Treatment delays among smear-positive pulmonary tuberculosis patients in Sudan: A comparative analysis between one rural and one urban setting in Sudan

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Sudan

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A thesis submitted in partial fulfilment of the requirement for the degree of Master of

Public Health by

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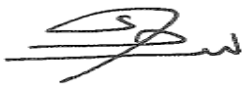
Signature 

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Abstract

Background
Delay in TB diagnosis and treatment exacerbates its morbidity, mortality and increases transmission of the disease within the community.

General Objective
The main objective of this study is to perform a comparative analysis of two national studies addressing delays in diagnosis and treatment of new smear-positive pulmonary tuberculosis in two different contexts (urban and rural) and review the findings against current published evidence in order to provide evidence-based recommendations to Sudan NTP towards improving national TB prevention and care activities.

Methodology
The methodology applied was descriptive and comparative analysis of two national studies against current published evidence.

Results
The main factors significantly associated with longer pre-treatment period at rural setting were divorced/widow, higher income, and use of traditional self-medication before reaching any health provider. Factors significantly associated with longer patient's period at rural setting were middle age, lower educational level, prolonged walking distance to the TBMU and lower sputum grading for AFB. Factors significantly associated with longer health system's period at rural setting were female, divorced/widow, higher level of education, higher monthly income, large family size, and failure to suspect TB as explained by not requesting X-ray examination.

Conclusions and Recommendations
Generally, all the three periods were longer at rural than urban setting. Despite having some significant socioeconomic factors contributing to prolonged patient's period, nevertheless, the contribution of the same socioeconomic factors in addition to other factors have contributed to a lower suspicion index among the health providers which was reflected in the significantly longer health system's period at rural setting. Despite the clear guidance by the National TB control Programme (NTP) on the importance of performing sputum examination to all patients presenting with cough for more than two weeks, most of the health providers still consider some other factors before applying the TB management guidelines. Sudan NTP is highly recommended to disseminate and enforce the application of the national TB management guidelines among all health providers. Other recommendations to the NTP include enhancing the public health education on TB and interdisciplinary approach to tackle socioeconomic barriers to TB healthcare.

Key words
Tuberculosis; Sudan; smear-positive; delays

Word count **11,308**

List of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
AFB	Acid Fast Bacilli
ANOVA	Analysis of Variance
BCG	Bacille Calmette-Guerin
DALYs	Disability-Adjusted Life Years
DOTS	Directly Observed Treatment, Short Course Strategy
Epi-Lab	The Epidemiological Laboratory-Sudan
FMOH	Federal Ministry of Health
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
HIV+TB	Tuberculosis patients with positive HIV status
HSD	Honestly Significant Difference
KIT	Koninklijk Instituut voor de Tropen (Royal Tropical Institute)
MDG	Millennium Development Goal
MDR	Multi Drug Resistant
MSE	Mean Squared Error
NGO	Non-governmental Organization
NHS	National Health Service
NTP	National Tuberculosis Programme
PLHIV	People Living with HIV/AIDS
PPM	Public Private Mix
SD	Standard Deviation
SPSS	Statistical Package for Social Science
TB	Tuberculosis
TBMU	Tuberculosis Management Unit
UNDP	United Nations Development Programme
UNFPA	United Nation Population Fund
USD	United States Dollar
VU	Vrije Universiteit (Free University)
WHO	World Health Organization
XDR-TB	Extensive Drug Resistant Tuberculosis

Introduction

I graduated from Faculty of Medicine, University of Khartoum, Sudan in 2000. I completed my medical internship in Sudan Public Teaching Hospitals during the period (December 2000 - May 2002). To refine and tune my counseling skills to multicultural communities, I integrated into the National Health Service (NHS) workforce in United Kingdom during the period Jan 2005 – July 2006. In 2009, I joined The Epidemiological Laboratory (Epi-Lab); this is a Sudanese non-profit non-governmental organization (NGO) , and a collaborating centre of World Health Organization (WHO).

My last appointment was as Epi-Lab TB REACH Project Coordinator. TB REACH is a new initiative launched by Stop TB Partnership in January 2010. The main objective of TB REACH is to promote early and increased case detection of infectious tuberculosis cases, ensure their timely treatment while maintaining high cure rates within the National TB Program. The overall objective of the post was to achieve Epi-Lab TB REACH project through coordination and oversight of all activities as well as playing the linkage between Sudan NTP, TB REACH Secretariat and Epi-Lab. The post had availed me the chance to participate in the global fight against TB and to adopt and implement innovative approaches and interventions to timely capture infectious TB cases among highly vulnerable and hard-to-reach communities.

Tuberculosis still poses a major public health problem in Sudan. TB case detection and management are far below WHO recommended targets. The total number of TB cases notified to national TB programme in 2011 was 50% of total number of expected incident cases. Furthermore, treatment success rate for new smear positive and/or culture-positive cases was only 80% in 2010 lagging behind WHO recommended target of 85% success rate for newly diagnosed smear-positive pulmonary TB cases.[1] Therefore, there is an urgent need to close the case-detection gap and reduce the risk of poor treatment outcomes. In order to do so we need to better understand the factors that delay accurate diagnosis and appropriate treatment initiation.

The main objective of this study is to perform a comparative analysis of two national studies that addressed delays in diagnosis and treatment of new smear-positive pulmonary tuberculosis at two different settings (urban and rural) and review the findings against current published evidence in order to provide evidence-based recommendations to Sudan NTP towards improving national TB prevention and care activities.

Chapter 1: Background Information: Country Profile

Demography

"Sudan is the third largest country on the African continent". It extends over a total area of 1.8 million square kilometres in Northeast Africa. The total population is 33, 419,625 people and the annual population growth rate is 2.5%. Life expectancy at birth (2011) was 54 years for male and 57 years for female. The population pyramid of Sudan shows a relatively young population with 62% being less than 25 years. The annual rate of urbanization is 3.7% per annum and around 50% of the population currently resides in urban areas.[2] Internally displaced populations are 4 million and predominately reside in Khartoum and Darfur states.[3]

Economic Situation

Sudan has enormous natural resources such as agriculture and animal resources, natural gas, oil, and minerals. Agriculture stands out as the major employment sector and currently constitutes the main source of income for over 80% of the Sudanese population. The annual growth rate of Sudan Gross domestic product (GDP) had recently demonstrated a sharp declining trend from 11.5% in 2007 to only 2.8% in 2011 mainly due to loss of oil revenues following secession of South Sudan in 2011. According to Human Development Index report (2013), Sudan's social and economic development deteriorated over the last decade, standing at position 171 out 186 in 2012 compared to position 150 in 2009 while GDP per capita dropped from 2,200 in 2008 to 1,270 in 2011. Sudan is currently classified among the least developed countries in the world with almost 50% of the population living below the poverty line.[2]

National Health System

The health system in Sudan is a decentralized three-layered hierarchical system: federal, state and locality. The federal level is concerned with policy formulation and governance in terms of coordination and supervision while the state government and localities implement those policies. Apart from ministry of health, health services are provided through uniform health facilities, non-governmental organizations, and private health sector. Provision of health services is organized through three levels; primary, secondary, and tertiary. The heath system is currently facing several challenges; profound shortage in human and financial resources, political instability, and recurrent flood and droughts.[4] Critical shortage in human resources for health is mainly attributed to high attrition and low production rates of healthcare workers.[5] The shortfall in financial resources is explicitly demonstrated by the fact that only 8% of GPD is devoted to health and the general government expenditure on health is only 11% of total general governmental expenditure; far below 2001 Abuja declaration signatory target (15%).[6] Following economic recession and liberation in early 1990s, the government introduced user-fees payment at the point of health service

delivery in order to reach a balance between the shortfall in financial resources and the health needs of the Sudanese population. Despite the fact that the interim constitution (2005) stipulates equal access and free primary healthcare to all Sudanese citizens, out-of-pocket health expenditure accounts for 69% of the total health expenditure.[6-7] Moreover regional and urban-rural disparities in health services distribution with a preferential access to those residing at affluent urban sites have further perpetuated the inequalities in health indicators across the regions and states.[8]

Epidemiological Profile

Sudan's epidemiological profile is currently under transition and demonstrates a rising double burden pattern with non-communicable diseases approaching high ranks among top causes of mortality and collectively accounting for 44% of all deaths. According to WHO region classification, Sudan belongs to Middle East and North African region. Nevertheless, its burden of disease corresponds to sub-Saharan African disease pattern with communicable diseases; lower respiratory tract infections, diarrhoea, malaria, HIV/AIDS, and tuberculosis, ranking high among top causes of premature death and disability. Due to recent changes in lifestyle following globalization, and industrialization, non-communicable diseases; diabetes, hypertension, cardiovascular diseases, cancer and road traffic accidents, are currently posing extra burden on the existing health system.[9-10]

Tuberculosis

Tuberculosis is an airborne infectious disease caused by Mycobacterium tuberculosis. It typically affects the lungs where it is called pulmonary tuberculosis; the infectious form of TB. It can also affect other body organs where it is called extra-pulmonary tuberculosis; the non-infectious form of TB.[11] It is estimated that one-third of the world population is infected with mycobacterium tuberculosis (latent TB). People with latent TB have no symptoms of tuberculosis and cannot yet transmit the disease. The lifetime risk to develop tuberculosis disease if infected is 10%. However, the risk of falling ill with tuberculosis is much higher in people with immune-compromised system such as those living with HIV, diabetes, malnutrition as well as tobacco users. People living with HIV have 21-34 times higher risk of developing TB disease.[12] The risk of developing TB disease is two to three times higher among diabetic patients and two-and-a-half times higher in smokers. Globally, diabetes is linked to 10% of TB cases while smoking is related to another 20% of TB cases.[13-14] TB predominately affects the economically productive age group (15-54) and strikes hard on people of low socio-economic status with a further downfall into poverty trap due to loss of income.[15-18]

People with active tuberculosis have symptoms of productive cough, haemoptysis, chest pains, fever, night sweating, and weight loss. If untreated, one single pulmonary tuberculosis case can infect 10-15 other people over the course of a year. According to natural history of Tuberculosis, 50% of patients will die if left untreated within 3-5 years while 25% remains alive with chronic infectious TB. The remaining 25% of patients will survive through self-cure. Nevertheless, if tuberculosis is poorly treated, 65% of cases will eventually die prematurely.[12]

Global TB Burden

World Health Organization declared tuberculosis as a public health emergency in 1993. Globally, the estimated number of people falling ill with TB in 2011 was 8.7 million including 1.1 million people co-infected with HIV. Nevertheless, only 5.8 million TB cases were notified to national TB programs; accounting for two-thirds of all estimated TB cases worldwide. TB epidemic strikes hard on children. In 2011, almost half a million children fell ill with TB of whom 64,000 children lost their lives to TB. Tuberculosis is fuelled by the concomitant epidemic of TB/HIV in addition to the persistent rise in multidrug resistance TB cases (MDR-TB). It is estimated that 500,000 new MDR-TB cases occurred in 2011. Globally, 84 countries have reported a severe form of MDR-TB cases named extensive drug resistant TB (XDR-TB) that is resistant to other two classes of anti-tuberculosis drugs, accounting for almost 9% of all MDR-TB cases.[11]

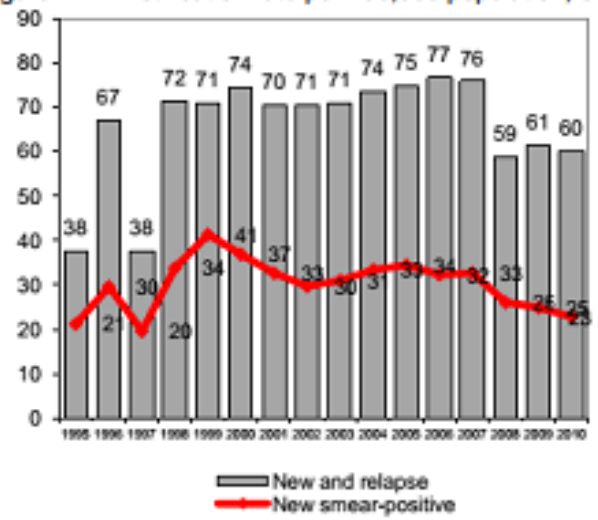
According to WHO global burden of disease report (2012), TB stands as the second infectious cause of death worldwide; second only to HIV.[11] The death toll continues to claim more lives with 1.4 million dying from TB in 2011 including 430,000 people co-infected with HIV. Tuberculosis is the major killer in HIV co-infected people. One in four deaths among people living with HIV/AIDs (PLWHA) is attributed to HIV-related TB. TB stands among the top killers of women worldwide accounting for half a million deaths among women in 2011. Low and middle income countries shoulder 95% of TB deaths. In 2010, 10 million orphan children lost their parents to TB.[12]

Following implementation of directly observed treatment, short course strategy (DOTS), STOP TB Strategy, and TB/HIV collaborative activities, a declining trend in the estimated new TB infections is noted worldwide; 2.6 million cases in 2009 compared to 3.1 million cases in 2001. Globally, 51 million TB cases were successfully treated and 20 million TB deaths were averted between 1995 and 2011. The death toll has decreased dramatically since 1990; approaching 41% decrease in TB mortality rate. Between 2005 and 2011, 1.3 million deaths were averted following implementation of TB/HIV collaborative activities.[19]

National TB Burden

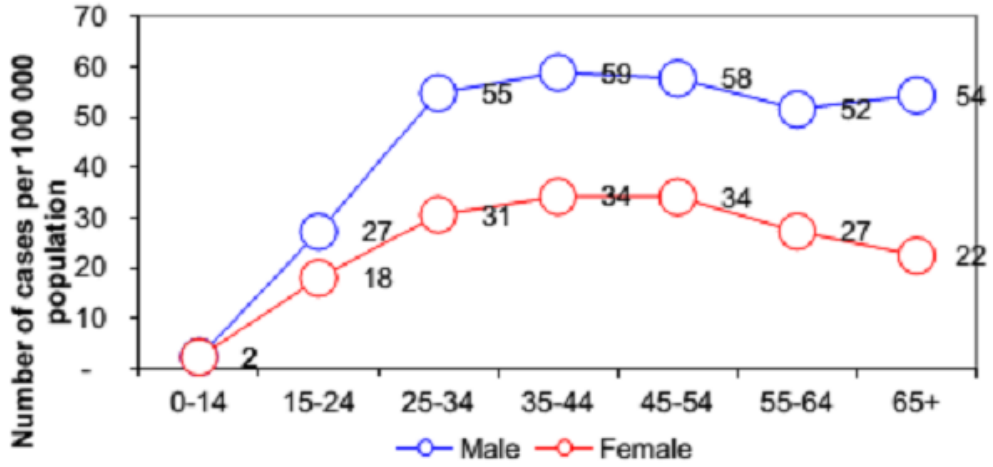
Sudan stands among the seven countries that shoulder 95% of TB burden in the Eastern Mediterranean Region in 2010.[20] The trend of notification of TB cases in Sudan (1995-2010) ranged between 38 to 77 new and relapse cases per 100,000 of population (Figure 1).[21] According to WHO TB country profiles (2011), it is estimated that the total number of TB cases was 69,000 (34,000 - 120,000) including 40,000 incidence (includes HIV+TB) (33,000 - 48,000), and 2,800 incidence (TB+HIV only) (2,100 - 3,600). Nevertheless, only half of estimated incidence of TB cases (20,385) had been notified to Sudan National Tuberculosis Program (NTP) in 2011; 18,636 new cases and 1,749 retreatment cases whereas the total number of new smear-positive TB cases notified to Sudan NTP was 7,266 cases. TB notification rate of men is almost twice as that of women with a male-to-female ratio of 1.9 (Figure 2).[21] In 2011, 2,584 children fell ill with TB. It is estimated that the total number of MDR-TB cases among notified pulmonary TB cases was 590 cases in 2011; 250 MDR-TB cases (70-430) among new cases and 340 MDR-TB cases (120-550) among retreatment cases. Nevertheless, the number of MDR-TB cases reported to be enrolled in MDR-TB treatment was only 80 cases in 2011.[1]

Figure 1: TB notification rate per 100,000 population, Sudan



Source: Adopted from Notification rate in the 7 high burden countries of the East Mediterranean Region. Reference number: 21

Figure 2: Notified new smear-positive cases per age groups and sex, Sudan, 2010



Source: Adopted from Notification rate in the 7 high burden countries of the East Mediterranean Region. Reference number: 21

According to WHO global burden of disease report (2012), TB stands at position 12 among top causes of premature death at the national level and position 16 among top causes of years of life lost due to disability and premature death (DALYs).[10] While HIV/AIDS stands at position 4 among top causes of premature death and DALYs in Sudan further fuelling TB epidemic. In 2011, it is estimated that TB mortality rate (excludes HIV+TB) was 22 per 100,000 (9.2-40 per 100,000) accounting for 7,500 deaths (3,200-14,000).[1]

TB Prevention and Care Strategies

According to Golub, TB prevention and care strategies are[22]:

- "Case-finding and treatment of active disease"
- "Treatment of latent TB infection"
- "Vaccination with Bacille Calmette-Guerin (BCG)"

The main principle of TB control is based on the first strategy since the cornerstone in TB prevention and care is to break the cycle of TB transmission through early diagnosis and prompt treatment of all infectious TB cases. Whereas, the other two approaches have minimal impact on reducing incidence of tuberculosis.[22]

Passive TB case-finding methodology

Passive TB case-finding strategy is currently the WHO recommended strategy for TB case-finding among the general population.[23] It depends on self-referral of symptomatic TB patients who voluntarily present to health services for medical attention. This strategy is feasible and effective in detecting the most infectious TB cases. Nevertheless, it requires high index of suspicion among health provider and early health care-seeking behaviour of people with presumptive active TB. Moreover, it does not address

vulnerable populations who despite being at higher risk of developing tuberculosis, cannot seek or access healthcare either due to social stigma, physical or financial barriers. Globally, prevalence surveys have shown that many cases of active TB are missed and remain undetected despite scaling up and decentralization of TB diagnostics and treatment services.[24] Currently, there are one-third of global TB cases not yet detected or notified to NTP.[11]

Active TB case-finding methodology

Active TB case-finding strategy entails looking systematically for cases with active tuberculosis and latent TB infection before they present themselves for medical attention. This strategy proactively identifies potential TB cases leading to early and increased TB case detection and treatment.[25] It prevents further transmission of active pulmonary TB within the community and is recommended by WHO for specific high risk groups; namely people living with HIV, prisoners and household contacts of infectious TB case. [26-27] The drawbacks of this strategy are it overburdens national TB programs since it is a resource-intensive strategy and mandates quality diagnostics and treatment services.[24] Therefore, it is considered less cost-effective compared to passive case-finding except for high risk groups.[(i)]

[i] Considerable debate aroused whether it violates principle ethics and patient rights as well as potentially treating people without TB due to false-positive results during screening.[24]

Chapter 2: Problem Statement, Justification, Objectives, and Methodology

Problem Statement, and Justification

Sudan NTP was established in 1995 and declared 100% DOTS coverage in 2003 (one tuberculosis management unit per each 100,000 population). Nevertheless, tuberculosis still poses a major public health problem in Sudan. TB case notification is far below WHO recommended target. Moreover, TB treatment success rate for new smear-positive and/or culture-positive cases was only 80% in 2010 lagging behind WHO recommended success rate of 85%. Furthermore, only 80 MDR-TB patients were enrolled in MDR-TB treatment out of the estimated 590 MDR-TB cases.[1] Therefore, there is an urgent need to close the case-detection gap and reduce the risk of poor treatment outcomes. In order to do so we need to better understand the factors that delay accurate diagnosis and appropriate treatment initiation.

Delay in TB diagnosis and treatment have negative repercussions on TB prevention and care. TB patients who present late at TB management unit (TBMU) will have more advanced tuberculosis disease and less favourable treatment outcome. Moreover, patients with infectious form of tuberculosis will continue to transmit the disease in the community.[26-27] "The risk of exposure to tuberculosis bacilli is related to the number of incident TB cases in the community, the duration of their infectiousness, and the number and nature of interaction between a case and a susceptible contact per unit of time of infectiousness".[28] The major objectives of TB prevention and care is to decrease TB-related mortality, prevent further transmission of the disease and TB-related morbidity as well as preventing the development of MDR-TB disease. Stop TB Partnership target is to halve TB prevalence and death rates by 2015 compared to 1990 levels whereas TB-related millennium development goal 6, target 8 (MDG6c) is to have halted and begun to reverse the incidence of tuberculosis by 2015.

The total pre-treatment period among newly diagnosed TB patients is defined as the time interval between onset of TB symptoms and start of anti-tuberculosis treatment. It is further subdivided into patient's period and health system's period. Patient's period is defined as the time interval between onset of TB symptoms and first contact with a formal heath care provider and is usually determined by patient health seeking behaviour. While Health system's period is defined as the time interval between patient's first contact with a formal health care provider and start of anti-tuberculosis treatment.[29]

Health-seeking behaviour among TB patients is influenced by patient's socioeconomic status, cultural and traditional norms prevalent within the community as well as the perceived quality of health-care facilities. Whereas, access to TB care is usually determined by patient's socioeconomic characteristics, coverage and accessibility to quality TB health services, patient's presenting complaint, health provider's practice towards TB symptoms, and level of coordination of the health system.[15,30-38]

General Objective

Two cross sectional multistage descriptive and analytical studies addressing delayed TB diagnosis and treatment among newly diagnosed smear-positive TB patients were conducted at primary healthcare settings in Sudan.[39,40] They consecutively explored the effect of several factors such as patient's socioeconomic characteristics, knowledge about TB, distance from TBMU, presenting complaint, and private practitioner consultation on TB diagnosis and management at two different settings.

The main objective of this study is to perform a comparative analysis of the results of these two studies, specifically addressing delays in diagnosis and treatment of new smear-positive pulmonary tuberculosis in two different contexts (urban and rural settings) and review the findings against current published evidence in order to provide evidence-based recommendations to Sudan NTP towards improving national TB prevention and care activities.

Specific Objectives

I. To define and compare the magnitude and contributions of patient's and health system's period in the total pre-treatment period among newly diagnosed smear-positive TB patients in the two national studies against current literature.

II. To identify and compare the most important socioeconomic factors, cultural and beliefs factors, and disease factors that influence total pre-treatment period, patient's period and health system's period.

III. To identify and compare the most important health system factors that influence total pre-treatment period, patient's period and health system's period.

IV. To make recommendations based on the findings of comparative analysis and literature review to Sudan National NTP in order to improve national TB prevention and care activities.

Methodology

This study adopted descriptive and comparative analysis of the two national studies as well as literature review to answer the study objectives.

Conceptual Framework

During my quest for a suitable conceptual framework for this study, I identified several conceptual frameworks that address health-seeking behaviour and health services utilization such as Andersen model, Kroeger's model, and Health belief model.[41,42,43] However, I chose to adapt Mckinlay's framework for utilization of health services since it managed to encompass the key determinants in patient's pathway to TB healthcare. Originally, the framework has six distinct approaches:[44]

1. "Economic (income, health insurance cover, cost of health services and availability of free medical care)"
2. "Socio-demographic (age, sex, education, religion, and ethnicity)"
3. "Geographic (geographical proximity of services)"
4. "Socio-psychological (motivation, perception, and learning)"
5. "Socio-cultural (values, norms, beliefs, definition of illness, and lifestyles)"
6. "Organizational or delivery system (structure and processes in healthcare organization)"

In order to facilitate the flow of the study analysis, I grouped the six approaches into three main categories:

1. Socioeconomic factors (economic and socio-demographic approaches)
2. Cultural and beliefs factors (social-psychological and socio-cultural approaches)
3. Health system factors (geographic and organizational or delivery system approach)

Furthermore, I added a fourth category; disease factor[ii] to finalize the analytical approach for this study. Worthy of note, all those four categories are interrelated.

[ii] Sputum smear positivity grade acts as a proxy for the severity of the disease

Figure 3: Thesis Conceptual Framework

Analytical approach to early diagnosis and treatment of smear-positive pulmonary TB patients	
Socioeconomic factors	Age, sex, marital status, educational status, occupation, monthly income, and housing condition
Cultural and beliefs factors	Knowledge and perceptions of TB symptoms*, self-medication, and reasons for coming to TBMU
Disease factors	Severity of disease (sputum smear positivity grading)**
Health system factors	Geographical and financial accessibility to general health services and TBMUs, type of health provider consulted before TBMU, and investigation requested by other health providers, referral system between general health services and TBMUs, actual and perceived quality of general health services and TBMUs***

* Not included in thesis analytical process as the two national studies approached this factor differently
** Sputum smear positivity grading acts as a proxy to severity of tuberculosis disease
***Geographical and financial accessibility to general health services, referral system between general health services and TBMUs, actual and perceived quality of health services/TBMUs have not be addressed in thesis analytical process due to deficient data sets.

Comparative Analysis of the Two National Studies

To analyze the two sets of raw data, statistical package for social science (SPSS version 14) was used. Statistical tests applied were parametric and non-parametric tests depending on the type of independent variables. For numerical data that are normally distributed, parametric tests such as independent-samples t-test and one-way analysis of variance (ANOVA) test were utilized to measure mean difference between the two studies. Furthermore, post-hoc multiple comparisons test; Tukey's HSD (Honestly Significant Difference) test was applied to measure the relations among the groups analyzed. The significance level was determined at 95% confidence interval, p value <0.05. Mann-Whitney U and Kruskal Wallis tests were applied when the assumption of normality was violated for numerical variables. On the other hand, cross tabulations and Chi-square test (Fisher's Exact test and Pearson Chi-Square test) were applied to examine the association between categorical variables.

The two national studies basically share the same objectives and largely adopted the same study methodology for data collection and analytical process.

General objective for the national studies

To determine the magnitude of the total pre-treatment period among newly diagnosed smear-positive pulmonary cases presenting to NTP management units.

Specific objectives

- To determine the magnitude and contributions of patient and health system delays in the total pre-treatment period.
- To determine the magnitude and contributions of both medical providers and TBMUs period in the total health system's period.
- To investigate the possible contributing factors that may explain the delays in diagnosing and treatment of newly diagnosed smear-positive TB patients.

Methodology

Study Design

The design of the two national studies was a cross sectional descriptive and analytical design. While the first study was conducted at an urban setting; primary health care facilities in Khartoum state, during the period 20th of August to 25th of October 2003, the second study was conducted at a rural setting; primary health care facilities in Gazeira state, during the period 17th of July 2005 to 11th of January 2006.[39,40] It is assumed that in the two year gap between the two studies, no significant changes occurred in the implementation of the national TB programme.

Study Settings

Khartoum State is the capital state of Sudan. Its population was estimated to be 6 million in 2002. Administratively, Khartoum state is subdivided into 7 provinces; Khartoum, Jabel Awlia, Khartoum North, Sharg El Neil, Omdurman, Karari, and Ombada.[45]TB health services in Khartoum state are administratively under three different health authorities; Sudan Federal Ministry of Health, Khartoum state Ministry of Health and Sudan Council of Churches. Khartoum state had declared 100% DOTS coverage in 2002.[45]

Gazeira State is the second largest state in Sudan. Its population was estimated to be 3.5 million in 2006. The majority of its populations are rural population (77.3%). Administratively, Gazeira state was subdivided into 6 provinces; Gaziera, Kamleen, Om el Gura, Managil, Hasahisa, and Butana.[45] TB health services in Gazeira state are administratively under Sudan NTP. Gazeira state adopted DOTS in 1996 and declared 100% DOTS coverage in 2002.[45]

Sampling and recruitment of the study population

The target population was newly diagnosed smear-positive TB patients presenting to Sudan NTP management units at the two study sites.

Inclusion Criteria [(iii)]

[(iii)] The first study excluded newly smear-positive TB cases that were on anti-tuberculosis treatment for more than 5 weeks in order to minimize recall bias.

- Age group 15 years old and above
- Willingness to participate at the study

Sampling Technique

A multistage random sampling technique was utilized to select provinces and TBMUs at which the study took place.

Stage 1: The provinces were selected through a random lottery technique.

Stage 2: At the provincial level in Khartoum state, 1-4 TBMUs with a new smear-positive notification rate of more than 10 cases per quarter were selected by a simple lottery randomization technique. While in Gazeira state, all TBMUs at the provincial level with a new smear-positive notification rate per year of 30 cases or more were selected for the study.[iv]

Stage 3: All eligible smear-positive TB cases registered during the data collection period were recruited at each selected TBMU.

Sample Size

Both studies utilized student's formula to calculate its sample size and to determine its statistical power.

$$N = \frac{Z2 \times P(1-P)}{E^2}$$

N = number of observations needed
Z = 1.96 (confidence interval of 95%)
P = estimated prevalence (proportion of patient with total pre-treatment period of more than 6 weeks)
E = allowable error (0.05)

The research hypothesis of Khartoum study was that the proportion of newly smear-positive TB patients who experienced more than 6 weeks pre-treatment period is 80%. This estimation was based on the findings of two previous studies (pre-treatment period of 6-9 weeks) conducted in Sudan and Ethiopia.[46,47] Gazeira study adopted the same formula to calculate the statistical power of its sample size.

Both studies experienced 0% refusal rate. Khartoum study recruited all eligible 267 patients during data collection period. Nevertheless, analysis was conducted for only 253 respondents since 14 questionnaires were

[iv] Since Khartoum state disproportionally contributes to one-third of total TB case notifications in Sudan, the cut-off point of the number of new smear-positive TB cases per selected TBMU was set a little bit higher in Khartoum state compared to Gazeira state.

deficient in essential information. Gazeira study had recruited all 216 eligible patients during data collection period.

Data Collection

Data collection was conducted through semi-structured questionnaires by well trained data assistants. The questionnaire design was divided into the following parts; socio-demographic characteristics of the respondent, information related to the respondent's current TB illness and health-seeking behaviour, the practice of TB and non-TB health care providers.[v]

To maximize the validity of the data collected in Khartoum study, complementary data collection technique was utilized to cross match the data collected such as date of smear examination, sputum positivity grading, and date of treatment initiation with TBMU patients register books and TBMU Laboratory register books. While in Gazeira study, the questionnaire design was arranged in a way that some questions validated each other.

Data Analysis

Both studies utilized SPSS for their data entry and data analytical procedures. Khartoum study adopted SPSS version 11 while Gazeira study adopted SPSS version 12.

Variables and Definitions:

The following definitions were utilized by both studies to determine the magnitude of pre-treatment period and the magnitude and contributions of patient's period, health system's period, health provider period, and TBMU period to the total pre-treatment period.

Dependant variables

Total Pre-treatment Period
Time period from onset of symptoms to start of anti-TB treatment

Patient's Period
Time period from onset of symptoms to the first contact with medical provider

Health System's Period
Time period between first visit to a medical provider and the initiation of anti-tuberculosis treatment

TBMU's Period

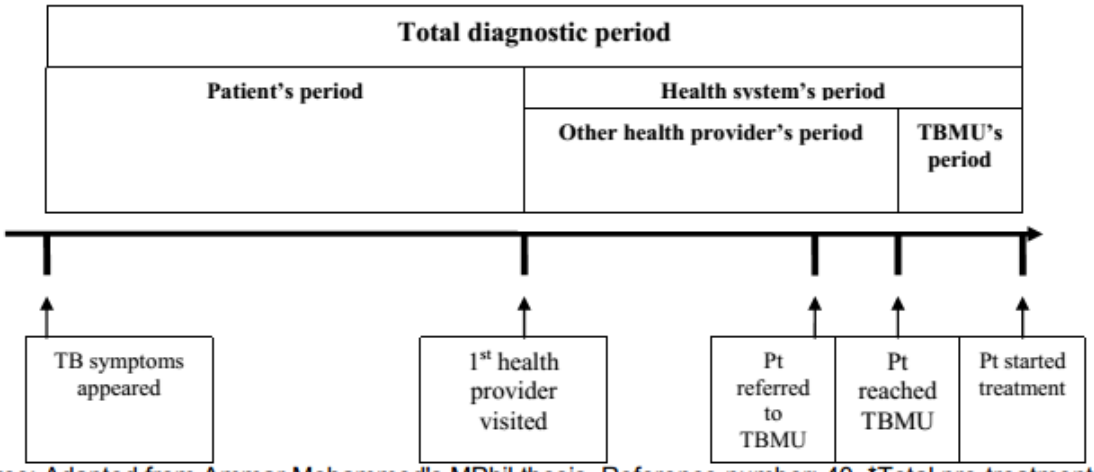
[v] Please see annexes 1 and 2 for the questionnaires.

Time interval between patient's first contact with TB management unit and start of anti-tuberculosis treatment

Other Health Provider's Period

Time interval between patient's first contact with non-TB health care provider and referral and receipt of the patient by a TBMU.[40]

Figure 4: The relationship between total pre-treatment*, patient's period, and health system's period



Source: Adapted from Ammar Mohammed's MPhil thesis. Reference number: 40. *Total pre-treatment period as per definition is equivalent to total diagnostic period in figure (4). The figure was adapted since it originally illustrated values of the mean and standard deviation for each period.

Independent variables: All common variables between the two national studies were included in the comparative analysis except type of investigation requested at TBMU and number of health providers visited prior to TBMU.

- **Patient's socioeconomic factors;** age, sex, marital status, education, occupation, monthly income, and housing condition (family size).
- **Cultural and beliefs factors including TB awareness:** Patient's health-seeking behaviour in terms of self-medication, type of self-medication (traditional medication and medical drugs, i.e. modern drugs), and reasons for coming to TBMU.
- **Disease factors:** The sputum smear grading for acid fast bacilli (AFB) as a proxy indicator for the severity of the disease.[(vi)]
- **Health system factor:**
  I. Distance from the TBMU: the walking distance in minutes between patient's house and TBMU.
  II. Type of health provider before TBMU [(vii)]:Health providers were categorized into three groups; group 1: public health-care providers,

[(vi)] The level of sputum smear grading for AFB ranges from scanty to 3 +++ according to the TBMU laboratory register book

group 2: private health-care providers, and group 3: other health providers (Pharmacy or NGO clinic)

III. Investigation requested by other health providers

Literature Search Strategy

A literature review was conducted as a background to this study. Full journal articles and reports were retrieved utilizing search engine such as Google scholar, Pubmed, KIT Library and VU Database. The following websites were accessed; Sudan FMoH, WHO, UNDP, and UNFPA to find and access full reports and publications. Additional articles were identified by searching the reference lists of primary studies.

Key words used to search for relevant documents were: Tuberculosis; Sudan NTP; smear-positive pulmonary tuberculosis; transmission; case-finding; active case-finding; passive case-finding; diagnosis; pre-treatment delay; patient delay; health system delay; care-seeking behaviour; TB control; diagnostic delay; treatment delay; poor resource settings; DOTS; diagnostic delay; delay in health-seeking; poverty; gender.

Inclusion factors: Only English articles were included. Time period specified for this search was 1997-2013.

[(vii)] Health provider: Qualified medical provider who has received formal medical education and has a license to practice health care as a doctor or medical assistant

Chapter 3: Results

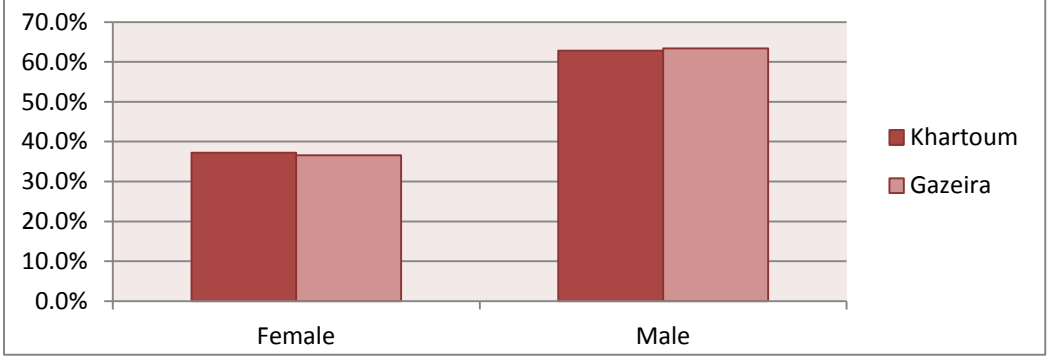
Overview of the two study populations

The total number of newly smear-positive TB patients recruited into the study sample from both studies was 469 (253 cases from Khartoum and 216 cases from Gazeira).

Gender

Both study samples demonstrated a male predominance with a male to female ratio of almost 2:1. On cross tabulation of data by gender and type of study setting, no statistically significant difference was revealed in gender split between the two study samples {Fisher's Exact test, p=0.924}.

Figure 5: The distribution of study respondents per sex in Khartoum and Gazeira states

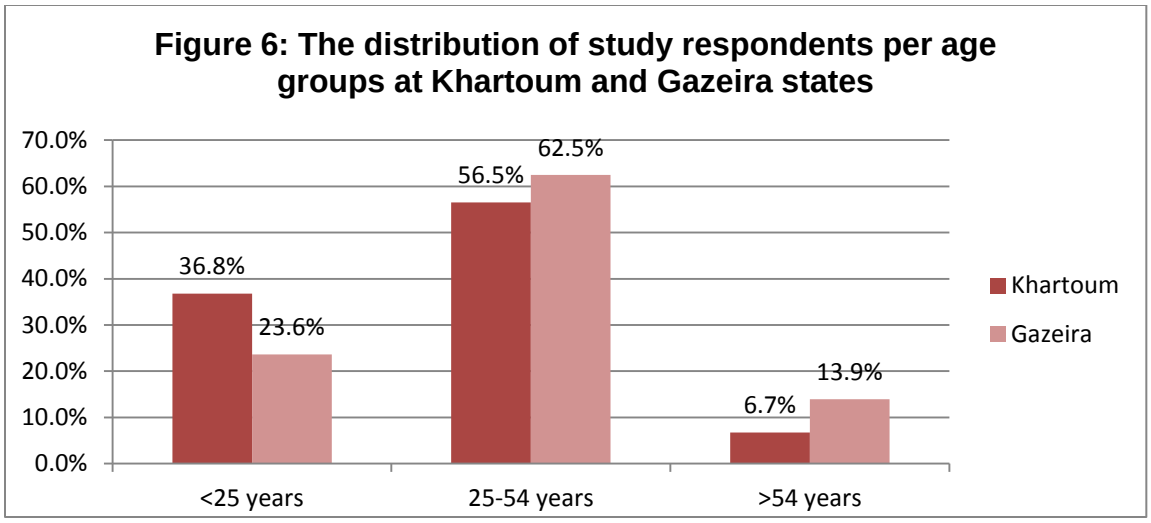


Age

The mean age for Khartoum study population was 30.82±12.356 (median= 27, mean rank= 209.79) while that of Gazeira study was 36.43±14.942 (median= 33, mean rank= 264.53). Mann-Whitney U test revealed a statistically significant difference between the two study samples {Z= -4.363, p<0.001}.

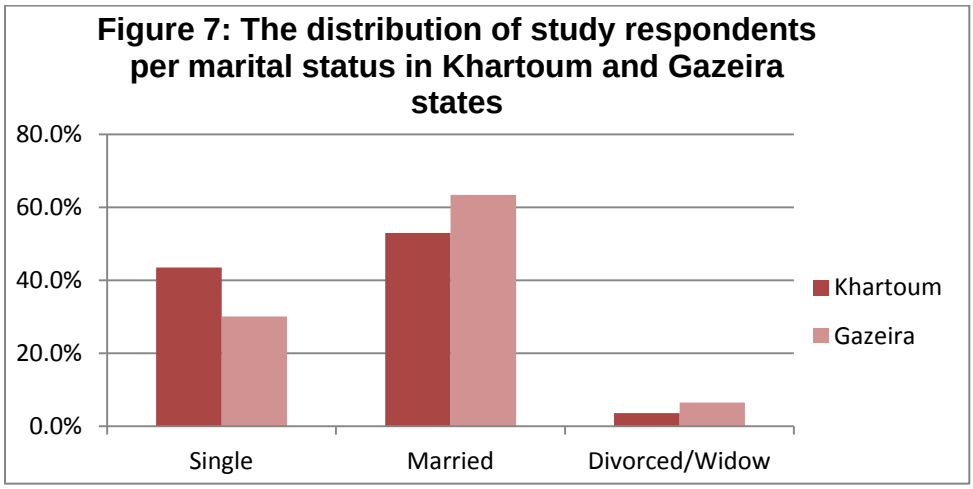
Age Group

The majority of study respondents were in the economically productive age group (25-54 years); with 56.5% in Khartoum and 62.5% in Gazeira. While 36.8% of Khartoum's study respondents were <25 years old and 6.7% were >54 years old, 23.6% of Gazeira's study respondents were <25 years old and 13.9% were >54 years old. Pearson Chi-Square test revealed a statistically significant difference in age distribution between the two study samples {X^2 (2) = 13.239, p<0.001}.



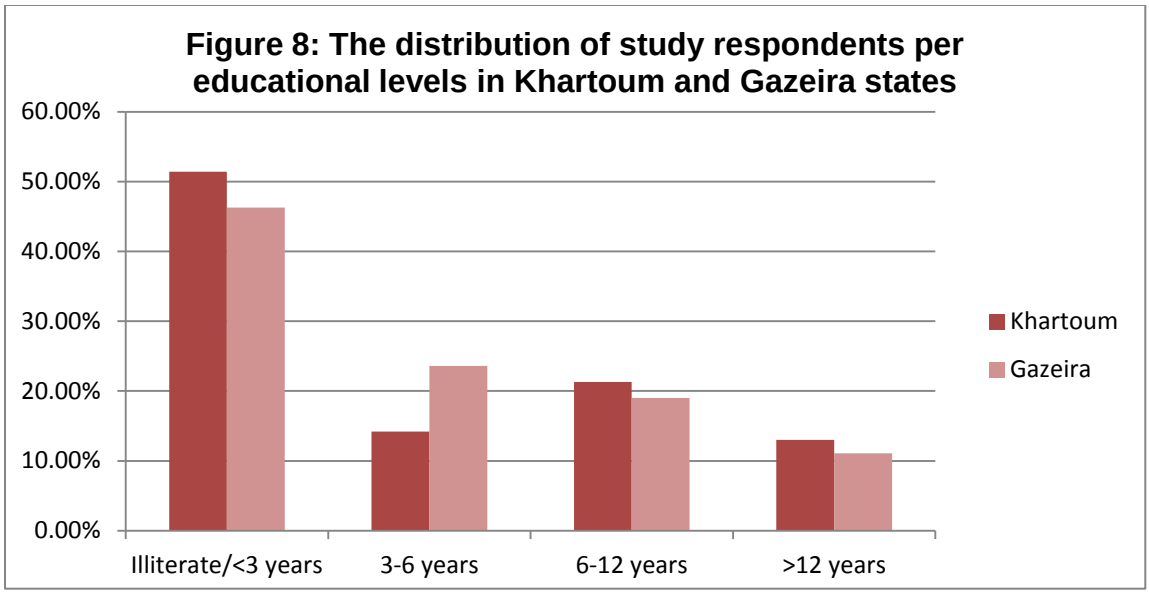
Marital Status

In Khartoum study, the majority of respondents were either married (53%) or single (43.5%). While in Gazeira study, almost two-thirds of respondents (63.4%) were married while 30.1% were single and 6.5% were either divorced/widow. Pearson Chi-Square test revealed a statistically significant difference in marital status between the two study samples {X^2 (2) = 9.834, p=0.007}.



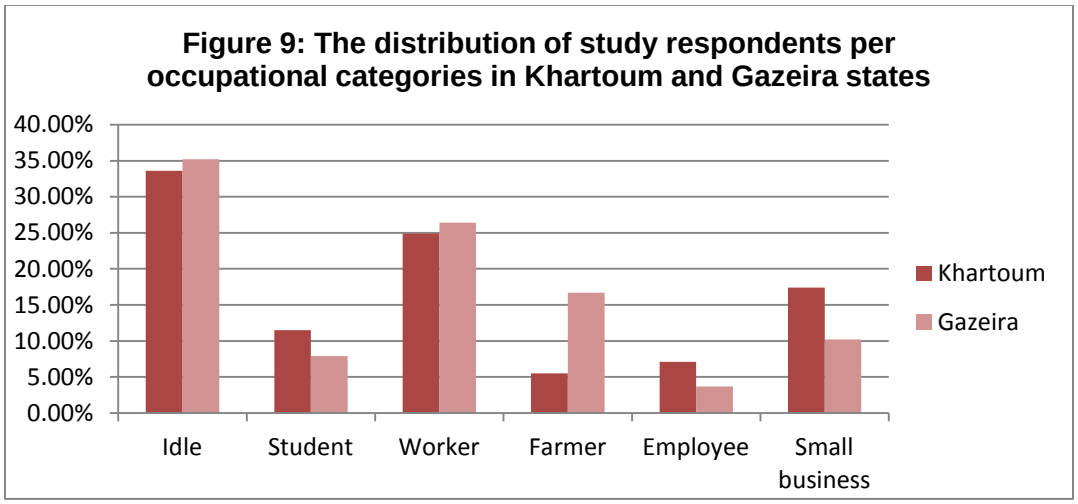
Educational Level

Illiteracy strikes hard among study respondents at both settings as 51.4% of patients in Khartoum state and 46.3% in Gazeira state were illiterate. Respondents with more than 12 years of formal education constituted the least proportion with only 13.0% respondents in Khartoum state and 11.1% of respondents in Gazeira state. According to Pearson Chi-Square test, there was no significant difference in educational levels between the two study samples {X^2 (3) = 6.823, p=0.078}.



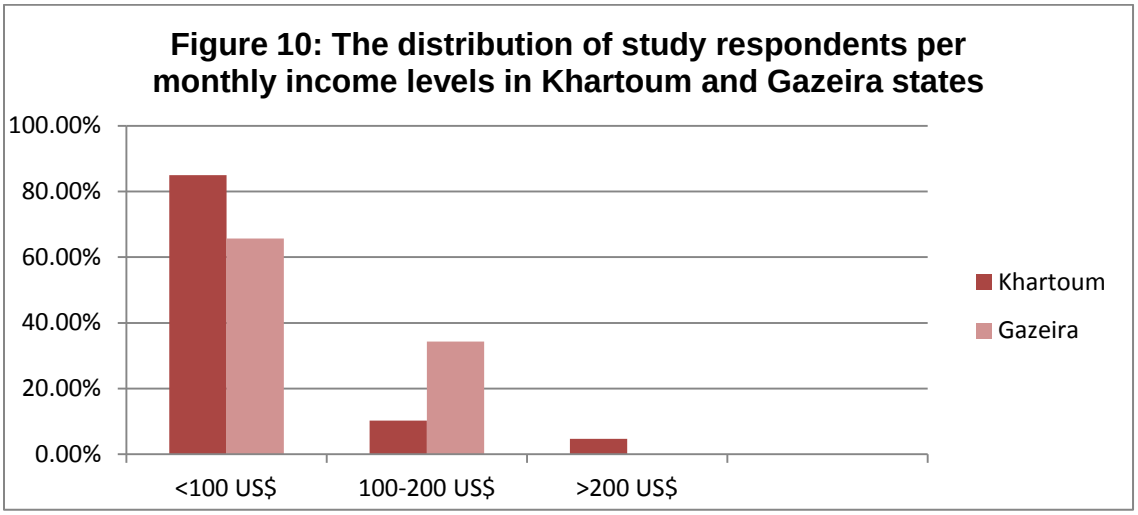
Occupation

Respondents who were idle represented almost one-third of the two study samples (33.6% at Khartoum and 35.2% in Gazeira state). While workers accounted for up to one-quarter of the two study samples (24.9% in Khartoum state and 26.4% in Gazeira state). Among Khartoum respondents, 17.4% were running small business, 11.5% were students, 7.1% were governmental employees, and 5.5% were farmers. On the other hand, 16.7% of Gazeira respondents were farmers, 10.2% were running small business, 7.9% were students, and 3.7% were governmental employees. Pearson Chi-Square test revealed a statistically significant difference in the distribution of occupation between the two study samples with higher proportion of farmers in Gazeira and higher proportion of respondents running small business in Khartoum. $\{X^2 (5) = 22.011, p<0.001\}$.



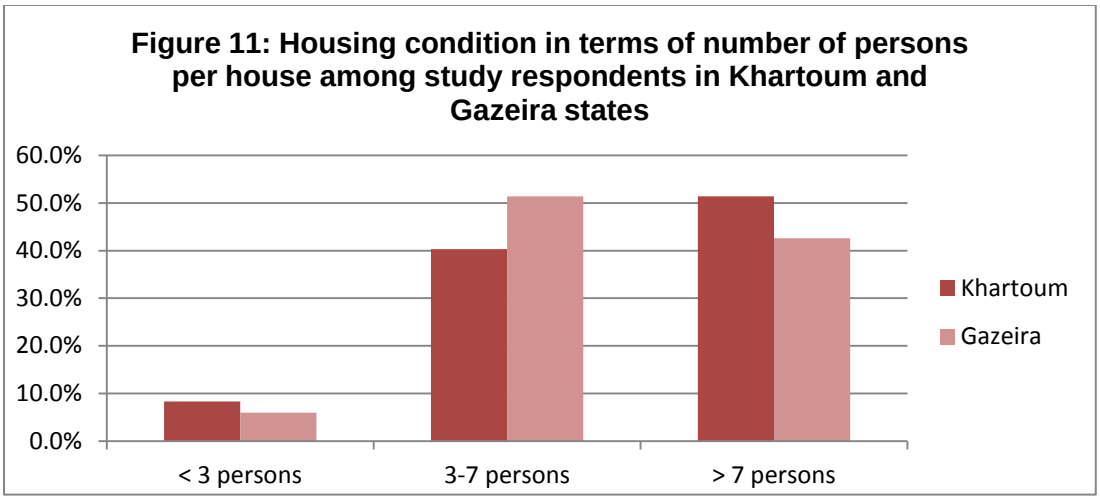
Monthly Income

Among Khartoum respondents, the majority (85.0%) reported less than 100 USD monthly income while 10.3% claimed 100–200 USD monthly income. On the other hand, almost two-thirds of Gazeira respondents (65.7%) claimed less than 100USD monthly income and one-third (34.3%) reported 100-200USD monthly income. The distribution of monthly income between the two study samples was statistically significant according to Pearson Chi-Square test {X^2 (2) = 47.343, p<0.001}.



Housing condition (Family size)

The majority of study respondents were sharing house with more than 3 persons at the two study settings. Among Khartoum study's respondents, the percentages of patients sharing house with 3-7 persons and more than 7 persons were 40.3% and 51.4% respectively. While in Gazeira state, the percentage of respondents sharing house with 3-7 persons and more than 7 persons were 51.4% and 42.6% respectively. Pearson Chi-Square test revealed no statistical difference in the number of family members between the two study samples {X^2 (2) = 5.885, p=0.053}.



Dependent variables

The total pre-treatment period

The mean total pre-treatment period was 66.75±44.19 days in Khartoum (median: 53 days, mean rank= 217.64) and 69.66±28.14 days in Gazeira (median: 64.5 days, mean rank= 255.33). While 59% of study sample had pre-treatment period of more than 6 weeks in Khartoum, 87.5% of study sample in Gazeira experienced such a delay. Mann-Whitney U test revealed a statistically significant difference between the two mean ranks {Z= -3.002, p= 0.003}.

Globally, the shortest length of median pre-treatment period (28 days) was reported in Vietnam and the longest one (336.5 days) in Afghanistan.[48,49] Two systematic reviews conducted by Storla and Sreeramareddy reported median diagnostic delay of 60-90 days and average total delay of 25-185 days respectively.[50,51]

Median total pre-treatment periods of about up to 2 months was reported in Pakistan (56 days), and Gambia, South India, and Nepal (60 days). Median total pre-treatment period of more than three months was reported by in Mwanza region, Tanzania (136 and 188 days), and Ghana (4 months).[26,53-57] A shorter median total pre-treatment period in Tanzania (84 days) was reported by a cross sectional review study of FIDELIS projects.[58]

Three different studies conducted in Ethiopia reported median total pre-treatment periods of 64, 70.5 and 80 days respectively.[29,47,59] A 70 days total pre-treatment period was reported in Malawi, and Nigeria.[60,61] While a recent study conducted in rural Nigeria reported a higher median total pre-treatment period of 77 days.[62]

The patient's period

The mean patient's period was 33.85±34.24 days in Khartoum (median: 21 days, mean rank= 214.69) and 36.61±23.13 days in Gazeira (median: 30 days, mean rank= 258.79). Mann-Whitney U test revealed a statistically significant difference between the two mean ranks {Z= -3.527, p<0.001}.

The shortest median patient period was reported in Gambia (2.1 days) while the longest one in Afghanistan (199 days).[26,49] Other studies reported patient period of 20 days (Ethiopia & south India), 21 days (Vietnam, Botswana, and Tanzania), 28 days (Ghana) 50 days (Nepal), 56 days (Nigeria), and 120 (Tanzania).[29,48,53-57,61-63]

Health system's period

The mean total health system's period was 32.88±30.73 days in Khartoum (median: 24 days) and 33.05±24.54 days in Gazeira (median: 28 days). Independent-samples t-test revealed insignificant statistical difference between the two means {t (467) = -0.065, p=0.948}.

The shortest median health system's period was reported in Ethiopia (6 days) followed by Vietnam (7 days). While the longest period was reported in Afghanistan (128.5 days).[47-49] Less than one month health system's periods were reported in Nigeria (14 days), Tanzania (15 days), Nepal (18 days), Thailand (19.6 days), and Ethiopia and Nigeria (21 days), South India (23 days), and Tanzania (26 days), Botswana (35 days).[53-56,60,62-65] Longer periods of more than one month were reported in Ethiopia (33.5 days), Botswana (35 days) and Gambia (58 days).[26,29,63]

Relationship between patient's period, health system's period and total pre-treatment period

In Khartoum state study, the patient's period ascribed to 51% of the total pre-treatment period whereas in Gazeira study, it accounted for up to 53% of the total pre-treatment period. This difference in the length of patient's period was statistically insignificant. Similarly, pre-treatment period was equally divided between patient's period and health system's period in Thailand, and Afghanistan.[49,64] On the other hand, patient's period ascribed to more than two-thirds of total pre-treatment period in Ethiopia, Vietnam, Tanzania, Nepal and Nigeria.[47,48,54,55,61,62] However, health system's period was longer than patient's period in Gambia, Botswana and Ghana.[26,57,63]

Independent variables[viii]

Socioeconomic factors

Age & Age group

There was no significant association between patient's age/age group and total pre-treatment period and health system's period in both settings. Similarly, age/age group had no significant association with patient's period in Khartoum. However, age group (25-54years) was significantly associated with longer patient's period in Gazeira.

Other studies conducted in Gambia, Thailand, Vietnam, Nigeria, and Pakistan reported longer pre-treatment period with older age (>25 years).[26,48,52,62,64] On the other hand, a longer total pre-treatment period associated with age group (< 45 years) compared to age group (>45 years) was reported in Tanzania (300 days versus 126 days respectively).[56] Worthy of note that a review study of FIDELIS's projects in Tanzania reported a longer pre-treatment period in patients falling in age groups (15-24) and (>65 years).[58]Longer patient's period associated with older age (>45 years) was reported in Tanzania, South India, and Ethiopia.[53,55,59]

Sex

The two national studies revealed no significant association between patient's sex and total pre-treatment period, and patient's period. Similarly, no significant association was found between sex and health system's period in Khartoum. However, female sex was significantly associated with longer health system's period in Gazeira state.

Total pre-treatment period was independent of sex in Gambia, Tanzania, and Afghanistan.[26,49,58] While studies conducted in Vietnam, Dar es Salam, and Bangladesh revealed a significant association between female sex and longer pre-treatment period.[48,65,66] On the other hand, male sex was associated with longer total pre-treatment period in Tanzania and Nigeria.[56,62]

Regarding patient's period, male sex was associated with longer patient's period in South India while it had no effect in Afghanistan.[49,53] Contrarily, female sex was associated with longer patient's period in Bangladesh and Dar es Salam.[65,66]

Marital Status

While Khartoum study revealed no significant association between patient's marital status and the three periods, Gazeira study demonstrated a

(viii) Please review table 1 (page 26 & 27) and table 2 (page 33) for the mean differences of the total pre-treatment period, patient's period, and health system's period in relation to patient's socioeconomic characteristics, cultural and beliefs factors, severity of the disease, and health system factors at Khartoum and Gazeira study settings

significant association between being widow/divorced and longer total pre-treatment period, and longer health system's period. No significant association was found between marital status and patient's period in Gazeira. Similarly, widow/divorced patients had longer pre-treatment period in Tanzania, and longer patient's period in Botswana.[56,63] However, being married was associated with longer health system's period in Botswana.[63]

Educational level

No significant association was demonstrated between patient's educational status and total pre-treatment period in both study settings. Similarly, no significant association was found between educational status and patient's period and health system's period in Khartoum. On the other hand, Gazeira study demonstrated a significant association between higher educational level (>12 years) and shorter patient's period and longer health system's period. Similarly, a negative correlation between patient's educational level and patient's period in South India, Tanzania and Chad.[53,55,71] However, pre-treatment period, patient's period, and health system's period were independent of educational level in Afghanistan.[49]

Occupation

No significant association was demonstrated between patient's occupation and total pre-treatment period in both study settings as well as in Afghanistan.[49] While Khartoum study demonstrated a significant association between farmers and longer patient's period, no significant association was found between occupation and health system's period in Khartoum. On the other hand, Gazeira study demonstrated no significant association between occupation and patient's period and health system's period. A recent study conducted in Pakistan revealed a longer total pre-treatment period in idle and unskilled worker compared to students, skilled workers and government servants.[52]

Monthly Income

Khartoum study showed no significant association between the three periods and patient's monthly income. On the other hand, Gazeira study revealed a significant association between higher income level (more than 100 USD) and longer total pre-treatment period and longer health's system period. However, no significant association was found between monthly income and patient's period in Gazeira. Contrarily, lower income level was associated with longer total pre-treatment period in Gambia and longer patient's period in South India, Zambia, and Chad.[18,26,53,71]

Housing condition (Family size)

Both Khartoum and Gazeira studies revealed no significant association between total pre-treatment period, patient's period and number of family members (family size). While Khartoum study revealed no significant

association between health system's period and family size, Gazeira study demonstrated a significant association between large family size (>3 persons) and longer health system's period. Similarly, large family size was associated with longer total pre-treatment period in Afghanistan.[49]

Cultural and beliefs factors

Self-medication

Around one-third of respondents practiced self-medication before visiting any medical health provider; 36.8% in Khartoum state and 33.3% in Gazeira state. Cross tabulation of data by type of study setting and whether self-medication was practiced revealed no statistical difference in health-seeking behaviour between the two study samples {Fisher's Exact test, p=0.497}.

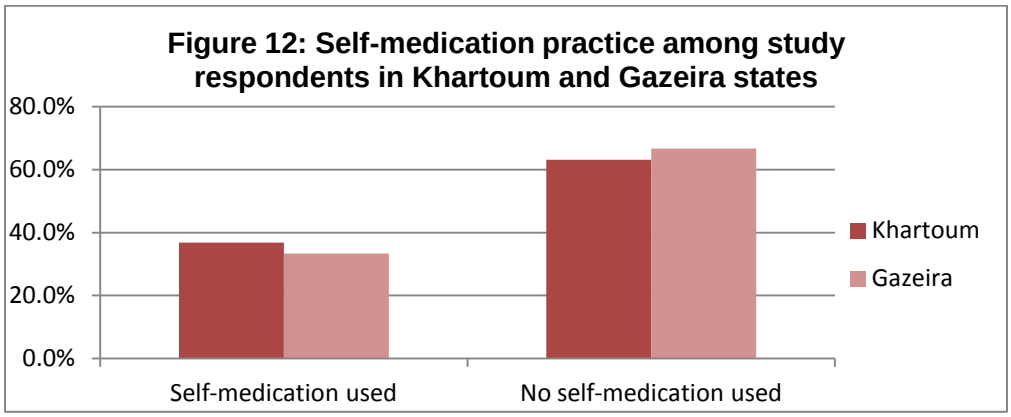


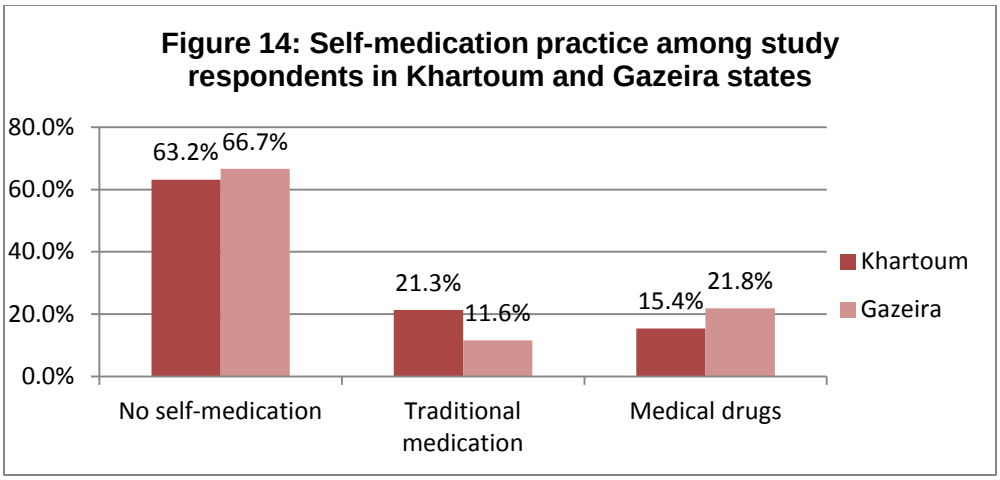
Figure 12: Self-medication practice among study respondents in Khartoum and Gazeira states

Relationship between self-medication and pre-treatment period, patient's period, and health system period

No significant association was demonstrated between self-medication and the three periods at both study settings. However, other studies conducted in Ethiopia and Afghanistan reported longer patient's period in patients resorted to self-medication.[29,49,59]

Type of self-medication

Around two- thirds of respondents did not resort to self-medication before visiting any medical health provider; 63.2% in Khartoum and 66.7% in Gazeira. However, 21.3% tried traditional medication in Khartoum compared to 11.6% in Gazeira. Cross tabulation of data by type of study setting and self-medication practice revealed a statistically significant difference in health-seeking behaviour between the two study samples with higher proportion of respondents using medical drugs in Gazeira {Pearson Chi-Square test: $X^2(2) = 9.37$, p=0.009}.



Relationship between type of self-medication and pre-treatment period, patient's period, and health system period

No significant association was found between type of self-medication and the three periods in Khartoum. On the other hand, Gazeira study demonstrated a significant association between resorting to traditional medication and longer pre-treatment period. However, no significant association was found between type of self-medication and patient's period and health system's period among Gazeira's study respondents. Contrarily, trial of self-medication was associated with longer patient's period in Afghanistan.[49]

Relationship between type of self-medication and length of patient's period

Study respondents were categorized into three groups with regard to self-medication practice; group 1: no self-medication, group 2: traditional medication, and group 3: medical drugs. One-way analysis of variance (ANOVA) test was applied to investigate the relationship between the length of the patient's period and self-medication practice. The ANOVA test revealed statistically insignificant difference between the three groups {$F(2,466) = 1.253$, $p= 0.287$}.

Table 1a: The relationship between total pre-treatment period, patient's period, health system's period and independent variables in Khartoum and Gazeira

Variable		Pre-treatment Period						Patient period						Health system period					
		Khartoum			Gazeira			Khartoum			Gazeira			Khartoum			Gazeira		
		mean	SD	P	mean	SD	P	mean	SD	P	mean	SD	P	mean	SD	p	mean	SD	p
Age group	<25	68.29	46.01	.441	67.67	26.17		31.56	29.06		32.63	21.56		36.68	35.94		35.04	26.81	
	25-54	64.39	42.87		72.30	28.19	.122	33.12	35.51	.062	**39.67**	23.69	**.035***	31.28	28.21	.864 (KW)	32.63	24.98	.786
	>54	78.12	45.63		61.13	30.08		52.53	44.83		29.57	21.17		25.59	15.00		31.57	18.18	
Sex**	Male	64.33	44.00	.258	67.93	27.65	.235	32.84	35.19	.541	38.11	24.15	.209	31.47	31.35	.344	29.82	24.71	**.010 ***
	Female	70.84	44.45		72.66	28.90		35.56	32.67		34.00	21.15		35.27	29.68		**38.66**	23.34	
Marital Status	Single	69.52	45.15	.332	72.00	30.85	**.005 *** (KW)	34.85	33.10	.762	39.98	27.97	0.529 (KW)	34.61	33.26	.429	32.02	26.59	**.002 ***
	Married	63.46	43.05		65.94	24.37		32.62	34.48		34.66	19.58		30.86	28.13		31.28	22.04	
	Divorced/ widow	81.78	48.90		**95.14**	36.47		39.89	46.39		39.93	29.66		41.89	36.35		**55.21**	28.72	
Educational level	Illiterate/< 3 years	64.43	40.16	.602	68.98	29.41	.644	35.92	34.68	.775	36.76	19.31	**<0.001 *** (KW)	28.50	23.13	**.416** (KW)	32.22	23.90	**.034 *** (KW)
	3-6 years	63.31	49.17		73.94	27.75		32.08	35.29		39.82	28.38		31.22	29.25		34.12	22.15	
	6-12 years	73.43	48.50		67.27	22.96		30.44	31.57		42.71	20.49		42.89	42.42		24.56	12.01	
	>12 years	68.70	47.16		67.46	32.14		33.18	36.46		**18.71**	22.18		**35.58**	33.30		**48.75**	38.20	
Occupation	idle	70.11	46.35	0.37 (KW)	73.45	26.78	0.17	36.38	34.43	**.009 *** (KW)	34.76	19.93	.116 (KW)	33.75	30.02	.206 (KW)	38.68	23.82	.129 (KW)
	Students	76.52	46.04		62.00	27.90		33.93	28.14		26.00	18.75		42.52	40.34		36.00	33.43	
	Worker	67.67	46.13		68.56	27.81		37.94	40.50		38.58	21.72		29.68	27.79		29.98	24.30	
	Farmer	71.57	43.25		65.94	27.39		**53.21**	47.07		34.72	22.33		18.36	15.69		31.22	17.57	
	Employee	60.11	44.08		73.00	32.18		15.67	17.57		49.13	29.85		44.39	43.05		23.88	7.38	
	Small buisness	53.68	34.31		70.18	34.15		24.34	22.20		44.59	34.05		29.34	24.07		25.59	30.55	

*** p <0.05; KW: Kruskal Wallis Test; and M-W: Mann-Whitney U Test**

**** Independent-samples t-test was applied to measure the mean difference of the three periods at each study setting whereas ANOVA test was applied to measure the mean difference of the three periods in relation to the remaining independent variables at each study setting**

Table 1b: The relationship between total pre-treatment period, patient's period, health system's period and independent variables in Khartoum and Gazeira

Variable		Pre-treatment Period						Patient period						Health system period					
		Khartoum			Gazeira			Khartoum			Gazeira			Khartoum			Gazeira		
		mean	SD	P	mean	SD	P	mean	SD	P	mean	SD	P	mean	SD	p	mean	SD	p
Monthly Income	<100 USD	67.17	43.43	.497	65.42	27.46	.002*	34.49	33.75	.349	38.13	24.01	.179	32.67	29.65	.939	27.29	18.30	<0.001* (KW)
	100-200 USD	58.85	53.16		**77.78**	27.83		25.42	38.24		33.68	21.19		33.31	41.45		**44.11**	30.62	
	>200 USD	76.25	37.14					40.58	33.92					35.83	24.95				
Housing Condition (number of family members	<3	67.00	37.34	.857	62.46	35.35	.391	43.48	37.24	.386	43.62	26.50	.576 (KW)	23.52	16.40	.313	**18.85**	18.93	.016* (KW)
	3-7 persons	64.90	43.36		71.90	29.42		32.18	32.97		35.63	19.77		32.69	28.37		36.27	27.43	
	>7	68.15	46.07		67.97	25.38		33.61	34.74		36.79	26.28		34.55	34.00		31.17	20.51	
Self-medication**	No	64.41	45.35	.271	69.09	27.11	.676	32.24	35.34	.327	35.27	23.67	.231	32.19	31.75	.639	33.82	25.66	.516
	Yes	70.76	42.07		70.79	30.27		36.62	32.26		39.28	21.93		34.08	29.04		31.51	22.21	
Type of self-medication	No self-medication	64.41	45.35	.259	69.09	27.11	.003*	32.24	35.34	.162	35.27	23.67	.104	32.19	31.75	.895	33.82	25.66	.073
	Traditional medication	66.00	37.29		**86.04**	27.93		31.69	26.45		45.84	22.97		34.20	27.03		40.20	23.34	
	Medical drugs	77.36	47.62		62.68	28.52		43.46	38.23		35.79	20.76		33.90	31.97		26.89	20.35	
Reasons for coming to TBMU	Self-referral	57.36	41.41	.171	68.19	32.05	.932	31.39	33.40	.792	40.79	21.57	.082	**26.00**	28.59	.006* (KW)	27.40	20.21	0.191 (KW)
	Relative/friend	73.73	50.49		70.11	29.66		32.58	30.96		30.14	21.98		41.15	40.79		39.98	33.67	
	Medical provider	68.76	43.87		69.98	26.45		34.85	35.11		37.45	23.71		33.88	29.39		32.53	21.65	

*** p <0.05; KW: Kruskal Wallis Test; and M-W: Mann-Whitney U Test**

**** Independent-samples t-test was applied to measure the mean difference of the three periods at each study setting whereas ANOVA test was applied to measure the mean difference of the three periods in relation to the remaining independent variables at each study setting**

Reasons for coming to TBMU

Reasons for coming to TBMU were categorized into three groups; self-referral, referral by a relative/friend, and referral by a medical health provider. The majority of respondents were referred to TBMU by a medical health provider; 67.6% in Khartoum and 60.2% in Gazeira. Nevertheless, self-referral to TBMU ranked second among Khartoum study's respondents (22.1%) and third among Gazeira study's respondents (19.4%). Pearson Chi-Square test revealed a statistically significant difference between the two study samples {X^2 (2) =9.353, p=0.009}.

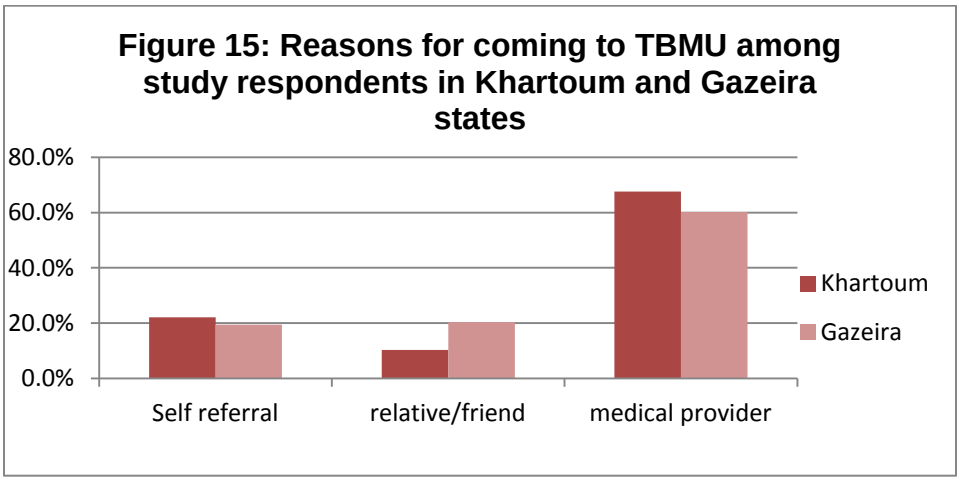


Figure 15: Reasons for coming to TBMU among study respondents in Khartoum and Gazeira states

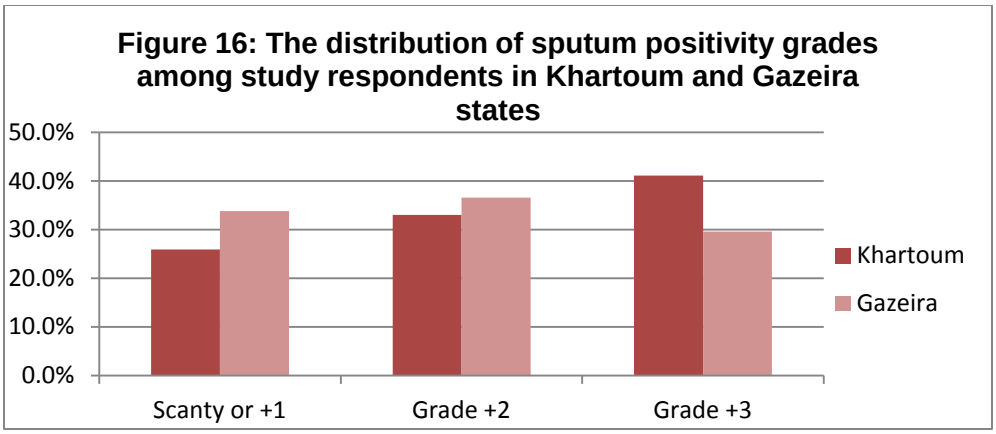
Relationship between reasons for coming to TBMU and pre-treatment period, patient's period, and health system period

No significant association was demonstrated between reasons for coming to TBMU and total pre-treatment period and patient's period in both settings. However, Khartoum study revealed a significant association between self-referral and shorter health system's period. On the other hand, Gazeira study revealed no significant association between reasons for coming to TBMU and health system's period.

Disease factors

Sputum smear grading

The majority of Khartoum's study respondents demonstrated grade +3 (41.1%) or grade +2 (33.0%) sputum smears. While the majority of Gazeira study patients' demonstrated grade +2 (36.6%) or scanty/+1 (33.8%) sputum smears. Pearson Chi-Square test revealed a statistically significant difference in the grading of sputum smears between the two study samples {X^2(2) = 6.148, p=0.046}.



Relationship between sputum smear grading and pre-treatment period, patient's period, and health system period

Both studies revealed no significant association between sputum smear grade and total pre-treatment period and health system's period. Similarly, Khartoum study demonstrated no significant association between sputum smear grade and patient's period. Contrarily, Gazeira study demonstrated a significant association between scanty/+1 sputum smear grade and longer patient's period. Furthermore, trends of longer pre-treatment period and patient's period were observed with smear-positive TB patients in Tanzania and Nepal.[54,56]

Relationship between sputum smear grade and length of patient's period

Study respondents were categorized into three groups with regard to sputum positivity grade; scanty or +1, grade +2, and grade +3. ANOVA test was applied to investigate the relationship between the length of the patient's period and sputum smear grade. The ANOVA test revealed a statistically significant difference between the three groups {F (2,398)= 4.596, MSE= 3527, p= 0.011}.

Post-hoc multiple comparison using Tukey HSD test indicated that the mean score of the first group (M=41.02, SD=29.446) was significantly different from second (M=32.84, SD=25.433) and third (M= 31.17, SD=28.315) groups. The mean score of the second group did not differ significantly from the third one.

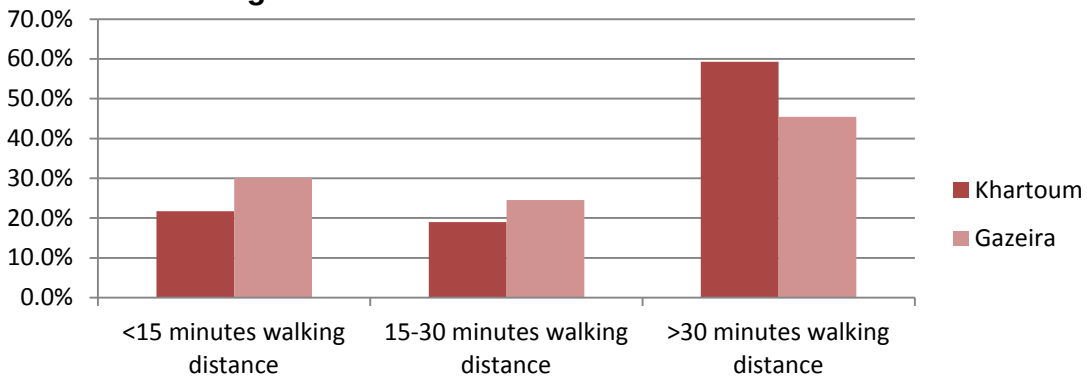
Health system factors

Distance to TBMU

Among Khartoum study's respondents, almost 60% of patients (59.3%) reported more than 30 minutes walking distance from their houses to TBMU compared to 21.7% of patients who had to walk for less than 15 minutes. On the other hand, 45.4% and 30.1% of Gazeira's study respondents reported more than 30 minutes and less than 15 minutes walking distance

respectively. According to Pearson Chi-Square test, the difference in walking distance to TBMU between the two studies was statistically significant {$X^2(2) = 9.122$, $p=0.010$}.

Figure 17: The distribution of study respondents per walking distance to TBMU in Khartoum and Gazeira states

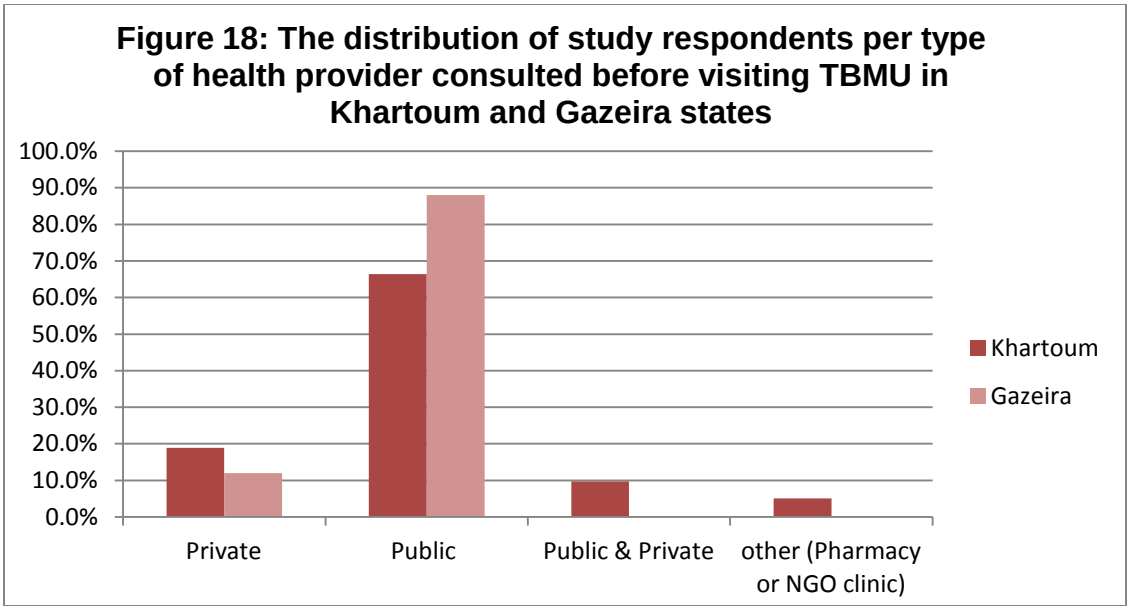


Relationship between walking distance to TBMU and pre-treatment period, patient's period, and health system period

Khartoum study showed no significant association between walking distance to TBMU and the three periods. Similarly, Gazeira study demonstrated no significant association between walking distance to TBMU and pre-treatment period. However, a significant association was found between walking distance to TBMU (15-30 minutes) and shorter patient's period and longer health system's period in Gazeira. Contrarily, longer patient's periods were associated with patients living (>2 km) in South India, (5 km) in Vietnam, (>10 km) in Ethiopia and Tanzania.[48,53,55,59]

Type of health provider before TBMU

Two-thirds of Khartoum study's respondents consulted public health care provider (66.4%) before visiting TBMU while 18.9% consulted private health-care provider and 9.7% consulted both providers. On the other hand, Gazeira study's respondents either consulted public (88.0%) or private health-care providers (12.0%). Pearson Chi-Square test revealed a statistically significant difference between the two studies with regard to type of health provider consulted before visiting TBMU {X^2 (3) = 41.691, $p<0.001$}.



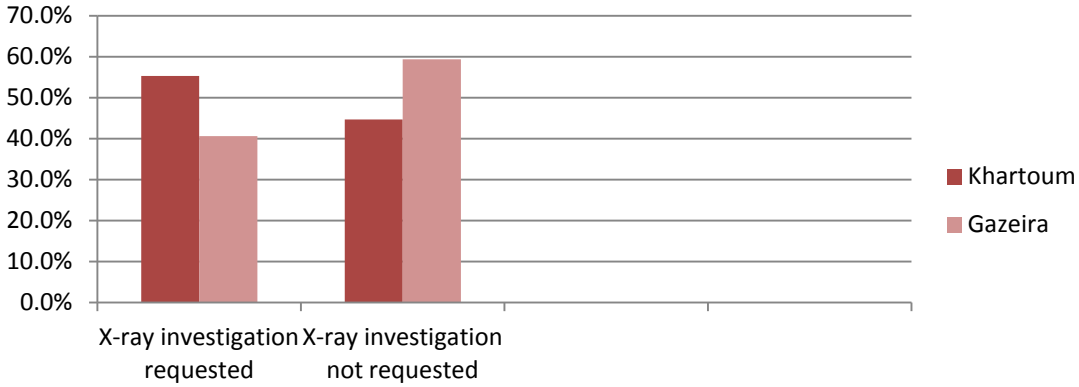
Relationship between type of health provider before TBMU and pre-treatment period, patient's period, and health system period

No significant association was found between type of health provider consulted before visiting TBMU and the three periods at both study settings. Contrarily, other studies showed significant association between private health providers and longer total pre-treatment period in Vietnam and South India, and longer patient's period in Afghanistan, and longer health system's period in Ethiopia, Vietnam, and South India.[29,48,49,53,59] On the other hand, public health providers were associated with longer patient's period in South India.[53]

Investigation requested by other health providers (X-ray)

In Khartoum, 55.3% of the respondents were requested to undertake X-ray examination by health providers compared to only 40.6% in Gazeira's. Fisher's Exact test revealed a statistically significant difference with regard to type of investigation requested by healthcare providers between the two study samples {p=0.004}.

Figure 19: The distribution of study respondents per type of investigation requested by health providers before visiting TBMU in Khartoum and Gazeira states



Relationship between type of investigation requested by other health providers and pre-treatment period, patient's period, and health system period

Khartoum study showed no significant association between type of investigation requested by health providers before visiting TBMU and the three periods. Similarly, Gazeira study showed no significant association between type of investigation requested by health providers before visiting TBMU and pre-treatment period and patient's period. However, x-ray examination was significantly associated with shorter health system's period in Gazeira.

Relationship between x-ray examination and length of health system's period

Study respondents were categorized into two groups; no X-ray examination requested and X-ray examination requested. The first group had longer health system's period (M= 40.30, SD= 27.737) compared to the second one (M= 32.48, SD=29.597). Independent-samples t-test revealed a statistically significant difference between the two means {t (385) = 2.684, P= 0.008}.

Table 1c: The relationship between total pre-treatment period, patient's period, health system's period and independent variables in Khartoum and Gazeira

Variable		Pre-treatment Period						Patient period						Health system period					
		Khartoum			Gazeira			Khartoum			Gazeira			Khartoum			Gazeira		
		mean	SD	P	mean	SD	P	mean	SD	P	mean	SD	P	mean	SD	p	mean	SD	p
Sputum smear grading	Scanty/+1	67.60	44.69	.776	74.07	26.53	.193	34.90	33.68	.845	**45.04**	25.75	**0.002*** (KW)	32.65	30.07	.924	29.03	19.64	0.134 (KW)
	Grade 2	62.41	35.72		65.78	27.87		31.75	29.54		33.68	21.90		30.61	26.86		32.10	24.86	
	Grade 3	63.08	41.82		69.41	29.92		31.66	34.59		30.59	18.55		31.47	23.92		38.81	28.20	
Walking distance to TB MU	<15 minutes	67.71	45.26	.546	71.35	30.71	.828	36.75	35.52	.326	37.51	22.09	**0.045***	30.93	33.48	.864	33.85	24.80	**.036***
	15-30 minutes	72.52	44.78		69.57	27.70		38.73	37.42		**29.94**	20.79		33.83	29.80		**39.62**	30.49	
	>30 minutes	64.55	43.73		68.58	26.81		31.23	32.65		39.61	24.46		33.29	30.15		28.97	19.73	
Type of health provider before TBMU	Private	66.24	36.32	.545	70.46	31.38	.877	28.34	31.22	.600	31.19	20.76	.204	37.95	29.42	.236	39.27	29.46	0.338 (KW)
	Public	69.67	44.84		69.55	27.76		35.61	34.65		37.35	23.39		34.02	29.58		32.20	23.75	
	Other (pharmacy or NGO clinic)	84.82	51.75					38.55	32.57					46.27	35.25				
	Both private and public	77.71	49.73					30.86	31.36					46.81	44.34				
Investigation requested by other health providers **	X-ray examination not requested	73.55	46.98	.372	73.90	27.55	.373	35.03	35.43	.664	31.93	19.70	0.051 (M-W)	38.56	30.94	.419	**41.97**	24.30	<0.001 *
	X-ray examination requested	68.16	41.74		69.90	30.33		33.03	32.07		41.91	28.52		35.06	32.17		27.99	24.06	

*** p <0.05; KW: Kruskal Wallis Test; and M-W: Mann-Whitney U Test**

**** Independent-samples t-test was applied to measure the mean difference of the three periods at each study setting whereas ANOVA test was applied to measure the mean difference of the three periods in relation to the remaining independent variables at each study setting**

Chapter 4: Discussion

Dependent variables

Total pre-treatment period

The median total pre-treatment period reported in Khartoum urban setting was significantly shorter than the median total pre-treatment period reported in Gazeira rural setting.

Similarly, a longer length of pre-treatment period at rural setting compared to urban setting was reported in Ghana and Gambia.[26,57] Contrarily, a longer length of pre-treatment period among urban dwellers rather than rural dwellers was reported in Nigeria.[62]

The length of median total pre-treatment period reported in Sudan; 53 days in Khartoum and 64.5 days in Gazeira, was consistent with reports from many countries in Africa and Asia, with the exception of Tanzania and Afghanistan, where the reported pre-treatment periods were roughly three to five times longer, and Vietnam where it was shorter by half. [26,47-49,50,52-54,56,60,61,64]

Patient's period

The median patient's period reported in Khartoum was significantly shorter than the median patient's period reported in Gazeira. Similarly, a longer length of patient's period at rural settings compared to urban settings was reported in Gambia, Tanzania, and Vietnam.[26,48,55] Contrarily, a longer length of patient's period was reported among urban patients compared to their rural counterparts in Nigeria.[62]

The length of median patient's period reported in Sudan; 21 days in Khartoum and 30 days in Gazeira, was consistent with reports from many countries in Africa and Asia except Nepal, Nigeria, and Afghanistan, where the reported patient's period were roughly two to eight times longer, and Gambia where it was extremely shorter accounting for only one-tenth of the median patient's period reported in Sudan. [26,29,48,49,53,54,57,61-64] The striking shortest length of patient's period in Gambia was attributed to variation in the definition of patient's period. In Gambia, patient's period was defined as the time interval between onset of symptoms and first visit to any health provider including patient's relatives, friends, and traditional healers. While in Sudan and other studies, patient's period was defined as the time interval between onset of symptoms and first visit to a formal health provider.

Health system period

The median health system's period reported at Khartoum urban setting was relatively shorter than the median health system's period reported at Gazeira rural setting though this difference was found to be statistically

insignificant. Similarly, a shorter length of health system's period at urban settings compared to rural settings was reported in Tanzania, and Vietnam.[48,55]

The length of median health system's period reported in Sudan; 24 days in Khartoum and 28 days in Gazeira, was consistent with reports from many countries in Africa, and Asia except Afghanistan where the reported health system's period was roughly five times longer, and Vietnam and Tanzania where it was shorter (only one-third in Vietnam and a half in Tanzania).[48,49,53,55,56,59,62]

The relationship between patient's period, health system's period, and total pre-treatment period

Total median pre-treatment period was almost equally divided between patient's period and health system's period at both national studies. Similar finding was described in both Thailand, and Afghanistan.[49,64] In most of other studies, a reciprocal relationship between patient's period and health system's period was demonstrated; the longer the patient's period was the shorter the health system's period would be.[47,48,54,55,57,61-63] This interesting finding was attributed to the fact that TB is more readily diagnosed among patients presenting at more advanced stages of the disease.

Independent Variables

Socioeconomic factors

Age

The median age of the study respondents in Khartoum was 27 years and it was relatively younger than the median age of their Gazeira's counterparts (33 years). The difference in mean age was found to be statistically significant between the two study samples. The relatively younger age at Khartoum urban setting could be attributed to higher risks of exposure to infection and progression to disease among urban dwellers compared to their rural counterparts. Higher risks among urban dwellers are attributed to higher population density, crowding, and poor ventilation at home at urban residence.[67] Globally, tuberculosis strikes hard on productive and reproductive segment of the society.

Total pre-treatment period, patient's period, and health system's period were independent of age in Khartoum. On the other hand, age group (24-54 years) was associated with longer patient's period in Gazeira. Khartoum study findings in relation to age and the three periods was similar to that reported in Afghanistan.[49] The association of longer patient's period with age group (24-54 years) reported in Gazeira was similar to that reported in Tanzania. Young farmers in Tanzania had longer patient's period compared to older age groups.[56] This finding was attributed to the probability that

young patients, farmers and daily wage earners delayed seeking health care in order to avoid loss of income and further financial constraints. However, other studies conducted at different contexts reported longer pre-treatment period, and patient's period with older age rather than young age as in Gazeira and Tanzanian studies. In Tanzania, South India, Nigeria, and Ethiopia, longer patient's periods were reported with older age (>45 years). This finding was attributed to the probability that "old people cannot access health facilities at preferred time as they depend on other people to access health-care".[53,55,59,62]

Sex

The gender split (male to female ratio) among of study respondents at both study settings was almost 2:1 reflecting the current national and global trends in TB notification rates. Considerable debate was aroused whether this gender difference in TB notification rates is due to inequality in access to health care or genuine biological difference with respect to TB susceptibility. Globally, socioeconomic and cultural barriers deter women from accessing health care. Women are financially dependent, have lower decision-making capacity and are more socially affected by the stigma attached to TB. On the other hand, lower prevalence of TB among women is partially attributed to the fact that women are biologically resistant to TB infection. However, women have a higher rate of progression of TB infection to tuberculosis disease as well as a higher TB fatality rate compared to men.[68,69]

In Khartoum study, the three periods were independent of sex. On the other hand, female sex was associated with longer health system's period in Gazeira. The association between female sex and longer health system period in Gazeira was attributed to lower index of suspicion for TB among health providers towards women with milder stages of the disease as well as avoidance of social stigma attached to TB and its negative repercussions on women's marital relations. Due to social stigma, woman's chance to get married if diagnosed with TB is reduced and she might suffer abandonment or divorce if already married.[43,66] However, other studies elsewhere attributed the association between female sex and longer health system's period to difference in care-seeking behaviour between men and women. Women often sought medical advice from private health providers and at lower level health facilities due to social commitments, financial constraints, and close proximity. Private health providers and low level health facilities often lack expertise in TB diagnosis and effective referral link to specialized TB diagnostic services. Furthermore, low level health facilities often lack trained staff, TB diagnostic laboratory, X-ray machines, and effective supervision, thereby potentially contribute to longer health system's period among women compared to men.[29,50,53,59,63,64]

Female sex was associated with longer pre-treatment period in Ghana, and Vietnam, Dar es Salam, and Bangladesh and longer patient's period in Dar es Salam, and Bangladesh. These associations were attributed to TB social stigmatization in Bangladesh and Vietnam.[31,57,65,66,70]

Marital status

More than a half of study population was married at both study settings. No significant association was found between marital status and the three periods in Khartoum although widow/divorced did seem to have longer length of all three periods. On the other hand, longer pre-treatment period and health system's period were reported among widow/divorced in Gazeira. Male TB patients had longer health system's period in Gazeira. The latter association was explained by the probability that widow/divorced TB male patients in Gazeira tend to avoid TB diagnosis so as not to jeopardize their social status in the community.[43] However, other studies reported longer pre-treatment period in Tanzania, and longer patient's period in Botswana among widow/divorced TB patients due to financial constraints.[56,63]

Educational level

Almost 50% of the study population was illiterate at both study settings. Higher educational level (>6 years) was insignificantly associated with longer health system's period in Khartoum. On the other hand, higher educational level (>12 years) was significantly associated with shorter patient's period and longer health system's period in Gazeira. A similar finding of shorter patient's period was reported in Nigeria.[62]

Illiteracy and low educational level are usually associated with low levels of TB knowledge, monthly income, and self-medication and hence delayed care-seeking behaviour and prolonged patient's period.[53,55,71] Contrarily, higher educational level is usually associated with knowledge of TB, and early care-seeking behaviour. Therefore, patients with higher level of education promptly seek medical advice. However, health providers face difficulties in reaching TB diagnosis among patients who present at early stages of the disease. Furthermore, health providers might have lower index of suspicion for TB towards patients of higher educational status.

Occupation

Almost one-third of the study population was idle at both study settings. Longer length of patient's period was demonstrated among farmers compared to employees in Khartoum. Farmers were more likely to have lower level of TB knowledge, and monthly income compared to governmental employees and hence delayed care-seeking behaviour. On the other hand, no significant association was found between occupational category and the three periods in Gazeira although employees and small

business respondents did seem to have longer pre-treatment period, longer patient's period, and shorter health system's period.

Monthly Income

More than two-thirds of study population was poor at both settings (monthly income of less than100 USD). No significant association was found between monthly income and the three periods in Khartoum, although respondents with higher monthly income (>200 USD) did seem to have longer length of all the three periods compared to other income categories. Similarly, longer length of total pre-treatment period and health's system period was significantly associated with higher income level (>100 USD) in Gazeira.

The unexpected finding of longer periods among TB patients of higher economic level was attributed in Gazeira study to early presentation at health facilities with milder form of the disease as well as lower index of suspicion for TB among health provider towards patients of higher economic status.

Contrarily to the findings reported in Khartoum and Gazeira, other studies elsewhere demonstrated longer patient's periods with low income level. Despite free TB diagnostic and treatment services, the additional costs incurred by patients (transportation, food, and loss of income) imposed financial constraints on poor patients with presumptive active TB, deterring them from seeking medical advice.[15,53,71]

Housing condition (Family size)

The majority of the study population was descending from sizable families; more than 40% were sharing house with more than 7 persons at both study settings. In Khartoum, no association was found between family size and the three periods. On the other hand, large family size was associated with longer health system's period in Gazeira similar to Afghanistan. The latter association was attributed to limited financial resources among households of large family size.[49]

Cultural and beliefs factors

Self-medication

Around one-third of study respondents practised self-medication at both study settings. No significant association was found between self-medication and the three periods at both study settings. However, resorting to self-medication did seem to be associated with longer patient's period at both study settings, similar to other studies conducted in Africa and Asia.[29,49,57,59,63] Patients resorting to self-medication often had low level of TB knowledge and underestimated the severity of their illness. This attitude might have serious repercussions on the patient's health; poor treatment

outcome, as well as transmission of the disease in the community through prolongation of the infectious period.

Other studies indicate that fear of social stigmatization and low TB Knowledge influenced care-seeking behaviour.[72] Confusion of TB and AIDS symptoms among TB patients resulted in delayed health-seeking behaviour in order to avoid social stigmatization attached to HIV if their HIV status turned out to be positive. However, high level of TB stigma was significantly associated with longer patient's period and shorter health system's period in Afghanistan and Vietnam.[48,49] This finding was related to the probability TB was more readily diagnosed among TB patients presenting at more advanced stages of the disease.[49]

Type of self-medication

More than one-third of the study population resorted first to traditional self-medication at both study settings. No association was found between type of self-medication and the three periods in Khartoum. However, self-medication with non-prescription medical drugs was apparently associated with longer pre-treatment period and longer patient's period in Khartoum. On the other hand, resorting to traditional medication was significantly associated with longer pre-treatment period in Gazeira. Similar finding was reported in Afghanistan.[49] Non-prescription medication has adverse effect on patient's health as it will temporarily alleviate TB symptoms and thereby, delaying appropriate care-seeking behaviour. Traditional medication was apparently associated with longer patient's period in Gazeira and this association could be attributed to patient's belief in the efficacy of traditional medication and hence delaying appropriate care-seeking behaviour.

Reasons for coming to TBMU

The majority of TB patients were referred by a health provider to TBMU at both study settings. Self-referral was reported by only one fifth of study respondents which might indicate a relatively low awareness level among the community about TB symptoms and availability of free TB diagnostics and treatment services.

Self-referral was significantly associated with shorter length of health system's period in Khartoum. On the other hand, Gazeira study demonstrated an insignificant association between self-referral and shorter health system's period. This association; despite been statistically insignificant at one study setting, underscored the potential impact of public education programme on enhancement of early care-seeking behaviour through raising community awareness on TB symptoms, its curability, and availability and accessibility of TB diagnostic and treatment services.

Disease factors

Sputum smear grading

Khartoum study population had higher grade of sputum smear positivity compared to Gazeira study population. This difference in sputum grading between the two national studies could be attributed to the probability that some respondents at Khartoum study were referred for TB diagnosis from other states with a subsequent progression of their illness prior to accurate diagnosis. It might also be attributed to lower level of self-medication with medical drugs among Khartoum study's respondents.

No significant association was found between sputum smear grade and the three periods in Khartoum although scanty/+1 sputum smear grade did seem to be associated with longer length of all three periods. On the other hand, scanty/+1 sputum smear grade was significantly associated with longer patient's period in Gazeira. The latter association could be attributed to resorting to self-medication among patients with milder form of the disease.

The finding that study respondents with scanty/+1 sputum positivity grade had longer patient's period compared to those with higher sputum grades could be attributed to the probability that TB patients with lower sputum grade had milder illness and therefore delayed care-seeking in hope their illness would self-cure.

Health system factors

Distance to TBMU

More than 40% of the study population reported more than 30 minutes walking distance to the nearest TBMU despite FMoH had declared 100% DOTS coverage in 2002 at the two states. This discrepancy might be explained by the probability that TB patients sought health care far away from their place of residence in order to avoid social isolation and stigma attached to TB health care. A similar finding was found in Nigeria where urban TB patients sought medical care at rural settings to avoid TB stigma and social isolation associated with seeking TB care at urban health facilities.[62]

No significant association between walking distance to TBMU and the three periods in Khartoum although patients living within 15-30 minutes walking distance to TBMU did seem to have longer length of the three periods in Khartoum. On the other hand, 15-30 minutes walking distance to TBMU was significantly associated with shorter patient's period and longer health system's period in Gazeira. This finding could be explained by the probability that health providers faced difficulties in reaching TB diagnosis among TB patients who presented at early stages of the disease. Similar to Khartoum

finding, longer walking distance was reported to be associated with longer patient's periods in many countries in Africa and Asia.[48,53,55,59]

Type of health provider before TBMU

More than two-thirds of the study populations consulted a public health provider before visiting TBMU. No significant association was found between type of health provider and the three periods at both study settings. Interestingly, patients who consulted both public and private health providers and other health providers (NGO clinics and pharmacies) apparently experienced longer length of all three periods in Khartoum. Furthermore, consulting a private health provider before visiting TBMU was apparently associated with shorter patient's period and longer health system's period at both study settings. The latter association was consistent with reports from other countries in Africa, and Asia.[29,53,59,64] This association was attributed to lack expertise in TB diagnosis and treatment among private health providers and weak referral system between public and private health sectors.[53,57,74] On the other hand, referring TB patients might impose physical and financial barriers on TB patients and hence deterring them from prompt arrival at TBMUs. However, patient's non-compliance with early referral advice contributed to longer length of health system's period in Gazeira.

Worthy of note, longer length of pre-treatment period and health system's period was reported among TB patients visiting traditional healers in Botswana and Ghana.[57,64] Visiting traditional healers was associated with longer health system's periods in Malawi, Kenya, Tanzania, Ghana, Botswana, and Nepal and longer patient's periods in Gambia, Nepal, Ethiopia, and Tanzania. [26,30,54,56,57,59,60,63,74]

Investigation requested by other health providers (X-ray)

More than half of Khartoum's study respondents (55.3%) were requested to undertake X-ray examination by health providers compared to only 40.6% of Gazeira study's respondents. No significant association was found between type of investigation requested and the three periods in Khartoum although failure to request X-ray examination did seem to be associated with longer length of all three periods in Khartoum. On the other hand, failure to request X-ray examination by other health providers was significantly associated longer health system's period in Gazeira and it did seem to be associated with longer pre-treatment period as well. Requesting X-ray examination probably indicated suspicion of TB diagnosis and thereby, shorter length of health system' period among respondents who performed the test.

Limitations of the comparative study

1. The analysis was limited to univariate analysis and no multivariate analysis was performed. Therefore, it is not possible to identify the variables most strongly correlated with the length of the three periods or the variables that influenced other variables.
2. Due to insufficient data, the study was incapable of exploring levels of TB knowledge, stigma, impact of non-formal health providers (i.e. traditional healers) as well as perceived and actual quality of health services.
3. Our findings cannot be extrapolated to all rural and urban settings in Sudan since baseline data sets were limited to only two national settings.
4. Both national studies depend on patient's retrospective memory and therefore reliability of data collected was subjected to recall bias and socially desirable answers.[(ix)]

Chapter 5: Conclusions & Recommendations

Conclusions

The median length of the three periods at Khartoum urban setting was shorter than median length reported at Gazeira rural setting. These findings were in line with reports from other countries except Nigeria where longer length of the three periods was associated with urban residence rather than rural residence. In Sudan, the median length of pre-treatment period, and patient's period was similar to other countries. However, the median health system's period reported in Sudan was relatively longer compared to other countries.

Total median pre-treatment period was almost equally divided between patient's period and health system's period in Sudan. However, other studies reported longer length of patient's period compared to health system' period. A reciprocal relationship between patient's period and health system's period was demonstrated; the longer the patient's period was the shorter the health system's period would be. This interesting finding was attributed to the fact that TB is more readily diagnosed among patients presenting at more advanced stages of the disease.

[(ix)] Recall bias and socially acceptable answers in terms of time of onset of symptoms, patient's health-seeking behaviour; self-medication & stigma

However, Khartoum study tried to minimize recall bias by enrolling only patients who started their treatment within the last 5 weeks as well as employing complementary data collection technique to validate the data collected. Whereas, Gazeira study designed its data collection tool (questionnaire) in a way some questions validated each other. Both studies recruited well trained data collectors to maximize the validity of the data collected and avoid socially desirable answers.

In Gazeira, being divorced/widow, higher monthly income, and resorting to self-medication with traditional medication were significantly associated with longer pre-treatment period. This finding underscored the imperative need to interdisciplinary approach to address socioeconomic barriers to TB diagnosis and treatment.

On the other hand, being divorced/widow, higher monthly income, and resorting to self-medication with medical drugs were associated with longer pre-treatment period in Khartoum though the association was found to be statistically insignificant.

In Gazeira, middle age and lower grade of sputum smear were associated with longer patient's period. Shorter walking distance to TBMU, and higher educational level were significantly associated with shorter patient's period in Gazeira. Index of suspicion for TB among health providers needs to be refined towards all patients with presumptive active tuberculosis irrespective of patient's socioeconomic characteristics.

In Gazeira, female, being divorced/widow, higher educational level, higher monthly income, large family size, 15-30 minutes walking distance to TBMU and not requesting X-ray examination by health providers were significantly associated with longer health system's period. On the other hand, self-referral to TBMU was significantly associated with shorter health system's period in Khartoum. However, longer health system's period did seem to be associated with female sex, being divorced/widow, higher educational level, large family size, 15-30 minutes walking distance, and failure to request X-ray examination by health providers in Khartoum.

Delayed care-seeking behaviour was demonstrated among patients with milder form of tuberculosis (patients with lower grade of sputum smear) and patients resorting to self-medication. Higher level of TB knowledge and awareness about availability of specialized TB diagnostics reflected by patient's self-referral was generally associated with shorter length of pre-treatment period and health system's period. Reporting more than 30 minutes to reach TBMU among study respondents despite FMoH had declared 100% DOTS coverage in 2002 might be attributed to patient's preference to access health care at remote health facilities in order to avoid social stigmatization associated with TB healthcare. Those associations underscored the potential impact of public health educational programs on enhancement of early and appropriate care-seeking behaviour among patients with presumptive active TB through raising community awareness about TB symptoms, its curability, negative impact of self-medication, availability, and accessibility of free TB diagnostic and treatment services.

Refined index of suspicion among health providers reflected by requesting x-ray examination facilitated early TB diagnosis and shortened health system's

period. Whereas, consulting private health-care providers prior to visiting TBMU was generally associated with longer health system's period compared to public health-care providers. The latter finding highlighted the imperative need to strengthening ongoing collaborative activities between Sudan NTP and the private health sector in terms of early referral, accurate diagnosis and timely treatment of TB patients.

Recommendations

Based on the study findings, the Sudan NTP is recommended to:

1. Concentrate on addressing the factors that predispose to longer length of health system's period in Sudan on both settings, this could be achieved through disseminating and enforcing the application of the national TB management guidelines among all health providers as well as refining the index of suspicion for TB among health providers (public and private health providers) towards all patients with presumptive active TB irrespective of gender, education, and monthly income levels.
2. Strengthen public health education about TB symptoms, its curability, and raise community awareness about availability of free specialized TB services in order to reduce stigma attached to TB and enhance early and appropriate care-seeking behaviour among patients with presumptive active TB.
3. Advocate for interdisciplinary approach to effectively address the socioeconomic barriers to TB prevention and care.

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Annex 1: Khartoum Study's Questionnaire

Delay in the diagnosis and treatment of new smear-positive pulmonary tuberculosis in Khartoum State

Respondent number: ☐☐

Date of filling the questionnaire: ……/……/2003

1. Age: …….. Years
2. Sex: Male ☐ Female ☐
3. Educational level *(number of years in formal education):*
   < 3 years ☐ 3-6 years ☐ 6-12 years ☐ > 12 years ☐
4. Duration of residence in the district:
   < 1 year ☐ 1-3 years ☐ > 3 years ☐
5. Occupation: ……..
6. Family monthly income:
   < 260,000 LS ☐ 260-520,000 LS ☐ > 520,000 LS ☐
7. Number of persons sharing the same house with you:
   <3 persons ☐ 3-7 persons ☐ > 7persons ☐
8. Distance from home to this health centre (TBMU). *(walking in minutes)*
   < 15 ☐ 15-30 ☐ > 30 ☐
9. What are the first complaints that you had experienced, which you think were related to your current illness?

Cough	☐	Loss of weight	☐
Sputum production	☐	Chest pain	☐
Fever	☐	Haemoptysis	☐
Night sweat	☐	Tiredness/ fatigue	☐
Other symptoms (specify)	☐	……	

10. Which of these symptoms urged you to seek medical care? ……
11. Have you tried self-medications? Yes ☐ No ☐
12. If yes, what type of medications you had tried? ……..

13. Had you suspected having tuberculosis? Yes ☐ No ☐

14. Had you have any previous knowledge about TB? Yes ☐ No ☐

15. What was the time period between the onset of your symptoms and your 1st visit to a medical provider? ……weeks

16. If this period was more than 3 weeks, what do you think the reasons for such long period?
……

17. Before reaching your current TB centre, what type of medical providers you had consulted?

Private provider ☐ Public provider ☐ Pharmacist ☐ Others (specify) ☐

18. How many medical providers you had consulted? ……..

19. How many visits did you carry to those providers? ……

20. What investigations (if any) that were performed by those providers?

Sputum ☐ X-ray ☐ Others ☐

21. What was the diagnosis, if any? ……..

22. What Type of medications you received, if any? ……

23. If anti-TB drugs, had you started these medications? ……

24. How did you reach this TB centre?

Referred by my medical provider ☐ Advised by a relative or a friend ☐

Came on my own ☐ Others (specify) ☐

25. If been referred by a medical provider, how many days it took you to reach this TB centre? ……

26. If more than 2 days, what were the reasons behind this delay?
……

27. How long it took you to reach this TB centre from your very first visit to a medical provider? ……

28. Which of the following investigations was/were performed in this TB centre?

Sputum ☐ X-ray ☐ Others ☐

29. How long it took from your first presentation in this TB centre until they requested sputum examination? ……

30. How long it took from request of sputum examination until you got the sputum results?

.....

31. If the period between requesting sputum examination and result collection was more than 3 days, what did you think was the reason behind such long period?

.....

32. Date of performing sputum examination (from lab. Register book): .....

33. Grading of sputum (Lab. Register) scanty ☐ +1 ☐ +2 ☐ +3 ☐

34. Date of registration (from district register book): .....

35. Date of start of treatment (from patient treatment card): .....

32. If the period between collection of sputum result and initiation of treatment was more than one day, what do you think was the reason behind such delay?

.....

Annex 2: Gazeira Study's Questionnaire

Delay in the diagnosis and treatment of new smear positive pulmonary TB in Gaziera State.

Respondent number ……../…… Date of filling ……../……../2005

1. Age: ……..Years
2. Sex: Male ☐ Female ☐
3. Education level (number of formal education in years)

Less than 3 years ☐ 3-6 Years ☐ 6-12 Years ☐ More than 12 years ☐

1. Marital status

Single ☐ Married ☐ Widow ☐ Divorced ☐

2. Where do you live (name of city or village): ……
3. Occupation: ……..
4. Family monthly income:

< 260,000 LS ☐ 260,000-520,000LS ☐ > 520,000LS ☐

5. Number of rooms in your house: …….
6. Number of persons sharing the same house with you: ……..
7. Distance from home to this health facility walking by foot

<15 minutes ☐ 15-30 minutes ☐ > 30 minutes ☐

8. What was/were the first symptoms that you had experienced that was/were related to your current illness?

Cough ☐ Loss of weight ☐ Sputum production ☐
Chest pain ☐ Fever ☐ Night sweating ☐
Tiredness ☐ Haemoptysis ☐ Others ☐

9. When was that in days?

<14 days ☐ 15-41days ☐ More than 42 days ☐

10. If more than 42 days then specify in days or months ……
11. Have you tried self-medications?

Yes ☐ No ☐

12. If yes what type of medications you used? ……..
13. What was the time period between the appearance of your first symptoms and your first visit to medical provider? ……. Days.
14. What type of medical provider you first visited?

Private clinic ☐ Public health facility ☐
Pharmacist ☐ Others (specify) ☐ …….

15. If it was public health facility, what was the mode of payment:

Health insurance ☐ Free ☐ Full payment ☐

16. Before reaching this center how many health providers you had consulted?.....

17. What investigations (if any) were performed by those providers?

Chest X-Ray ☐ Blood ☐ Sputum ☐ Others ☐

18. If sputum was done what was the result?

Positive ☐ Negative ☐

19. What was the diagnosis, if any? ……..

20. What type of medications you received, if any? ……..

21. How did you reach this TB centre?

Referred by my medical provider ☐ Advised by a friend or relative ☐

Came on my own ☐ Other (specify)……. ☐

22. If referred by medical provider, how many days it took to reach this TB centre?..... days.

23. How long it took you to reach this TB centre from your very first visit to a medical provider? ……days.

24. Which of the following investigations was/were performed in this TB centre?

Sputum ☐ Chest X-ray ☐ Others ☐

25. How long it took from your first presentation in this TB centre until they requested sputum examination? ……Days.

26. How long it took from request of sputum examination until you got the sputum results? ……Days.

27. If the period between requesting sputum examination and result collection was more than 3days, what did you think was the reasons behind this? ……..

28. Date of the collection of the first sample of sputum examination (from the TB laboratory register book? Day ……../ Month …….

29. grading of sputum result (from LRB):

Scanty ☐ +1 ☐ +2 ☐ +3 ☐

30. Date of registration at the TB district register book: Day……/Month ……..

Date of start of treatment (from patient treatment card): Day……. / Month……

Annex 3:

Table 3: The relationship between dependent and independent variables in Khartoum

Variable		Pre-treatment Period				Patient period				Health system period			
		Khartoum				Khartoum				Khartoum			
		mean	SD	median	P	mean	SD	median	P	mean	SD	Median	p
Age group	<25	68.29	46.01	67.00	.441	31.56	29.06	30.00	.062	36.68	35.94	30.00	0.864 (KW)
	25-54	64.39	42.87	56.00		33.12	35.51	21.00		31.28	28.21	30.00	
	>54	78.12	45.63	76.00		52.53	44.83	60.00		25.59	15.00	17.00	
Sex	Male	64.33	44.00	53.50	.258	32.84	35.19	21.00	.541	31.47	31.35	26.00	.344
	Female	70.84	44.45	71.50		35.56	32.67	26.00		35.27	29.68	34.50	
Marital Status	Single	69.52	45.15	64.50	.332	34.85	33.10	30.00	.762	34.61	33.26	29.50	.429
	Married	63.46	43.05	56.00		32.62	34.48	21.00		30.86	28.13	30.00	
	Divorced/widow	81.78	48.90	68.00		39.89	46.39	7.00		41.89	36.35	38.00	
Educational level	Illiterate/<3 years	64.43	40.16	61.00	.602	35.92	34.68	30.00	.775	28.50	23.13	30.00	**0.416 (KW)**
	3-6 years	63.31	49.17	41.00		32.08	35.29	14.50		31.22	29.25	23.00	
	6-12 years	73.43	48.50	63.00		30.44	31.57	21.00		42.89	42.42	30.00	
	>12 years	68.70	47.16	67.50		33.18	36.46	30.00		35.58	33.30	28.00	
Occupation	idle	70.11	46.35	67.00	0.365 (KW)	36.38	34.43	21.00	**0.009 (KW)**	33.75	30.02	32.00	0.206 (KW)
	Students	76.52	46.04	88.00		33.93	28.14	37.50		42.52	40.34	28.00	
	Worker	67.67	46.13	57.00		37.94	40.50	30.00		29.68	27.79	26.00	
	Farmer	71.57	43.25	63.00		53.21	47.07	30.00		18.36	15.69	16.00	
	Employee	60.11	44.08	41.00		15.67	17.57	3.00		44.39	43.05	36.00	
	Small buisness	53.68	34.31	53.50		24.34	22.20	21.00		29.34	24.07	26.50	
Monthly Income	<100 USD	67.17	43.43	61.00	.497	34.49	33.75	21.00	.349	32.67	29.65	30.00	.939
	100-200 USD	58.85	53.16	40.00		25.42	38.24	8.50		33.31	41.45	17.00	
	>200 USD	76.25	37.14	81		40.58	33.92	30.00		35.83	24.95	30.00	
Housing Condition	<3	67.00	37.34	60.00	.857	43.48	37.24	30.00	.386	23.52	16.40	30.00	.313

Variable		Pre-treatment Period				Patient period				Health system period			
		Khartoum				Khartoum				Khartoum			
		mean	SD	median	P	mean	SD	median	P	mean	SD	Median	p
(number of family members	3-7 persons	64.90	43.36	61.00		32.18	32.97	21.00		32.69	28.37	30.00	
	>7	68.15	46.07	56.00		33.61	34.74	21.00		34.55	34.00	27.00	
Self-medication	No	64.41	45.35	60.00	.271	32.24	35.34	60.00	.327	32.19	31.75	30.00	.639
	Yes	70.76	42.07	60.00		36.62	32.26	30.00		34.08	29.04	29.00	
Type of self-medication	No self-medication	64.41	45.35	60.00	.259	32.24	35.34	21.00	.162	32.19	31.75	30.00	.895
	Traditional medication	66.00	37.29	59.00		31.69	26.45	30.00		34.20	27.03	30.00	
	Medical drugs	77.36	47.62	69.00		43.46	38.23	22.00		33.90	31.97	23.00	
Reasons for coming to TBMU	Self-referral	57.36	41.41	65.00	.171	31.39	33.40	21.50	.792	26.00	28.59	28.00	0.006 (KW)
	Relative/friend	73.73	50.49	62.50		32.58	30.96	25.50		41.15	40.79	30.50	
	Medical provider	68.76	43.87	58.00		34.85	35.11	21.00		33.88	29.39	29.50	
Sputum smear grading	Scanty/+1	67.60	44.69	56.00	.776	34.90	33.68	21.00	.845	32.65	30.07	24.00	.924
	Grade 2	62.41	35.72	62.00		31.75	29.54	30.00		30.61	26.86	27.00	
	Grade 3	63.08	41.82	57.50		31.66	34.59	21.00		31.47	23.92	31.50	
Walking distance to TB MU	<15 minutes	67.71	45.26	59.50	.546	36.75	35.52	21.00	.326	30.93	33.48	26.50	.864
	15-30 minutes	72.52	44.78	61.00		38.73	37.42	30.00		33.83	29.80	35.00	
	>30 minutes	64.55	43.73	57.00		31.23	32.65	21.00		33.29	30.15	29.00	
Type of health provider before TBMU	Private	66.24	36.32	62.00	.545	28.34	31.22	21.00	.600	37.95	29.42	31.00	.236
	Public	69.67	44.84	58.00		35.61	34.65	30.00		34.02	29.58	28.00	
	Other (pharmacy or NGO clinic)	84.82	51.75	57.50		38.55	32.57	21.00		46.27	35.25	41.50	
	Both private and public	77.71	49.73	47.00		30.86	31.36	21.00		46.81	44.34	28.50	
Investigation requested by other health providers	X-ray examination not requested	73.55	46.98	61.00	.372	35.03	35.43	21.00	.664	38.56	30.94	29.00	.419
	X-ray examination requested	68.16	41.74	52.00		33.03	32.07	21.00		35.06	32.17	30.00	

* p <0.05; KW: Kruskal Wallis Test; and M-W: Mann-Whitney U Test

** Independent-samples t-test was applied to measure the mean difference of the three periods at each study setting whereas ANOVA test was applied to measure the mean difference of the three periods in relation to the remaining independent variables at each study setting

Annex 4:

Table 4: The relationship between dependent and independent variables in Gazeira

Variable		Pre-treatment Period Gazeira				Patient period Gazeira				Health system period Gazeira			
		mean	SD	median	P	mean	SD	median	P	mean	SD	median	p
Age group	<25	67.67	26.17	64.00	.122	32.63	21.56	25.50	**.035**	35.04	26.81	30.50	.786
	25-54	72.30	28.19	74.00		**39.67**	**23.69**	32.00		32.63	24.98	29.00	
	>54	61.13	30.08	51.50		29.57	21.17	21.00		31.57	18.18	29.50	
Sex	Male	67.93	27.65	65.00	.235	38.11	24.15	30.00	.209	29.82	24.71	27.00	**.010**
	Female	72.66	28.90	69.00		34.00	21.15	30.00		**38.66**	**23.34**	34.00	
Marital Status	Single	72.00	30.85	78.00	**0.005 (KW)**	39.98	27.97	35.00	0.529 (KW)	32.02	26.59	28.00	**.002**
	Married	65.94	24.37	62.00		34.66	19.58	30.00		31.28	22.04	29.00	
	Divorced/widow	95.14	36.47	90.00		39.93	29.66	30.00		55.21	28.72	65.00	
Educational level	Illiterate/<3 years	68.98	29.41	66.00	.644	36.76	19.31	30.00	**<0.001 (KW)**	32.22	23.90	29.00	**0.034 (KW)**
	3-6 years	73.94	27.75	76.00		39.82	28.38	30.00		34.12	22.15	32.00	
	6-12 years	67.27	22.96	64.00		42.71	20.49	40.00		24.56	12.01	25.00	
	>12 years	67.46	32.14	60.00		18.71	22.18	3.00		48.75	38.20	43.00	
Occupation	idle	73.45	26.78	69.00	.170	34.76	19.93	30.00	0.116 (KW)	38.68	23.82	35.00	0.129 (KW)
	Students	62.00	27.90	60.00		26.00	18.75	20.00		36.00	33.43	39.00	
	Worker	68.56	27.81	65.00		38.58	21.72	32.00		29.98	24.30	24.00	
	Farmer	65.94	27.39	58.00		34.72	22.33	30.00		31.22	17.57	30.00	
	Employee	73.00	32.18	89.00		49.13	29.85	60.00		23.88	7.38	23.00	
	Small buisness	70.18	34.15	80.00		44.59	34.05	30.00		25.59	30.55	17.00	
Monthly Income	<100 USD	65.42	27.46	63.00	**.002**	38.13	24.01	30.00	.179	27.29	18.30	26.00	**<0.001 (KW)**
	100-200 USD	77.78	27.83	81.00		33.68	21.19	30.00		44.11	30.62	36.50	
Housing Condition (number of family members	<3	62.46	35.35	64.00	.391	43.62	26.50	47.50	0.576 (KW)	18.85	18.93	16.50	**0.016 (KW)**
	3-7 persons	71.90	29.42	76.00		35.63	19.77	30.00		36.27	27.43	32.00	

Variable		Pre-treatment Period				Patient period				Health system period			
		Gazeira				Gazeira				Gazeira			
		mean	SD	median	P	mean	SD	median	P	mean	SD	median	p
	>7	67.97	25.38	58.50		36.79	26.28	30.00		31.17	20.51	29.00	
Self-medication	**No**	69.09	27.11	68.00	.676	35.27	23.67	30.00	.231	33.82	25.66	29.00	.516
	Yes	70.79	30.27	66.00		39.28	21.93	45.00		31.51	22.21	30.00	
Type of self-medication	**No self-medication**	69.09	27.11	68.00	**.003**	35.27	23.67	30.00	.104	33.82	25.66	29.00	.073
	Traditional medication	86.04	27.93	83.50		45.84	22.97	55.00		40.20	23.34	39.50	
	Medical drugs	62.68	28.52	57.00		35.79	20.76	30.00		26.89	20.35	26.00	
Reasons for coming to TBMU	**Self-referral**	68.19	32.05	58.00	.932	40.79	21.57	32.00	.082	27.40	20.21	25.50	0.191 (KW)
	Relative/friend	70.11	29.66	74.00		30.14	21.98	15.00		39.98	33.67	43.00	
	Medical provider	69.98	26.45	66.00		37.45	23.71	30.00		32.53	21.65	29.00	
Sputum smear grading	**Scanty/+1**	74.07	26.53	74.00	.193	45.04	25.75	35.00	**0.002 (KW)**	29.03	19.64	26.00	0.134 (KW)
	Grade 2	65.78	27.87	69.00		33.68	21.90	30.00		32.10	24.86	28.00	
	Grade 3	69.41	29.92	66.00		30.59	18.55	30.00		38.81	28.20	33.50	
Walking distance to TB MU	**<15 minutes**	71.35	30.71	65.00	.828	37.51	22.09	30.00	**.045**	33.85	24.80	28.00	**.036**
	15-30 minutes	69.57	27.70	69.00		29.94	20.79	26.00		39.62	30.49	34.00	
	>30 minutes	68.58	26.81	67.00		39.61	24.46	30.00		28.97	19.73	25.00	
Type of health provider before TBMU	**Private**	70.46	31.38	68.50	.877	31.19	20.76	30.00	.204	39.27	29.46	43.00	0.338 (KW)
	Public	69.55	27.76	67.00		37.35	23.39	30.00		32.20	23.75	29.00	
Investigation requested by other health providers	**X-ray examination not requested**	73.90	27.55	69.00	.373	31.93	19.70	30.00	**0.051 (M-W)**	41.97	24.30	33.00	**<0.001**
	X-ray examination requested	69.90	30.33	65.00		41.91	28.52	32.00		27.99	24.06	20.00	

* p <0.05; KW: Kruskal Wallis Test; and M-W: Mann-Whitney U Test** Independent-samples t-test was applied to measure the mean difference of the three periods at each study setting whereas ANOVA test was applied to measure the mean difference of the three periods in relation to the remaining independent variables at each study setting