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Prevalence and Outcomes of Tuberculosis Treatment in a Primary Care Center in Karachi, Pakistan

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Abstract

Background: Tuberculosis (TB) still remains a major health issue in Pakistan, despite the introduction of directly observed treatment short course strategy (DOTS) by World Health Organization (WHO) in 1995. Major progress towards the disease control, however is achieved after the revival of national tuberculosis control (NTP) program in 2001. Between 2002 and 2007, DOTS coverage increased from 44% to 99%, but there are still large and persistent gaps in detection and treatment. We conducted this study, to see prevalence and treatment outcome among TB patients who completed treatment under DOTS strategy over 15 years.

Primary endpoint: To determine treatment outcome of all types of TB from 2004 till 2018 in a primary health center (PHC) in Karachi.

Secondary endpoint: To determine the prevalence, predominant site, and number of new versus retreatment cases of TB.

Methods: It is a cross-sectional descriptive study, conducted at a PHC, affiliated with Family medicine department of Ziauddin University Hospital, Clifton, Karachi. This Center also functions as Basic Management Unit (BMU) for tuberculosis control under DOTS strategy since 2004, in collaboration with NTP, Pakistan. Data was collected from January 1st 2004 till December 31st 2018. Among all subjects who visited the center, those who had cough for more than 2 weeks, were screened for pulmonary tuberculosis (PTB). Extrapulmonary Tuberculosis (EPTB) was diagnosed on relevant investigations. After treatment completion, their outcome was analyzed.

Results: Out of 41615 patients who visited PHC center, 454 patients (1.1%) had TB. 74.7% subjects were diagnosed having PTB while 25.3% had EPTB. 81% subjects completed TB treatment, 1.32% failed to respond to the treatment, 1.1% subjects died during the course of the disease, 15% were lost to follow up and 1.32% moved to another facility. 94.9% (431) subjects were new patients, while 5% (23) were retreatment patients. 88% subjects of PTB were Sputum Smear Positive (SSP) and 12% had Sputum Smear Negative (SSN) PTB.

Conclusion: In conclusion, this study documented the prevalence of TB in a slum community of 100,000 inhabitants, who visited the PHC in their locality. Standard DOTS guidelines were used for screening, diagnosis and treatment of the subjects. Strengthening screening methods and diagnostic procedures, will bring about more confirmed cases of TB and under reporting will be reduced. Strict surveillance of subjects on treatment will improve treatment outcome, and will decrease future development of multi drug resistant TB (MDR TB).

Keywords: MDR TB; XDR TB; Gene x-pert

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Introduction

Pakistan is located in south Asia, bordered by India to the east, Afghanistan to the west, Iran to the Southwest, and China in the far northeast. It's a federation that comprises four provinces: Punjab, Khyber Pakhtunkhwa, Sindh and Baluchistan. Pakistan falls in the Low-and Middle Income Countries (LMIC), GDP per capita of $1,516 and worlds 6th most populous country (207 million populations according to 2017 census). Factors like poverty, malnutrition, poor housing and sanitation, inadequate health care facilities, population migration and urbanization, political instability and refugee crisis are key challenges in health care in the country.

Tuberculosis (TB) is one of the major public health problems in Pakistan, with the country ranking 5th among 30 high burden countries worldwide. According to WHO global TB report 2018, the incidence of TB in the general population is 267 per 100,000 populations in the country.

Pakistan's battle with TB continues, as it annually contributes 5 to 10 million new cases of TB worldwide [1]. Although the Government's incentives and logistical efforts in providing free treatment and diagnostics for TB cannot be underestimated, still curbing, the disease is far from eradication as it has emerged with new challenges of MDR and XDR TB. Till date there has been around 300 000 MDR-TB cases reported globally in 2012 with Pakistan being the 5th highest contributor to these [2]. Although the percentage of cured cases following treatment is always higher, the increased mortality and morbidity due to TB can equally be attributed to the failure of treatment and re-infection.

Studies conducted in neighboring countries of Pakistan, like China found treatment failure cases to be 29.4%, [3] whereas Iran had around 7% along with 5.5% of Relapse cases [4]. While India had a failure rate of 6% but 17% of the outcome of TB cases was on account of mortality due to the disease [5]. However, distant countries like Ethiopia reported only 1.2% of treatment failure rate [6]. Whereas Australia, having a very low burden of this disease, reported 7% deaths due to TB in 15 years but no treatment failure or relapses [7]. Data of 31 countries reviewed in Europe documented treatment Failure of 0.6% only and deaths by Tuberculosis to be 7.8% [8].

Our study aims to highlight the prevalence and epidemiology of TB so that we can track its outcome and inspire future research to help identify the determinants needed to control the disease and limit its spread and treatment failure.

Research Methodology

It is a cross-sectional descriptive study, conducted at a PHC, affiliated with Family medicine department of Ziauddin university hospital, Clifton Karachi. This Center also functions as Basic Management Unit (BMU) for tuberculosis control under DOTS strategy since 2004, in collaboration with NTP, Pakistan. Data was collected from January 1st 2004 till December 31st 2018. Among all subjects (men, women, and children) who visited the center, those who had cough for more than 2 weeks, were screened for Pulmonary Tuberculosis (PTB). Extrapulmonary Tuberculosis (EPTB) was diagnosed on relevant investigations. After treatment completion, their outcome was analyzed.

Those who had cough for more than 2 weeks and could produce phlegm, their sputum was tested for Acid Fast Bacilli (AFB) by microscopy or Gene X-pert. Hence they were divided into pulmonary smear positive or pulmonary smear negative TB. Subjects who were smear negative but had signs and symptoms suggestive of pulmonary TB such as chest pain, fever, weight loss, reduced appetite, weakness or fatigue, along with history of close TB contact were subjected to Chest X-ray (clinically diagnosed patients). Extrapulmonary TB involving lymph nodes, pleura, spine, CNS, and abdomen were diagnosed by bacteriology/histology of aspirated/biopsied specimen, CT/MRI scan. Patient's type was decided as "new case" (those who were never treated for TB in the past or had taken treatment for less than one month), or as a" retreatment cases" (those who had received one month or more of TB treatment in the past). Treatment regimens followed the Pakistan National TB Control program (NTP) treatment guidelines, as recommended by WHO. Treatment of new smear-positive/ smear negative pulmonary patients, consisted of initial intensive phase of 2 months of weight based, combination therapy (HRZE) containing Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E), followed by 4/6 months of HR in continuation phase once a day. Retreatment patients received 60 doses of streptomycin (S) along with 3 months of HRZE in the initial intensive phase, followed by continuation phase for 5/6 months of HRE, daily. Treatment facilitators directly observed drug administration during initial intensive phase in new patients and throughout the treatment in case of retreatment patients.

Treatment outcomes were assessed using WHO definitions, and were recorded in TB03 register. "Treatment success" is defined as either cure or treatment completed. "Cure" is defined as a patient who is registered as smear positive, has completed the duration of treatment, and becomes sputum smear negative at the end of the treatment and on at least one of previous occasion. "Treatment completed" is defined as smear negative or extra pulmonary cases completed duration of treatment successfully. "Failure" is defined as sputum smear-positive patient who remains or becomes smear positive at 5 months or later during treatment." Death" is defined as a patient who dies for any reason during the course of TB treatment." Lost to follow up" is defined as a case whose treatment was interrupted for two consecutive months or more after last medicine intake. "Not evaluated" is defined as cases for which no treatment outcome is assigned (includes" Transfer out "to another treatment unit and their treatment outcome is unknown). We analyzed TB treatment outcome data by using Statistical Package for the Social sciences (SPSS) version 20.

Results and Discussion

Out of 41615 patients who came to primary care center from Jan 1 2004 till December 31st 2018, 454 patients (1.1%) had Tuberculosis. Majority TB patients were females 245 (54%) while the rest 209 (46%) were males. Out of all Tuberculosis patients, 74.7% (339) subjects had pulmonary TB while 25.3% (115) had

Extrapulmonary TB. 94.9% (431) subjects were new patients while 5% (23) were retreatment patients **(Figure 1).**

Figure 2 refers to the treatment outcome of TB patients. As far as outcome is concerned, 81% (368 out of 454) subjects completed the Anti-Tubercular Treatment (ATT), 1.32% (6 out of 454) subjects had treatment failure, while 1.1% (5) subjects died during the course of the disease. 15% (69) patients were lost to follow up and 1.32% (6) moved to another facility so their outcome could not be documented.

Figure 3 refers to the status of sputum smears. 88% (227 out of 258) pulmonary TB patients were sputum smear positive. The rest 12% (31) were diagnosed as sputum smear negative patients.

Pakistan continues to face threat to its economy and the health of its population at the hands of TB. The closest to accurate incidence of the registered cases of Tuberculosis in Pakistan was reported to be around 497 per 100,000 populations in 2012 [9]; which is expected to have increased by now. This study aimed to contribute to similar studies conducted in different districts of Pakistan by highlighting the prevalence of TB and the outcome of its treatment.

Our study focused on the disease outcome. Many studies such as Fatima et al. compared initial loss to follow up in tertiary care setting with rural health care setting. Their study showed that rural care setting had less (2%) 10 patients with initial loss to follow up as compared to (10%) 86 patients in tertiary care setting [10].

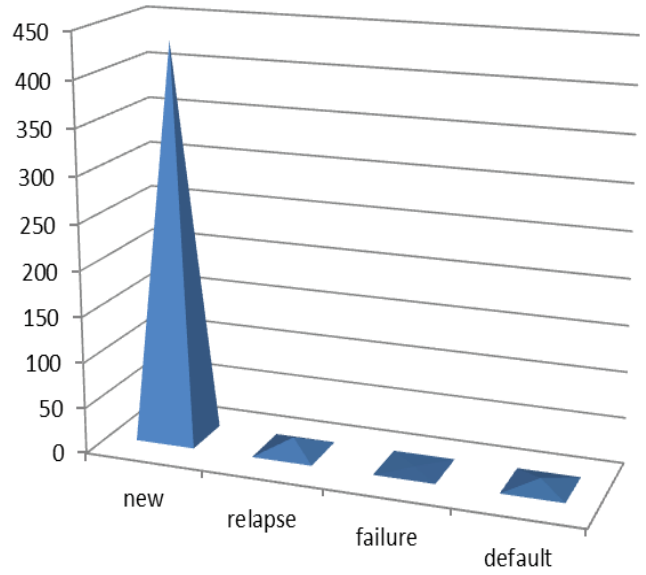

Figure 1 Number of new and retreatment cases of tuberculosis; retreatment categorized into relapses, failures and defaulters.

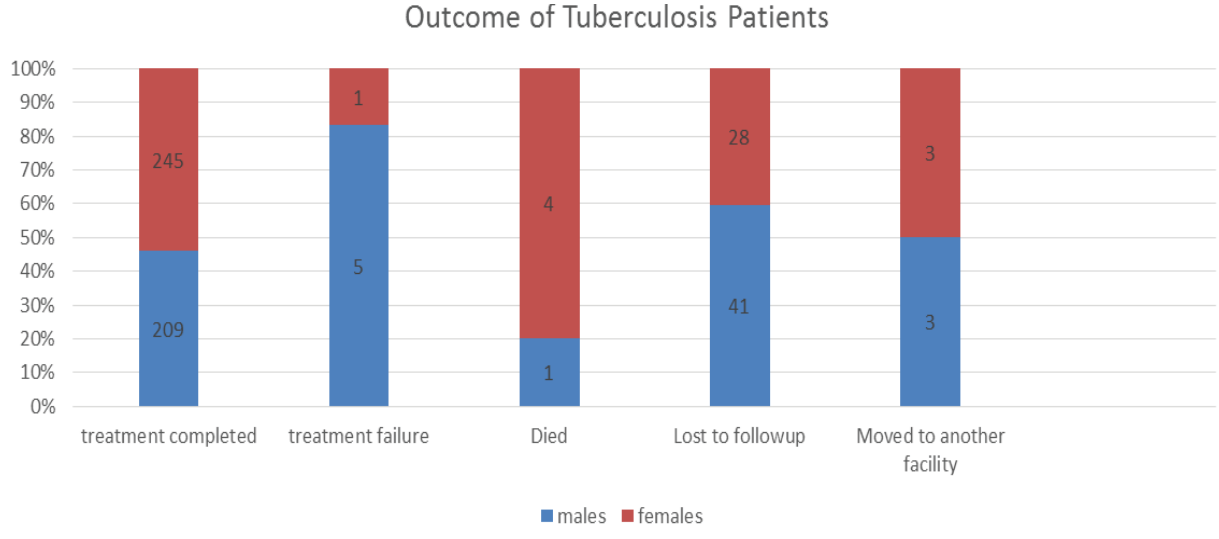

Figure 2 Proportion of outcome of tuberculosis patients.

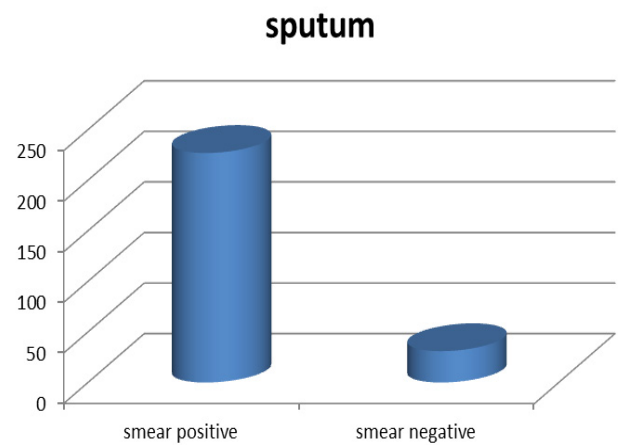

Figure 3 Number of pulmonary tuberculosis diagnosed as sputum smear positive or negative cases.

However, our study entirely focused on a PHC setting. In another study, treatment outcomes differed; 192 (39.0%) were cured, 276 (56.0%) had their treatment completed, 9 (1.8%) had died, 1 (0.2%) had treatment failure, 13 (2.6%) had a loss to follow up, and 1 (0.2%) transferred out [11]. Similarly, a study from Ethiopia demonstrated treatment outcome of TB patients; 376 (30.4%) of them had been cured, 767 (62.1%) had completed their treatment, 48 (3.9%) had died, 30 (2.4%) were defaulted, and the remaining 15 (1.2%) had failed the treatment [6]. Another study from Ethiopia showed that those TB patients evaluated for treatment outcome; 952 (60.1%) of them had successful treatment outcome and 632 (39.9%) of them had unsuccessful treatment outcome. Of the patients with unsuccessful treatment outcome, 281 (17.7%) had died, 13 (0.8%) had treatment failure, and 338 (21.3%) were lost to follow-up [12]. A study from Thailand assessing TB among healthcare workers showed treatment outcomes; 44.7% of patients were cured, and 55.3% of patients completed treatment and none of the patients relapsed. 13.2% patients had developed adverse drug reactions. The survival status for long-term follow-up was 1.3% with smear-positive Pulmonary TB who died 1 year after the end of treatment from the primary disease [13]. Our study showed that 81% (368 out of 454) subjects completed the treatment, 1.32% (6 out of 454) subjects had treatment failure, while 1.1% (5) subjects died during the course of the disease, 15% (69) were lost to follow up and 1.32% (6) moved to another facility. We can see a general trend that many patients actually complete their treatment and only a few have treatment failures, or die or are lost to follow up. Those with loss to follow up are at a higher risk for increased morbidity and mortality and pose potential threats to the community as well [14].

After reviewing all the data from 2004 to 2018, the current study was able to record a total of 454 cases of TB from the entire pool of patients. Similar to our study, a research conducted at Shangla identified 493 total TB cases [15], however, it was at a 150 bed DHQ Hospital whereas our study focused on a single PHC in Karachi which is most frequently visited by people from its own colony. Alternatively, a retrospective study in Mansehra, only took into account data of over one year, from 1st January to 31st December 2013 and included a total of 625 patients under TB treatment [16]. Likewise, another retrospective study conducted in Bahawalpur in 2014 included 690 TB cases [11]. Conversely a study featured on a larger scale that extracted data from 12 random districts of Pakistan had its data collected through the NTP- TB Register, non-NTP public health facilities, private health facilities and private laboratory facilities which identified a total of 8346 cases of TB [9]. Additionally another study that took place in three tertiary hospitals in Quetta documented 1110 TB patients after smear testing [17]. Amongst the neighboring countries of Pakistan, China had reported around 472,596 TB cases between 1992 to 2015, from Chongqing [18] whereas a total of 224,480 cases were recorded in 6 cities of Shandong between 2005 to 2017 [19]. Comparatively, in India, 409 cases were reviewed between May 2014-June 2016 from Puducherry and Tamil Nadu [20] and 510 TB patients were included for analysis from central India in 2014 [21], which is similar to our own data. Subsequently, WHO reported 16 000 TB cases in Iraq and 12,000 TB cases in Iran in the year of 2017 [22]. However these numbers showed the prevalence of the disease in the whole country rather than focusing on specific regions. While Saudi Arabia alone had 32,435 registered TB cases between 2005 and 2012, most of them were non-Saudi [23]. Moreover of the 10.0 million new cases of TB reported annually [1] majority were contributed by these countries including Pakistan.

Significantly, although not known why, the disease has shown a predilection towards the female gender in most studies in Pakistan where they make up more than 50% of the total subjects just like in our study regardless of the place where they were conducted. Namely Manshera and Quetta alone recorded 57% females [16] and 58% females [17] respectively, who had TB. However, there was some variation between the prevalence of two districts within the same city of Khyber-Pakhtunkhwa specifically in Dir Lower Valley and Shangla. Dir Lower Valley having 49.5% males and 50.5% females [24] and Shangla having 52.5% males and 47.5% females [15]. Similarly, Bhawalpur also highlighted a male predominant pattern; 51.7% males and 48.3% Females [11] However China showed a consistent male majority amongst its TB cases with 70.82% males in Shandong [19] 60.3% in Northwest China [25] 71.3% in Chongqing [18] and around 71.6% of the total cases being males in a study conducted at a provincial level in almost 21 provinces of China [26] Likewise, India also had 75.1% male TB cases in a study conducted in Puducherry and Tamil Nadu [20] and 62.9% males in another study conducted in central India [21]. Similarly Saudi Arabia also had higher incidence for males than for females from 2009 to 2012 [23]. This entirely contrasts with our results. However, there is no literature as to why the disease is more common in one gender and how it is influenced by geographical variation in different areas of Pakistan.

TB could also present with extra pulmonary manifestations leading to systemic diseases. The study by Jacob et al. demonstrated EPTB among 223 individuals out of 857 who had been identified positive by sputum smear test [27]. Very similarly, a study regarding prevalence of TB in Kotli, Azad Kashmir showed less extrapulmonary (23%) patients in comparison with pulmonary

TB patients (76.99%) [28]. Ahmad et al. [15] briefly state that only 22.7% of patients had extrapulmonary tuberculosis. A Nepalese comparison study showed 48.5% patients had extrapulmonary TB and 51.5% had Pulmonary TB. Only 16.4% of pulmonary TB patients had hilar lymph node enlargement and/or pleural pathology (unilateral or bilateral). 16.5% of total extra pulmonary patients had concurrent PTB [29]. In addition, a study in Cameroon showed the prevalence of bacteriologically confirmed EPTB as 41.3%. The affected sites were the lymph nodes (68.9%) and the pleural cavity (15.6%) [30]. Similarly a study in Ghana, showed 21.8% patients had EPTB while 78.2% patients had PTB. 32.8% of the EPTB patients had disseminated TB, while 18.4% had their pleura affected. 2.9% of EPTB cases had various sites affected including pericardial, genitourinary, skin, and breast disease [31]. Similarly, our study had less patients with EPTB as compared to PTB as that is more commonly seen.

Taking all the registered TB cases into account, most have been newly diagnosed cases in all the studies conducted in Pakistan. Manshera reported 85.4% of its 534 TB patients as new cases [16]. Similar results were observed in Bhawalpur where a total of 611 (88.6%) out of 690 cases were classified under new cases [11]. Likewise 93.5% of the 493 cases in Shangla were new [15]. The same trends can be seen in the neighboring countries of Pakistan as well, with China having 205,716 (91.64%) new cases out of the total 224,480 cases in one study [19]. Our study also reciprocated these results markedly closely reporting 94.9% (431) of the subjects as new patients out of the total 454 cases of TB. Whereas India had 395 (77%) Category I (New) cases out of the total 510 [21]. However, the pattern in our study can be explained by the number and type of risk factors that influence the spread of TB and its outcome and have stayed constant throughout Pakistan with slight regional variations only. Much research has been conducted on identification of these risk factors whereas poor control of the spread of the disease, compliance of the patient and awareness of the disease can be seen as potential areas for improvement in the future.

An important parameter to identify TB is through sputum smear testing. Many studies, like ours, had performed sputum smear testing and identified the causative bacteria. Ejaz et al. demonstrated 233 smear-positive TB cases. Of these 161 were positive on culture. They also had 108 smear-negative definite TB cases and 88 of these had ≥ 5 colonies on culture [32]. Another study, regarding detection of tuberculosis in high risk groups of Pakistan (2014), showed that 7747 patients visiting general practitioners were screened and 1410 (18.2%) came out smear-positive. In contrast to our study, their study focused on TB detection in general camps as well, which allowed them to detect the disease before symptoms appeared [33]. Jacob et al. also performed smear testing to identify TB patients. 1010 (9.1%) were smear positive and 634 were identified smear negative [27]. A study in Western China for pulmonary tuberculosis showed that 78.4% patients who had two sputum smears examined turned out to be smear negative as well as culture negative. In addition, 6.4% were bacteriologically confirmed cases and of them 49.5% were smear positive cases and 93.1% were culture positive cases [34]. A relatively similar but interesting study conducted in Central Jail Bangladesh regarding prevalence of tuberculosis showed 77% of inmates had positive smear microscopy results and 23% cases were negative for smear microscopy but positive for culture [35]. These studies are similar to ours, as the majority (227) of the patients in our setup was sputum smear positive as compared to 31 patients who came out negative. Smear testing is integral to identification. However, it should be noted that some cases may come out smear negative as the test is less sensitive. Therefore, other quick methods like Gene x-pert should be available on site in order to get a definitive diagnosis.

Limitation

A major limitation to our study was that the sample should have been diverse to represent the whole community. Our focus was only on patients who presented at the PHC and their routinely recorded data was used to represent the prevalence of tuberculosis.

Conclusion

In conclusion, this study documented the prevalence of TB in a PHC using common methods to detect the disease. Strengthening the surveillance and diagnostic methods will bring about confirmed cases of TB and underreporting will be reduced.

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