam, Tanzania.** BMC Public Health, 2009, 9:278.

Paper III

Ngadaya, E.S., Mfinanga, G.S., Wandwalo, E.R. & Morkve, O. (2009) **Delay in tuberculosis case detection in Pwani region, Tanzania. A cross sectional study.** BMC Health Services Research 2009, 9:196doi:10.1186/1472-6963-9-196.

Paper IV

Ngadaya, E.S., Robberstad, B, Wandwalo, E.R., Mfinanga, G.S., & Morkve, O. **Patients and household costs associated with tuberculosis diagnosis: Can Tanzanian poor afford free tuberculosis diagnostic services? (Submitted: BMC PUBLIC HEALTH)**

Contents

ABBREVIATIONS

AFB   Acid fast bacilli

AIDS   Acquired Immune Deficiency Syndrome

CTRL   Central Tuberculosis Reference Laboratory

DALYs   Disability adjusted life years

DOTS   Direct Observed treatment Strategy

DTLC   District tuberculosis and leprosy coordinator

EPTB   Extra pulmonary tuberculosis

FP   Family planning

GDP   Gross Domestic Product

HIV   Human immunodeficiency virus

IUATLD   International Union against tuberculosis and lung diseases

MCH   Maternal and child health

MOHSW   Ministry of Health and Social Welfare

NIMR   National Institute for Medical Research

NTLP   National Tuberculosis and Leprosy control Programme

OPD   Out patients department

PMTCT   Prevention of maternal to child transmission of HIV

PTB   Pulmonary Tuberculosis

SD   Standard deviation

TB	Tuberculosis
TSH	Tanzanian shilling
TDHS	Tanzania demographic and health survey
USD	United states dollar
VCT	Voluntary Counselling and Testing
WHO	World health Organisation

1. INTRODUCTION AND LITERATURE REVIEW

1.1 General

Tuberculosis is a growing threat, a global health burden and the leading cause of adult death above any other infectious disease especially in the developing world [1]. The HIV/AIDS pandemic has caused a resurgence of TB. Globally, it is estimated that, 7-15% of new cases of TB are also HIV/AIDS co-infected; Sub Saharan Africa accounts for 75% of these case [1-3]. Nearly 60% of HIV infected individuals in Sub Saharan Africa are women, but TB case detection in many countries is lower in women than in men[4]. In Tanzania, women account for 58% of all HIV infected cases but less than two fifths of new smear positive TB cases notified in the country in 2007 were women [5-6]. WHO recommends TB case detection through passive case finding rather than active case finding. However, TB case detection through passive case finding has remained lower in many sub Saharan countries and active case finding through mass screening and house-to-house surveys were neither practical nor cost effective [7-8] .

1.2 Pulmonary tuberculosis diseases, causes and transmission.

Pulmonary tuberculosis is a lung disease caused by *Mycobacterium tuberculosis* or occasionally by other bacteria that are members of what is known as the *mycobacterium complex (m. bovis, m. africanum, m. microti, m. cannetti m. pinnipedii and m. caprae).*

A typical pulmonary tuberculosis disease is characterised by chronic cough with or without blood stained sputum, low grade evening fever, weight loss, night sweat, chest tightness and chest pain. The micro-organisms usually enter the body by inhalation of infected droplet nuclei from a person with pulmonary tuberculosis. Individual risk of infection depends on the concentration of infected droplets in the

air, extent of exposure to droplei nuclei and the susceptibility of an individual to infection [9]. Good ventilation removes nuclei droplets and so prevents nuclei from being inhaled by a person. Direct sunlight kills the tubercle bacilli within minutes, but they can survive in the dark for many hours (24-48 hours) [9]. Sputum smear-positive pulmonary tuberculosis patients are much more infectious than those with smear-negative sputum [10].

1.3   TB and HIV

The natural history of many diseases including TB has been reverted by HIV/AIDS. The advent of the HIV/AIDS pandemic has lead to an increase of TB especially in Sub Saharan Africa [1-2, 11]. Though globally, TB prevalence is on a decline by more than 20 percent, the disease has tripled in the high burden HIV countries [12]. HIV has been the driving force for TB and has modified the natural history of the TB disease. While, as earlier stated, 7-15% of all new TB cases in adults are also HIV co-infected globally, in WHO African region the figure is 31% and in Tanzania is even higher at 50% [2-3, 6]. The diagnosis of tuberculosis is more difficult in individuals with HIV/AIDS [13]. Immunosuppression caused by HIV/AIDS predisposes a previously TB infected individual to develop disease [14] . The annual risk of developing TB disease in a person co infected with HIV/AIDS increases about 20 times, from 0.4% to 8% [14]. TB/HIV co infected individuals usually have atypical TB presentation [15]. With the advent of HIV/AIDS, there is increase in extra pulmonary TB cases (EPTB), atypical findings in chest x-ray and increase in smear negative pulmonary TB cases [15-16].

1.4   Global TB burden

It is estimated that, one third of the world's population is infected with TB [1]. One in ten infected people develops active TB in their life time, and 1.8 million people die from the disease annually [1]. Tuberculosis is disproportionally distributed globally

with the majority of new TB cases occurring in Asia and Sub Saharan Africa [1, 17-18]. The proportion of people who become sick with TB each year is stable or falling worldwide, but the absolute number of new cases is still increasing, partly because of population growth [19]. Regional comparisons of the estimated number of cases in 2007 show that most were in Asia (55%) and Africa (31%) [1]. Nearly 80% of the global burden of tuberculosis is contributed by only 22 countries. In 2006 and 2007, Tanzania ranked 14 and 15 respectively [1, 19]. The top five countries with high TB burden are India, China, Indonesia, Nigeria and South Africa [1].

1.5   The burden of tuberculosis in Tanzania.

In more than twenty years after launching of the National Tuberculosis and Leprosy Programme (NTLP) in Tanzania, tuberculosis continues to be among the major public health problems in the country. Following the advent of the HIV/AIDS epidemic in the country, the number of tuberculosis cases has steadily increased from 11,753 in 1983 to about 62,092 in the year 2007, more than five-folds [20]. The majority appear in the economically active age group (15-54 years), the same age group affected by HIV/AIDS [20-21]. The situation is worse in urban areas like Dar-es-Salaam, which for almost two decades has contributed about 25% of cases notified in the country [20]. Apart from HIV/AIDS, other factors that contribute to the rapid increase of tuberculosis in Tanzania include population growth and urbanisation [6, 21]. A study by Range et al, showed that, between 1991-1998 TB case notifications rates increased from 54 to 74 per 100,000 populations [21]. Sixty percent of this increase was related to HIV/AIDS [21]. Annual reports of the NTLP have shown the same trends [20]. According to these reports, between 2006 and 2007, the notification rate per 100,000 population declined by 3.3% [6]. Case detection rate for new smear positive cases was 51% in 2007 while that of all new cases was 48% [1]. Out of all TB cases notified in 2007, ninety three percent were new case [1].

1.6   Global Policies and challenges for Tuberculosis control

For decades, tuberculosis control has been a major subject of concern on the world agenda. In the year 1991, the world health Assembly recognised TB to be a major neglected health problem and called for much greater international effort to control the disease. However, for almost two decades now the situation has not improved especially in low income countries, where the burden is overshadowed by stigma, ignorance, poverty and poor diagnostic facilities [22-25]. WHO estimates that case detection in many countries is very low [1], therefore, large numbers of cases are undiagnosed and continue to spread the infection in various communities. The WHO has set two targets for global TB control: 70% detection of incident cases, and 85% successful treatment. Theoretically, reduction of TB is expected once these two targets are met. The global target of detecting at least 70% of TB cases is still a challenge in most of the sub Saharan countries. Tuberculosis control aims at reducing the spread of infection through early case detection and prompt treatment. It is through case detection that the source of infection can be identified and through early treatment that the chain of transmission can be broken and thereby preventing unnecessary deaths. Community studies on active case findings have not been recommended in developing countries [8, 26-28] partly because of the high cost. Pronyk et al in South Africa managed to detect only 6 patients through active case finding among a population of 56,000 [27]. In addition to that, most of their patients had previously attended a health facility without being recognized as TB suspects, implying delayed diagnosis [27]**.** WHO recommends TB case detection through passive rather than active case finding. However, TB case notification is still low in most of the developing world. While globally 62% of new smear positive cases were detected in 2006 under DOTS, in 2007 the figure was 63% [1]. Overall treatment success rate in 2007 was 86%, slightly above WHO target of 85% [1]. While good TB treatment success rates has been achieved under DOTS, low case detection rates remain an obstacle to the long-term success of TB control programs [1, 29-30].

1.7   Active TB case finding: Historical perspective and success.

After the advent of anti-TB drugs, there was a significant change of TB case finding, from case detection and isolation to case detection and treatment. Different TB case detection strategies have been used over the last century from mass radiography, house to house surveys, out-patient case detection and enhanced case findings. Mass radiography was the first active case finding strategy in industrialized countries before 1960's [7]. In 1945, mass radiography was conducted in the developing world where a greater proportion of army recruits from India were found to have TB [7]. Another mass radiography study conducted in Delhi, India among 90% of civil servants revealed a significant number of undiagnosed TB [7] . However, in the late 1950's, the use of mass radiography in the developing world was found not to be practical, primarily due to its high cost and under-developed public health infrastructures [31]. From early 1960s, studies in developing countries revealed that the majority of patients were aware of their TB symptoms and had sought care for these symptoms prior to their diagnosis [7, 32]. It was therefore concluded that, with the strong health system infrastructures, the majority of symptomatic cases could be detected [7, 32]. From the 1970's and onwards, house-to-house TB case detection studies using different methodologies from symptom survey, tuberculin skin testing and mass radiography were conducted. House-to-house symptoms screening and sputum collection in South Korea found health facilities screening to be more efficient, even though household visits detected almost three times more cases than the health facilities screening [7]. A prevalence survey conducted in KwaZulu, South Africa concluded that active case finding would be necessary if TB incidence was to be reduced; however it was too costly and therefore impractical [33]. Kenyan investigators tested several different case detection strategies in a series of studies in the late 1970s and 1980s [34-36]. Though house-to-house surveys yielded the highest proportion of the estimated annual incidence of smear-positive cases, it was found to be cumbersome, costly and time-consuming, and therefore considered to be an impractical strategy for many developing countries with limited resources [26, 28, 36].

1.8   Tanzania Tuberculosis control and case detection rates.

Tanzania total population is projected at 38 million people [37] of which the majority are females. The healthcare system in Tanzania is fairly well distributed with over 90% of the population living within 10km from a health facility [38-39]. Tanzania is among the countries with the highest TB and HIV burdens [1, 4]. The HIV prevalence among TB patients is almost 50% [1], higher in urban settings compared to rural areas. TB case detection in Tanzania is mainly through passive case finding. Passive as opposed to active TB case finding is when symptomatic patients present themselves to the outpatients department (OPD) with a cough of two or more weeks with or without accompanying symptoms, and are screened for TB. None of the case finding activities are conducted at the maternal and child health (MCH) clinics or family planning (FP) clinics.   Directly Observed Short course therapy (DOTS) coverage in Tanzania is 100% but for more than a decade case detection rates of new smear positives cases has shown a decreasing tendency [1]. TB diagnosis is mainly by smear microscope and TB activities are monitored routinely through NTLP [40].

1.9   Challenges for early TB case finding

A successful TB program requires specific behaviours from both patients and healthcare providers in order to facilitate successful TB case detection and prompt treatment. In many communities where TB incidence is high, the major force driving the epidemic is transmission, and long delay from the onset of disease to start of treatment. Patients' health seeking behaviour and factors within the healthcare systems are the main determinants of the delay.

Health system: Healthcare providers are expected to successfully offer sputum smear examination to patients, conduct tests adequately and timely, and monitor TB medicine intake [1, 40]. However, inadequate TB knowledge among health workers and the lack of diagnostic facilities may delay patients diagnosis and treatment [41]. Studies have shown that, the majority of people with cough seek appropriate help

early but the problem is within the healthcare system. Less than a quarter of people who attended a health facility in Ghana with cough of more than 2 weeks were investigated for TB at their first visit [42]. Another study from Kampala Uganda showed a total delay of up to 22 weeks among those who first approached government health centres. The major contributor to the total delay was health system [43]. Studies conducted in Botswana, Ghana and Ethiopia identified healthcare system as the main cause of delay as well [44-46].

Patients health seeking behaviour: How an individual define his/her ill-health condition depends on a variety of factors, such as ignorance, poverty and stigma associated with the disease. Lack of knowledge may lead to under- or over-estimation of the duration of illness [47]. Poverty and ignorance can also influence individual health seeking behaviour. It can influence the way the poor perceive their illness, when and where to seek care, type and quality of care received and whether they achieve successful outcome or not. Such barriers delay health care seeking and lengthen the overall process of achieving cure, resulting in greater expense and lost income, which in turn increase poverty [48-49]. Late reporting to a health facility after onset of cough symptoms was among the causes of delay to initiate TB treatment in Mwanza and Dar es Salaam [41, 50]. A significant number of patients first reported to traditional healers in Mwanza [50] which may contribute to their delay. A study conducted in Kampala Uganda revealed that the majority of patients first presented to a private clinic or pharmacy after having respiratory symptoms, thus delaying to seek proper medical care [43]. Due to the similarities in symptoms between TB and HIV/AIDS, TB is highly stigmatized [51-52]. A study conducted in a high HIV prevalence area in Thailand revealed that TB is highly stigmatized because people with symptoms related to TB are regarded as having HIV rather than TB [53]. This could be a major drawback in case detection as patients may fear to present themselves for care, especially those patients who suspected themselves of having HIV/AIDS [53-54].

1.10   TB in women: burden and historical perspective.

TB kills more women than all causes of maternal death combined [55]. Globally less than half of the new smear positive TB cases notified in 2007 were females [1]. In Tanzania less than two fifth of smear positive TB patients detected in 2005 were females [6]. The impact of TB on women is more intense when considering repeated child bearing, malnutrition and low social economic status of women, HIV/AIDS and stigma attached to TB. Once infected with TB, women in the reproductive age group are more susceptible to develop active TB than men of the same age group [56]. TB in pregnant women has been a topic of concern and controversy. It was believed that, enlarging gravid uterus improved the course of TB disease [57]. However, in the middle of 20th century it was shown that change of intra-thoracic pressure due to descend of the diaphragm following delivery, accompanied by hormonal fluctuation and low nutrition increase the susceptibility to pulmonary TB [58]. Towards the beginning of 21st century, it was revealed that, if properly and adequate treated with anti-TB chemotherapy, pregnant women are not at a higher risk than non pregnant women [59]. Several factors have been associated with low case detection among women, some being cultural, social, low social economic status of women and women's tendency of placing family matters above their own health [60-61]. Under-reporting of TB cases among women could explain the low notification rate of TB among women since it is known that the prevalence of infection is similar in males and females until adolescence [62]. After adolescence TB notification rates in many developing countries show men's disease rates exceeding that of women [62]. This have been associated with greater exposure because of higher social and economic activities among adult males than females [63].

1.11   Expanding TB case finding activities to other clinics.

Extension of TB case finding activities to other clinics has been recommended in other studies and may contribute to reducing delay in initiating treatment. A study

conducted in Haiti showed that a high proportion of people with cough attending voluntary HIV counselling and testing (VCT) clinics had TB [64] and it was recommended to extend TB case finding activities to VCT clinics. Furthermore, TB screening during antenatal care (ANC) was recommended in a study by Kali on combining PMTCT clinics with active case finding for tuberculosis [65]. In this study, significant numbers of HIV-infected pregnant women were found to have previously undiagnosed, smear-negative, culture-confirmed TB. Sangala et al in Malawi demonstrated that intervention aiming at extending TB case finding to ANC was acceptable [66]. In addition to the acceptability of extending TB case finding activities to other clinics, screening of patients with short duration of cough of one week has revealed undiagnosed smear positive TB cases in Malawi [67]. Furthermore, a study conducted in Brazil revealed that the probability of having TB was not related to cough duration [68].

1.12   Economic burden of TB

The burden of tuberculosis in Africa and other low income countries is significant. It affects social and economic livelihoods of the individual patients, families and the country economy at large. TB affects the economic welfare of people in at least two ways. First, the disease necessitates costly healthcare seeking thus reducing the proportion of income available for other types of consumption and investments. Second, TB sickness reduces the ability of people to perform their usual productive activities, further diminishing the economic capabilities of poor households [69].

High direct costs before TB diagnosis, during the course of diagnosis and during treatment among patients and households have been reported in other studies [48, 69-70]. The economic burden to TB patients just before registration into a TB clinic was for example demonstrated to be a barrier for prompt diagnosis in Zambia [69]. A study in Bangladesh showed that, households with a TB patient spend 20% of the households annual income on private medical expenses before the patient visited public TB clinic [48]. The average patient and household costs before TB diagnosis

was 209% of the mean monthly income in Malawi and 158% in Zambia [69, 71]. In a study conducted in Zambia, one third of TB patients stopped working due to TB illness [69]. Furthermore, the majority of wage earners had to stop work because of TB in Uganda, where subsistence farmers reported lower productivity for the same reason [70]. It was further revealed that the average time lost was unbearable and that patients on average lost income comparable to almost 90% of Gross Domestic Product (GDP) per capita [70].

Loss of income and increased expenditure following TB illness may subject poor families to remain with debt and, in consequence, having to sell their assets, which subsequently may result in increased poverty. Two fifths of households with TB patient in Bangladesh sold their assets to cover the cost associated with TB [48]. Research in India revealed that one fifth of rural patients and two fifth of urban patients borrowed money to pay for expenses due to TB [49]. All these findings suggest that reducing diagnostic delay could reduce costs, improve welfare, increase households' productivity and their income. High pre-diagnosis costs can be substantial especially among the poor and may deter patients from seeking care early and therefore jeopardize the efforts made by National TB control programs in meeting the Millennium development goals.

2. RATIONALE OF THE STUDY AND STUDY OBJECTIVES

2.1 Rationale of the study:

Infectious pulmonary tuberculosis is often not detected until a late stage, even though patients may have attended health facilities during the initial stage of the disease [41, 50, 72]. The period during which infected people fall ill, but before they are diagnosed and effectively treated, is critical because of substantial pre-diagnosis costs. This is a particular cause for worry because of long delay in TB case detection leading to ongoing transmission caused by poor patients who can't afford pre diagnosis expenses. Thus, there is a need for looking into other ways of detecting TB cases early within the recommended passive case finding strategy in order to reduce delay and cost.

The majority of Tanzanian are poor, they consume less than the national poverty line of 0.4USD per person per day [39]. In the year 2007, the average monthly household income at national level was 31USD [39], while for a household in Dar es Salaam the average was 63 USD [39]. On clinical and epidemiological grounds, emphasis has rightly always been laid on early diagnosis of tuberculosis. But due to ignorance and poverty, delay in TB case detection is still a problem in many African countries causing high patients and households cots. Like in many other developing countries, TB case-finding in Tanzania depend on self-referred patients to the health facilities. A patient must have cough of two weeks or more to be suspected [40] and only patients with long duration of cough are screened for TB by smear microscopy [40, 73]. Under current passive case finding, Tanzania as a country is detecting less than WHO estimates, since only those who report to the OPD with chronic cough with or without some other constitutional symptoms for TB are suspected and investigated. However, with the current health system situation in the country, it is less likely for patients with short duration of cough to queue at the health facility for care; most of them will first take self medication from drug shops and pharmacies as reported in

other studies [46, 74]. Furthermore, ignorance may also make patients to underestimate the duration of their illness as it was previously reported in Tanzania [47] and therefore, reduce their chances of being suspected early. In addition, it is not necessary for someone to cough for two weeks or more for mycobacterium to be evident in the sputum[68]. Moreover, incorporation into maternal and child health clinics, information about the risks of tuberculosis in young women was recommended by Holmes in 1998 [62].

Despite low TB case detection in Tanzania, no single study has tried to intensify passive TB case finding, by expanding TB case detection activities into FP and MCH clinics as well as screening all patients with cough, regardless of the duration, attending OPD, FP and MCH clinics. Pre-diagnosis costs and how they may affect health seeking behaviour are also not well documented. The present study was conducted under normal operational conditions using the routine diagnostic technique for TB. Cough is a primary symptom used in this study as advocated by NTLP [40]. A study from India also found that, using cough as a primary symptom among OPD attendees, 65% of all prevalent smear positive TB cases would be detected [75]. Sputum microscopy is the main diagnostic technique for TB as it is cheap and quick, most available and reliable. Sputum culture is not done as a routine procedure, but can be done in zonal laboratories and in the National Reference Laboratory for drug sensitivity surveillance and follow up of retreatment patients with treatment failure or relapse [40].

2.2   Goal

The main goal of the study was to contribute towards reducing diagnostic delay and identifying factors associated with tuberculosis management delay in Coastal (Pwani) regions.

2.3   Main objective

To establish the effect of intensifying passive TB case finding: study delays in TB management and determine patients' and households' costs associated with TB passive case finding in Dar es Salaam and Pwani regions, Tanzania.

2.4   Specific objectives

i.   To determine the prevalence of pulmonary tuberculosis among all patients who reported cough, regardless of duration, attending OPD in Dar es Salaam.

ii.   To determine the proportion of smear positive TB cases among women with cough attending FP and MCH clinics in Dar es Salaam.

iii.   To determine the magnitude of, and factors responsible for TB management delay in Pwani.

iv.   To determine patients' and households' cost associated with TB healthcare seeking in Dar es Salaam.

3.   METHODS

3.1   Study design and area.

We conducted a cross sectional hospital based study in Dar es Salaam and Pwani region between 2007 and 2008. The two regions are adjacent to each other and they are located along the coastal area of Tanzania as shown in figure 1 below.

Coast (Pwani) region is bordered to the East by Dar-es-Salaam and the Indian Ocean, to the North by the Tanga Region, to the South by the Lindi Region and to the West by the Morogoro Region. Residents of Pwanit are of different ethnicity, though mainly Zaramo. They are mostly engaged in low income generating activities and small scale farming. According to the 2002 census report, Pwani region has a total population of 889,154 with 440,161 males and 448,993 females [76]. The region is administratively divided into six districts namely Bagamoyo, Kibaha, Kisarawe, Mkuranga, Rufiji and Mafia. The study was conducted in Bagamoyo, Kibaha, Mkuranga and Kisarawe. The total population in the four districts where we conducted our study was as follows; Bagamoyo 230,164; Kibaha132, 045; Kisarawe 95,614 and Mkuranga187, 428 [76]. The literacy level among males and females in Pwani was 75.7% and 72.5% respectively, compared to 80.0% and 67.3% for the country at large [77]. The majority of the residents live below one dollar a day [39]. HIV/AIDS prevalence in the region is 5.3% [78] slightly lower than the national figure of 6.0%. TB case notification is still very low like in other regions of Tanzania [20].

Dar es Salaam is the country's richest city and a regionally important economic centre. The city is administratively divided into three municipalities namely Kinondoni to the north, Ilala in the center and Temeke to the south of the city. The study was conducted in all municipalities of Dar es Salaam. According to the 2002 census report, Dar es Salaam has a total population of 2,497,940 with 1,261,077

males and 1,236,863 females [76]. Kinondoni alone has the total population of 1,088,867 with 549,929 males and 538,938 females. Ilala and Temeke have the total population of 637,573 and 771,500 respectively. Total male and female population in Ilala is 321,903 and 315,670 respectively, while that of Temeke is 389,245 males and 382,255 females [76]. The population is relatively young with the majority aged less than 25 years [76]. Population growth following urbanization is also high making the city to have mixed ethnicity. Since Dar es Salaam is close to Pwani region, residents between the two regions easily interact. The surrounding villages and towns of Pwani focus on Dar es Salaam as the market for their products and the source of supplies and consumer goods. The majority of the residents are involved in small scale businesses. Percent literacy level among males and females in Dar es Salaam was 94.5% and 87.4% respectively [77]. For the past ten years, Dar es Salaam has accounted for a quarter of all TB cases notified in the country. Like in other parts of the country, TB services are free in all government facilities. Health facilities in Dar es Salaam are well distributed, while 75% of the population lives within 2km from a health facility, more than 95% are within 6 kilometers [39].

Figure I: Map of Tanzania:
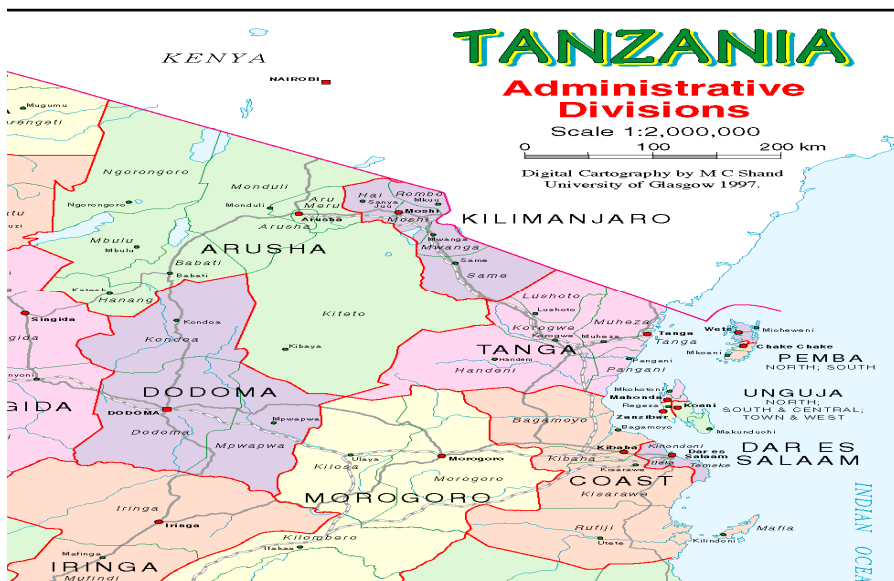
3.2   **Study population**.

3.2.1 Selection of districts.

All three municipals of Dar es Salaam and four out of six districts of Pwani regions were included in the study. From the list of all districts in Pwani, we randomly selected four namely; Bagamoyo, Kibaha, Kisarawe and Mkuranga.

3.2.2 Selection of health facilities:

In Dar es Salaam, the study included municipal hospitals and government health centers. All municipal hospitals namely; Temeke, Ilala and Mwananyamala were purposefully selected due to their large number of patients. In addition, we also selected randomly one health center from each municipal from a list of all government health centers. The selected health centers included Zakiem in Temeke, Tabata in Ilala, and Magomeni in Kinondoni, making a total of three health centers in Dar es Salaam.

In the four districts of Pwani region, we included all four district hospitals plus a random sample of 10% of all health facilities which offer TB services. In total we included the four hospitals, four health centers and eight dispensaries from Pwani region.

3.2.3 Selection of study participants:

Study participants for detection of pulmonary tuberculosis among patients with cough attending Outpatient departments in Dar Es Salaam (paper I) involved patients aged 5 years and above and complaining of cough. Study participants for pulmonary tuberculosis among women with cough attending FP and MCH clinics in Dar Es Salaam (paper II) involved women with cough aged 15 years and above. All

participants enrolled through OPD, FP and MCH were screened for TB by sputum microscopy, regardless of the duration of cough.

Exclusion criteria for the study participants (paper I and II) comprised patients who were already diagnosed with tuberculosis at the time of the study or who were already on anti TB drugs, non-consenting patients and patients who were unable to collaborate because of psychiatric disease.

To study delays in tuberculosis case detection (Paper III) we recruited smear positive TB patients diagnosed as having TB within three months prior to the commencement of the study in Pwani region.

Study participants for patients and household costs associated with TB health care seeking (paper IV) included patients aged 15 years and above who had just been diagnosed with TB. Patients were excluded if they were less than fifteen years of age, insane or non-consenting.

Table 1: Summary of the study participants and tools.

Paper	Title	Study population	Number of patients/sputum samples collected.	Study tools
Paper I	Detection of pulmonary tuberculosis among patients with cough attending outpatient departments in Dar Es Salaam, Tanzania: does duration of cough matter?	All patients aged five years and above, with cough, regardless of duration, attending out-patient department.	2274 patients	OPD registers, laboratory registers/ records.
Paper II	Pulmonary tuberculosis among women with cough attending FP	Women with cough, regardless of	749 women	FP and MCH registers,

	and MCH clinics in Dar es Salaam, Tanzania.	duration, attending FP and MCH clinics		Laboratory registers/records.
Paper III	Delay in Tuberculosis case detection in Pwani Region, Tanzania. A cross sectional Study.	Smear positive TB patients ages 15 years and above.	226 smear positive TB patients	Structured questionnaires, TB treatment cards
Paper IV	Patients and household cost associated with tuberculosis diagnosis: Can Tanzanian poor afford free TB diagnosis services?	Patients aged 15 years and above and who had just been diagnosed with TB.	123 TB patients	Structured questionnaires

3.3   Data collection methods:

We recruited study participants in four different locations: general OPD clinics, MCH clinics, FP clinics and DOTS clinics.

Figure II: Flow chart of study subjects.

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                    ┌──────────────────────┐
                    │  All study subjects  │
                    │  3,372.              │
                    └──────────────────────┘
              ┌─────────────┴──────────────┐
              ▼                            ▼
   ┌────────────────────┐      ┌────────────────────┐
   │ 3,023 TB suspects  │      │ 349 TB patients    │
   │ from OPD, MCH and  │      │ from DOTS clinics  │
   └────────────────────┘      └────────────────────┘
      ┌──────┴───────┐            ┌──────┴───────┐
      ▼              ▼            ▼              ▼
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2274 patients with cough, regardless of duration, attending OPD.	749 women with cough, regardless of duration, attending FP and MCH	123 recently diagnosed TB patients	226 smear positive TB patients attending DOTS clinics.
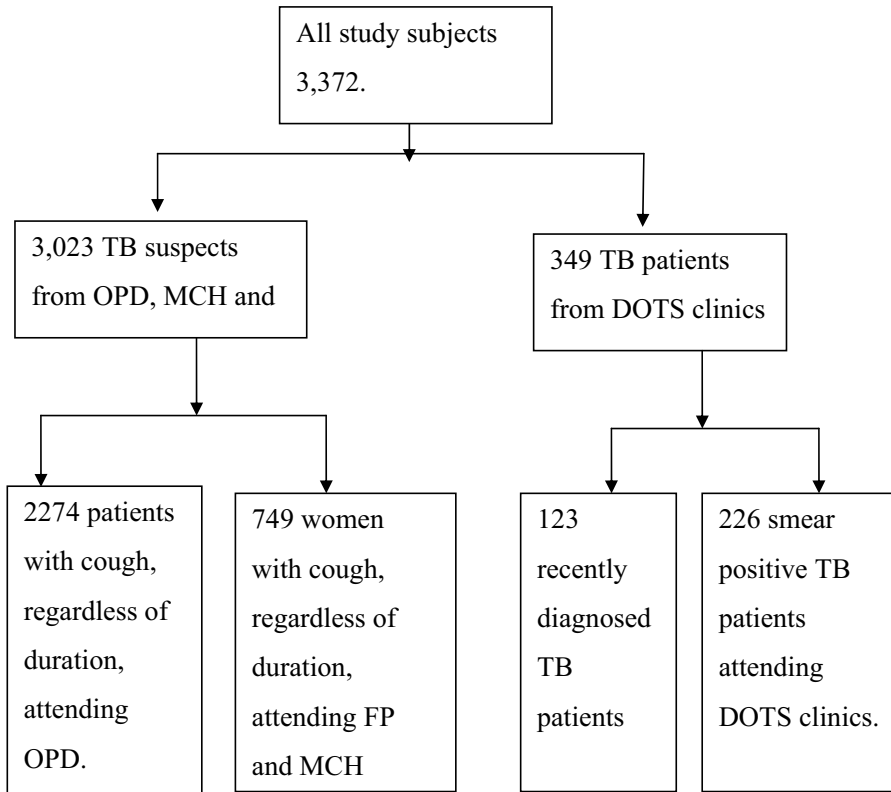
3.3.1 Training of personnel.

Before commencement of the study, we trained the research team on the study questionnaires and data collection procedures. The team comprised of research coordinators, clinical officers, laboratory personnel and research assistants.

3.3.2 Recruitment of study participants from the OPD, MCH and FP clinics:

In the OPD clinics, clinical officers registered in a separate study register all patients reported to have been coughing. At the MCH and FP clinics, clinical officers asked the patients whether they had a cough. If so, they requested the patients to submit

sputum samples as per national guidelines for TB suspects. Variables recorded were name, socio-demographic characteristics, area of residence, cough duration in days or weeks, areas they visited for care, number of visits made and sputum results. Sputum request forms were used for sputum investigations. Study laboratory registers were used to record patients smear results.

3.3.3 Recruitment of study participants and data collection for assessing delay in TB management:

We interviewed the patients using a structured questionnaire which included open and close-ended questions. To ensure that all smear positive patients were enrolled, we identified all smear positive patients who had been diagnosed within three months prior to the day of interview. A maximum of two weeks was used to collect information at each facility, depending on the number of smear positive patients available in the facility and number of patients coming to collect drugs. The information collected included: socio-demographic characteristics, knowledge about TB, place of first consultation and time spent to go to the nearest health facility. Other information collected were date of onset of pulmonary symptoms, date of first visit to a health facility, dates of collection of all three sputum samples, and date of starting treatment. If a patient did not remember the exact dates, then the patient was asked if it was at the beginning of the month, at mid month or at the end of the month. The beginning of the month was labeled as 5th, mid month was labeled as 15th and end of the month was labeled as 25th of the respective month. Patient TB treatment cards were also used to look at the date treatment was started.

3.3.4 Recruitment of study participants from the DOTS Clinics for identifying patients and households cost before TB diagnosis:

In all facilities, a list of all TB patients aged 15 years and above who had been diagnosed within the last two days was made as they appeared in the TB treatment registers. From this list, every second patient who came for TB treatment was

selected, and after informed verbal consent, they were interviewed using a structured questionnaire. Associated healthcare seeking expenditures and loss of income incurred by the patients, caregivers and families while seeking care for TB symptoms were registered. Interviewers were trained to elicit answers with a series of supplementary questions. Patients were asked about when their current TB symptoms started, where they visited for healthcare, number of visits made to each healthcare facility, including traditional healers, number of visits they were escorted on, as well as travel time and cost they encountered. Other information requested included: time spent in each facility, consultation, laboratory and treatment cost. Cost for buying food or drink while going to each place and any other out of pocket cost was also noted. In addition, we asked questions concerning income from different sources for each member of the household before and during illness. Questionnaires also contained information on patients' socio-demographic characteristics.

Cost estimation: The conceptual framework for the measurement of patient and household cost were drawn from general guidelines for cost analysis [79]. Costs were estimated during TB healthcare seeking, which is the period from the onset of symptoms to the diagnosis. Two types of costs commonly associated with using healthcare services were measured: direct and indirect cost. Direct costs include all financial expenditure by the patient and care taker such as on consultation, registration, traditional healers and remedies, investigations, drugs and food bought when seeking care. Direct costs also included transport costs – the amount spent by the patient and/or caregiver on transport to travel to each health facility. Indirect costs included patients' and households' income loss, and loss of time from production and employment activities related to disease and accessing care. Economic losses from all sources were also calculated. We estimated time loss by assuming that there are 22 working days in a month and 8 working hours in a day. Time loss was converted to monetary values based on the average reported patient income before illness. Patients with no income before illness were excluded in the calculation of mean patients' income.

3.3.5 Collection of sputum, microbiology and diagnosis of TB.

All patients were requested to submit three sputum samples in a form of spot, morning, and spot. Spot specimens were collected on the day the patient is suspected to have tuberculosis, morning samples were collected early in the morning of the second day and the third specimen was collected on submission of the morning specimen. A total of 9069 sputum samples were collected in a 50 ml screw cap. Smear microscopy was done by routine Ziehl Nielsen staining technique for acid fast bacilli in each respective facility laboratory. A patient was diagnosed to be smear positive if he/she had at least two sputum smears positive for acid fast bacilli. Smear positive results were classified and recorded according to the standard WHO/IUATLD protocol. Acid Fast Bacilli seen per high power field was classified as 1-9 per100 immersion fields, +1 for 10-99AFB per 100 fields, +2 for 1-10 AFB per 1 field and +3 for >10 AFB per 1 field.

3.3.6 Quality control:

Research assistants were trained on research tools and data collection procedures. In addition, training was also conducted to make sure that procedures for smear microscopy were according to the National standards. Study clinicians were responsible to register all patients with cough and their smear results in the study registers. At the end of the week, the study coordinators compared smear results recorded in the patients' registers with patients' results in the laboratory registers. The study was conducted at a time when the Central Tuberculosis Reference Laboratory (CTRL) had an ongoing quality assurance project. The quality check for the submitted samples was done according to routine National Tuberculosis and Leprosy Control Program (NTLP) guidelines [40].

3.4   Study Management.

3.4.1 OPD, MCH, FP and DOTS clinics:

Clinicians were placed in the OPD of each selected facility as well as at the FP and MCH clinics. One laboratory personnel in each facility was responsible for performing smear microscopy and record the results in the laboratory registers and laboratory request forms. They were also directing patients to send their laboratory results to the respective clinicians.

One research assistant was placed at each of the MCH and FP registration areas. They were responsible for asking all women about cough and direct them to study clinicians. The research coordinators checked the records filled by clinicians and research assistants for completeness and consistency. Their main responsibility was to ensure that the study protocol and guidelines were followed. They were also responsible for filing the questionnaires and keeping the registers for further review by the principal investigator, before data entry. Data was double entered by the data entry clerks.

3.5   Data management and statistical analysis.

3.5.1 General:

Completed questionnaires were coded by numbers and double entered in a computer software Epi-data version 3.1 [80]. Coding procedure was done to allow computer entries of responses for open questions and combinations of multiple responses to respective questions in the questionnaire. Cross-checking and data cleaning was done. Data was then transferred to Statistical Package for Social Sciences version 11.5 for windows (SPSS Inc, Chicago, USA) for analysis. The variables were categorized to form groups of interest for comparison analysis.

3.5.2 OPD, MCH and FP data:

The outcome variable was diagnosis of smear positive TB. We explored possible associations between cough duration and smear results, clinic of diagnosis, place of first presentation and number of visits made prior to diagnosis. Pearson chi- square and Wald statistic were used to compare group difference for categorical variables. Differences were considered statistically significant if $p \leq 5\%$. We estimated risk factors for smear positivity by logistic regression, with 95% confidence interval (CI) given for odds ratios (OR), indicating a statistically significant relationship if the 95% CI did not include 1. Adjusted OR with 95 % CI were also calculated. Nineteen (1.3%) patients had only one smear positive sputum sample and were excluded from the analysis.

3.5.3 DOTS clinic data:

Risk factors for delay were estimated by bivariate logistic regression with 95% CI given for OR. The means(SDs) and medians (ranges) were used for estimation of time delay from onset of illness to reporting for the first time to health facilities and to initiation of treatment.

3.5.4 Cost analysis:

We divided our study population into two groups of poor and less poor, using average income of 63 USD for Dar es Salaam [39] as cut off. Patients with below 63 USD were regarded as poor and those above 63 USD as less poor. Mean and median direct, indirect and total costs for both patients and households were determined. All costs and incomes are presented in USD 2007 and the exchange rate from Tanzanian shillings to USD used was TZS 1,279.1 per one USD [39].

3.6   Operational definitions

Patient delay: the time interval between the day of experiencing for the first time one of the current pulmonary symptoms to the day the patient sought medical advice for the first time. Interval that exceeded 30 days was considered as patient delay [41, 50].

Health facility delay: the time interval between first consultation at a health facility to the day the treatment was initiated. We considered a time interval of more than 5 days as health facility delay [41].

Total delay: the sum of the patient and health facility delay.

Knowledge about TB: Patients who knew that TB can be spread from one person to another by coughing/sneezing were defined as having "good knowledge on TB transmission". Patients who mentioned prolonged cough plus two other symptoms from the following: fever, night sweat, chest pain, difficult in breathing, weight loss and coughing blood were defined as having "good knowledge of TB symptoms"[41].

3.7   Ethical Clearance:

The proposal was granted ethical clearance by the Tanzania Medical Research Coordinating Committee. Permission to conduct the study was also sought from the local authorities. Informed verbal consent was obtained from each interviewee before enrolment into the study. For those below the age of 18 years permission was sought from their parents or caretakers. Patients with one smear positive sputum sample (Paper I and II) were referred to the district tuberculosis and leprosy coordinator (DTLC) for treatment and follow up using NTLP procedures. All patients with PTB (Paper I and II) were also referred to the DTLC for treatment. Non-TB patients were treated according to the diagnosis made.

4. KEY FINDINGS

4.1 Detection of Pulmonary Tuberculosis among Patients with cough attending Outpatient departments (Paper 1):

We enrolled 2274 patients, out of these, 2214 (97.4%) remembered their cough duration. One thousand nine hundred and seventy three patients (89.1%) coughed for two weeks or more compared to 241 (10.9%) patients who coughed for less than 2 weeks. Of those who coughed for two weeks or more, 250 (12.7%) had smear positive PTB, and of those who had coughed for less than two weeks, 21 (8.7%) had smear positive PTB. There was no statistically significant difference in proportion of smear positive tuberculosis between the two comparison groups (Pearson Chi-Square 3.2; p = 0.074). We therefore concluded that detection of smear positive PTB among patients who had coughed for less than two weeks was as high as for those who had coughed for more than two weeks among patients attending outpatients departments in Dar es Salaam.

4.2 Pulmonary tuberculosis among women with cough attending clinics for family planning and maternal and child health (Paper II)

We enrolled all women with a cough, attending family planning clinics and those who escorted their children for MCH services.

We enrolled a total of 749 TB suspects. Five hundred and twenty nine patients (70.6%) were from MCH clinics. Mean (SD) age was 27.6 (5.2) years. A total of 616 (82.2%) suspects were coughing for less than two weeks as compared to 133 (17.8%), who coughed for two or more weeks. Among the 616 who had coughed for less than two weeks, 14 (2.3%) were smear positive TB patients, and of the 133 who had coughed for two or more weeks, 13 (9.8%) were smear positive TB patients. Risk factors associated with smear positive results were having attended more than one

visit to any facility prior to diagnosis (OR=6.8; 95%CI 2.57- 18.0) and having HIV/AIDS (OR= 4.4; 95%CI 1.65-11.96). Long duration of cough was not a risk factor for being smear positive (OR=1.6; 95%CI 0.59-4.49). Therefore, we concluded that the proportion of smear positive TB patients among women with cough attending FP and MCH clinics was 3.8%. The probability of having smear positive TB did not depend on cough duration.

4.3   Delay in tuberculosis case detection (Paper III):

The aim of this study was to estimate the extent and factors responsible for delay in TB case detection in Pwani. Delays were divided into patient, health facility and total delay.

Of the 226 smear positive TB patients enrolled from DOTS clinics, results were available for 206. The majority (66.5%) of the patients were males. Mean age for males and females were 37.3 and 33.7 years respectively. Mean (SD) total delay was 125.5 (98.5) days (median 90). Out of 206 patients, 79 (38.35%) delayed to seek TB healthcare. Health facility delay was observed among 121 (58.7%) patients. Risk factors for patients delay was poor knowledge that chest pain may be a TB symptom (OR= 2.9; 95%CI 1.20- 7.03) and the belief that TB is always associated with HIV/AIDS (OR=2.7; 95%CI 1.39-5.23). Patients who presented with chest pain were (OR= 0.2; 95%CI 0.10-0.61) less likely to delay compared to those with no chest pain.

4.4   Patients and household costs associated with tuberculosis diagnosis (Paper IV):

One hundred and twenty three patients were enrolled. Based on average income, their households were categorised as "poor" or "less poor".

We found that, almost two fifths of patients stopped working due to TB illness with an average of 77 days off. About two thirds reported income reduction, but there was no significant difference between the poor and the less poor. Before diagnosis,

overall, tuberculosis caused on average 25 lost work days. About half of the patients who stopped working were head and the main bread earner for their households. TB patients loose on average almost half of their mean monthly income, and the loss is relatively larger for the poorest patients. At the household level, income was most severely affected in relative terms for the poorest households, with a reduction of 36% (13 USD). The overall households mean monthly income for both groups dropped by 28% (from USD 134.4 to USD 90.7). The overall total costs for the entire household amounted to USD 57, which is equivalent to more that two fifths of the mean monthly income. Poor households spent 150% of their mean monthly income compared to 43% among the less poor household. Indirect cost contributed to almost two thirds of the total cost. We concluded that economic burden of TB healthcare seeking is high, especially among the poorest households, and this may severely prohibit optimal health seeking behaviour.

5.   DISCUSSION

5.1   General methodological issues.

5.1.1   Study design:

Cross sectional study design is considered appropriate in assessing disease prevalence and therefore important for health planning and resource allocation in resource constrained countries. Thus, it was the best study design for our study because we were looking at the prevalence of smear positive TB among patients with cough, determine extent of delay and cost before TB diagnosis. Although it is not as easy to precisely estimate risk in cross sectional studies as it is in cohort studies, the sub groups within our study could be compared and odds ratios calculated, so as to grossly estimate risk factors as part of cross sectional analytical design. The study findings can not be applied to patients with symptoms of TB other than cough (Paper I and II) since the study subjects were patients with cough only. Neither can the findings be generalized to smear negative and other types of TB (Paper III), as we only studied smear positive patients. In addition, private facilities and dispensaries were not sampled in our study (paper I, II and IV), this may reduce the representativeness and hence generalisability of our findings.

5.2   Biases:

5.2.1 Selection bias:

Our study is subject to selection bias, due to the fact that the universe for this study was different from the general population. This may affect generalization of the study findings. Selection bias could be avoided by including patients with cough from the general population. However, due to financial and time constraints we were not able to do a community based survey. Furthermore, TB case finding routines in Tanzania

are through out-patient departments. Except for research purposes, none of the TB case finding activities are conducted at the community level.

5.3 Recall bias

Failure to recall the duration of cough (paper I and II) might lead to mislabeling of patient and therefore under or over estimating the relationship between duration of cough and smear results. However, efforts were made to validate the data by repeated questioning. Furthermore, wrong estimations of the dates (paper III) might lead to the wrong calculation of delays. However, efforts were made to estimate the dates by using periods of the months, holidays etc. As earlier stated, if a patient did not remember the exact dates, he/she was asked if it was at the beginning of the month, at mid month or at end of the month. The beginning of the month was labeled as 5th, mid month was labeled as 15th and end of the month was labeled as 25th of each respective month. Patient TB treatment cards were also used to look at the date treatment was initiated. Monthly income and cost estimation are also subject to recall bias (paper IV). This bias could over- or underestimates the income and cost for TB healthcare seeking. In trying to reduce this bias, we validated our data throughout the interview by repeated questioning and comparisons of patient cost information with known market prices. Though consumption expenditure provide more reliable information of household income [39], the mean household income of 134.4 US$ before illness obtained in this study is almost similar to the 121.1 US$ which is the mean households monthly expenditure for Dar es Salaam reported in 2007 by Tanzania households and budgetary surveys (THBS) [39]. The THBS mostly focus on consumption expenditure information in poverty analysis [39].

5.4   Discussion of the results

TB case finding

DOTS coverage in Tanzania is reported to be 100%, [1] but case detection rates of new smear positive cases have shown a decreasing tendency from 61% in 1995 to 51% in 2007 [1]. WHO recommends passive over active case finding. However, passive case finding depends on patients self awareness, their ability to seek care, as well as affordability of the healthcare. In addition, it also depends on health workers knowledge of TB and their alertness in suspecting patients. Ignorance among health care workers and TB patients contributed to delay in commencing treatment [41, 43, 50, 72, 81]. As a consequence, delayed treatment may eventually cost life and increase the time spent due to inappropriate and ineffective treatment. The effect is even more devastating in the current HIV era where the majority of TB patients are also HIV co-infected [1, 6]. Studies suggest that the probability of being smear positive does not depend on the duration of cough, and that the majority of patients who report to the health facilities have long duration of cough [50, 68, 82-84], though they may report the opposite. Thus, with the DOTS coverage of 100%, efforts are needed to increase detection of infectious cases to reverse the current TB situation in the country. With the existing HIV trends, it may pay off to consider screening all patients with a cough attending OPD as well as expanding TB case findings into other clinics.

Prevalence of smear positive PTB among patients with cough

The proportion of smear positive pulmonary TB among patients who had coughed for less than two weeks was as high as for those who had coughed for two weeks or more. This could probably be explained (though not investigated in this study) partly by patients' ignorance and their perception of duration of their illness. In addition, such patients could have visited several other health facilities that could have suspected TB if medical personnel had proper awareness of TB. However, health

seeking behavior of the study participants before they presented at the out-patient departments was not investigated. Screening, regardless of cough duration, could shorten the duration of TB transmission, as it might reduce diagnostic delays. This is important, especially for individuals co-infected with HIV/AIDS, as it could reduce morbidity and mortality.

Thus, taking into consideration the still increasing prevalence of TB/HIV co-infection, it may pay off to screen for TB, regardless of cough duration, if we really intend to eradicate TB by the year 2050 [85]. A study conducted in Brazil, a country with prevalence of HIV/AIDS in the adult population of less than 1% and annual incidence of smear positive TB patients/100,000 population of 26, reported that the probability of detecting TB case does not depend on the duration of cough [68]. Our study in Tanzania, where prevalence of HIV/AIDS is 7% and annual incidence of new smear positive TB patients/100,000 population is 120, support this finding [1, 78].

Effect of expanding TB case detection in MCH and FP clinics.

The proportion of women with active pulmonary tuberculosis among coughers attending MCH and FP clinics was 3.8%. However, none of the TB screening activities are done routinely in MCH and FP clinics. Our study indicates that pulmonary tuberculosis among MCH and FP attendees with a history of cough is not significantly less frequent, when the duration of the cough is shorter than two weeks. This is also similar to a study conducted in Brazil [68]. Using the current criteria for TB suspicion and only relying on OPD attendees, we might be delaying quite a big number of TB cases, since only those who report at the OPD with a cough of more than two weeks will be screened for TB under the routine program.

The majority of the smear positive women were more likely to have visited government hospitals and made more than one visit without being suspected. Failing to suspect women is consistent with other studies conducted in Vietnam and Tanzania, where factors like poor knowledge of recognizing and reporting TB

symptoms and ignorance among healthcare workers were associated with delay in TB case detection among women [41, 86]. They could also have first visited healthcare posts where they were not properly taken care of, e.g. medical stores and traditional healers. Lack of awareness by health personnel and lack of TB diagnostic services could also offer an explanation [60, 86-87]. Apart from the delay in being suspected, fewer smear positive women than men were detected [1, 17, 82]. Though we did not investigate the reason for this, one study has shown that, women are unable to produce good and quality sputum [88]. Other risk factors associated with smear positive results among women with cough attending MCH and FP clinics were having HIV/AIDS. This is contrary to other studies where HIV/AIDS positive patients were more likely to be smear negative [89-90]. Though not investigated in this study, but shown in another study, possibly the level of immune suppression of our study patients was not so severe to the extent of affecting their TB presentation [91].

Worthy to note also is the fact that women who had a long duration of cough were more likely to attend MCH than FP clinics. MCH clinics in the study areas were not only the clinics for checking under-fives wellbeing but also acted as referral clinics for the sick children. Studies have indicated that women place the needs of their children and other family activities above their own health. A study in India demonstrated that women tended to visit heath facilities for immunization and their children's wellbeing rather than for their own health [61].

Apparently, the expansion of TB case finding to other clinics and screening approach might increase laboratory workload. We therefore recommend that workload- and cost effectiveness studies should be conducted to look at the feasibility of the screening approaches.

Delay in TB case detection.

Delay in TB case detection is a serious matter; its magnitude has been reported in several other studies [41, 43, 50, 72, 92]. Though, TB diagnosis is said to be free of charge, the findings from our study show that the 'free of charge isn't free'. Before TB diagnosis, patients and households not only lose from suspending their jobs, but also from unbearable direct and indirect costs. Pre diagnosis high cost may delay poor patients from seeking care early. Delayed patients will serve as potential reservoirs for infection transmission in their communities. This is especially true when considering that one untreated infectious TB case is estimated to infect up to 15 people annually and over 20 during the natural course of untreated disease [10, 93]. Similar to a study conducted in Dar es Salaam, our study indicated that, on average, almost two fifth of patients delayed to seek care with a mean duration of more than two months [41]. Twenty five percent of patients in our study delayed to start treatment until more than three months. Similar results were obtained in Ethiopia [72]. The major contributor to the total delay observed in our study was the delay by patients (63%), but this was lower than what was reported in Mwanza [50]. Studies in Ethiopia and Nigeria also showed dominance of patients delay in the total delay [72, 81]. Delay in TB case finding jeopardizes the NTLP effort of fighting TB. It also increases the cost not only to the patients and households but also to the health services because of the prolonged ill health condition leading to repeated consultations.

Factors associated with patients delay

We have found that patients with poor knowledge that chest pain was one of the TB symptoms and those who believe that TB is always associated with HIV/AIDS delayed to seek TB healthcare. This finding is similar to a study conducted in Dar es Salaam [41]. Similarities of some of TB symptoms with that of HIV/AIDS and stigma associated with HIV/AIDS may offer an explanation. Patients with symptoms related to TB were regarded as having HIV rather than TB in Thailand [53]. This may delay patients from seeking appropriate care because of fear, especially those patients

who suspect themselves as having HIV/AIDS [53-54]. In addition, healthcare seeking observed in our study differs from other studies. Most patients in our study first sought help for their pulmonary symptoms in government hospitals, in contrast to a study in India, which showed a high proportion of TB patients first seeking healthcare in private facilities [94]. However, despite that, most patients in our study first sought healthcare for their pulmonary symptoms in government facilities, yet more than half were delayed from being suspected at their first visit, even if many of them (78.6%) had prolonged cough of more than two weeks prior to their first consultation.

Patients and households cost before diagnosis

TB imposes a considerable economic toll especially among the poor. The poorest in our sample spent on average more than what they received in a month. That means, TB left poor families without a buffer for other living cost, making them to depend on their relatives and friends for a living. Though not investigated in this study, other studies have shown that to cope with the burden of TB, families end up in debt, having to sell assets and even withdraw their children from school [48-49, 95]. As a consequence, poverty may increase.

The loss of income following TB healthcare seeking can be devastating. Similar to other studies [5-6, 21, 69, 95], our study also indicated that the productive segment of the household is mostly affected. Moreover, we found that before TB diagnosis, overall household mean monthly income dropped considerably and the poor suffered the burden more than the less poor. Income loss following TB healthcare seeking has also been reported in other studies conducted in Zambia, Uganda, Malawi and Tanzania [69-71, 96]. We found that tuberculosis caused on average 25 patients lost work days before diagnosis. This is almost the same as that reported in Zambia and Malawi [69, 71].   Though the two studies were conducted 10 years ago, unfortunately indirect cost before TB diagnosis seems to be the same.

Relatively, overall household cost for TB diagnosis reported in our study is lower than that reported in Zambia and Malawi [69, 71]. The household in our sample spent on average 57 USD which is equivalent to two fifths of their mean monthly incomes unlike Zambians (127%) and Malawi's (209%) [69, 71]. Difference in total monthly income used in calculating the cost in the three studies can serve an explanation. Other reasons can be due to the difference in the study areas, study population and time since 1998 and 2001 respectively when the study in Zambia and Malawi were conducted. Involving patients in the intensive phase in Malawi [71], and recall bias may also serve an explanation. Pre-diagnosis high cost has also been reported by other authors [97-98]. In our study, the poor spent less on fees, transportation and food. However, relative to their total income, poor patients were affected three times more than the less poor.

Cost by area of consultation

As expected, total cost was high among patients who attended traditional healers and private health facilities. Moreover, it is not surprising that the burden of cost in private facilities shown in our study is relatively higher among the poor families. Similarly, a study from Thailand showed that out of pocket expenditure for TB diagnosis was higher among the poor [98]. Studies in Nepal, Botswana and Tanzania have shown that patients who first visited traditional healers and/or private facilities had a longer delay in TB diagnosis [50, 92, 99-100] and this may also raise the cost of healthcare seeking.

6. PUBLIC IMPLICATION.

Our findings indicate that screening, regardless of cough duration, and expanding TB case detection activities to FP and MCH clinics might have a significant effect, especially among the poor. This could offer several benefits, such as increased early TB case detection by reducing TB diagnostic delay, and, as a consequence, reduced patients' cost associated with TB healthcare seeking. This should be of interest to NTLP, especially when considering patients' and health workers' ignorance, as well as atypical manifestations of TB among HIV positive individuals. In particular, this is important for individuals co-infected with HIV/AIDS, as it could reduce morbidity and mortality associated with delayed TB treatment.

On the operational research side, investing in conducting workload- and cost effectiveness studies of the screening approach, and expansion of the study to include other sites, could be important.

7.   CONCLUSIONS

1. The proportion of pulmonary tuberculosis cases among patients with cough attending a general OPD was 12.7% among those who had coughed for 2 weeks or more, and 8.7% among those who had coughed for less than 2 weeks. There was no statistically significant difference between the two groups

2. The proportion of smear positive TB patients among women with cough attending FP and MCH clinics was 3.8%. HIV infection and visit to any health facility prior to diagnosis were risk factors of having smear positive TB.

3. There was a considerable delay in TB case detection in Pwani, mainly due to patients' delay. Risk factors for delay included misconception about TB and HIV and poor knowledge of TB symptoms.

4. The economic burden of TB health care seeking was high, especially for the poorest households. Prior to diagnosis, TB patients lost on average 46% of their mean monthly income. At household level, mean monthly income dropped by 28%. Before diagnosis, poor households spent 150% of their mean monthly income, compared to 43% among the less poor.

8.   RECOMMENDATIONS.

1. Special efforts need to be made on intensifying TB case finding to reduce diagnostic delays, and, in turn, reduce the cost prior to diagnosis. This may be done through:

   o Screening for TB, regardless of cough duration, for all patients who report cough at OPD, FP and MCH clinics.

   o Expanding TB case detection activities to other clinics like FP and MCH clinics.

Source of data

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