Status of Tuberculosis Burden in War Affected Province, Khyber Pakhtunkhwa, Pakistan: Analysis of Quaterly Reported Cases

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Abstract: The present study was aimed to ascertain Tuberculosis (TB) morbidity in hospital patients of Khyber Pakhtunkhwa (KP), Pakistan. Record of 6549 suspects including 2318 (2241 new cases and 77 previously treated cases) confirmed positive patients was recovered from multiple hospitals of KP. Retrieved data was analyzed for various demographic parameters and TB types. Results indicated overall morbidity of 34.21% (2241/6549). Gender wise, 46.98% (1053) were males while 53.01% (1188) were females (P < 0.0001). Age wise, age group ≥15 was highly affected with 75.94% (1702) infection morbidity followed by age group 4-15 with 16.64% (373) and age group 0-4 with 7.40% (166) (P < 0.0001). On the basis of TB type, highest numbers comprised of pulmonary sputum smear positive cases with 36.09% (809) followed by extra-pulmonary Tuberculosis (EPTB) cases with 33.28% (746) and pulmonary sputum smear negative cases with 30.61% (686) (P < 0.0001). Among the previously treated cases (77), 77.92% (60) were relapse cases, 12.98% (10) were treatment failure cases while 9.09% (7) were treatment default cases. Conclusively, high number of TB cases were identified. The elevated TB morbidity in KP emphasize the need of improvement in the current TB management policy for effective eradication of the infection.
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1. Introduction

Tuberculosis (TB) is ranked the second major infectious disease [1] with high morbidity and mortality. Globally, the estimated morbidity in 2012 is 8.6 million while the annual death toll is 1.3 million [2]. Pakistan is one of the five countries which contribute enormous TB share to the overall TB burden [3]. Countrywide, the annual morbidity of TB is approximately 231 new cases in a population of 100000 [2].

The causative agent of TB is Mycobacterium Tuberculosis (MTB). It is an airborne non-motile acid fast facultative bacterium that mostly localize macrophages [4]. Pulmonary Tuberculosis (PTB) is the most common type of TB that affects the lungs. Extra-pulmonary Tuberculosis (EPTB) includes all forms of TB other than PTB [5]. EPTB is known to affect the lymph nodes, pleura, bones and joints, the genitourinary system and soft tissues. Of the total TB morbidity, approximately 47% cases in the country are attributed to PTB [3].

After disappearing from world public health agenda in the 1960s and 1970s, TB re-emerged as a serious health concern in the early 1990s [6]. The return of TB was escalated by various associated factors, including Human Immune Deficiency Virus (HIV) pandemic [6]. In the mid 1990s, Directly Observed Treatment Short-course (DOTS) strategy was introduced by World Health Organization (WHO) which was aimed to monitor and document TB cases [7]. However, due to limited coverage and implementation problems in several countries, the program could not be successfully expanded to the underdeveloped countries in its early years [8, 9]. Also, the emergence of multi drug resistant MTB (MDR-MTB) strains which exhibit resistance against the potent anti-TB drugs rifampicin and isonizid resulted in treatment inefficacy, relapse and mortality that posed serious complications in TB control [10, 11]. The extensively drug resistant TB (XDR-TB) that confer resistance to rifampicin, isonizid and second-line drugs used in TB treatment [12] further worsen the situation. Currently, XDR-TB is a serious health threat as its treatment is extremely complicated and the mortality rate in susceptible individuals such as HIV carriers is very high [13]. The annual world wide occurrence of resistant forms is estimated to be about 440,000 MDR-TB cases and 50,000 XDR-TB cases

[14, 15]. Pakistan is ahead of all the Eastern Mediterranean Region countries with an annual 9000 MDR-TB cases [16].

Khyber Pakhtunkhwa (KP) province lies in the northern part of Pakistan. This province has been greatly affected by the war against insurgency and natural calamities in the past few years. Studies on TB distribution from this area have been reported very limitedly. Therefore, the current study was planned to determine the latest status of TB morbidity for assessment of disease burden in this region.

2. Material and Methods
Plan of study

Various TB centers located in multiple districts of KP, Pakistan were visited during August 2015 to September 2015. TB patients record was retrieved after proper permission of hospitals administration. A total of 6549 TB suspects record was retrieved that consisted of 2318 confirmed TB positive patients, diagnosed either bacteriologically or clinically [17]. Of them, 2241 patients were identified as new TB cases while 77 patients were treated previously. To get the actual morbidity number, previously treated patients were excluded in determination of the total infection percent. The collected data was carefully arranged according to the time of retrieval into two quarters i.e quarter I and quarter II. Further, patients

record was classified into categories and analyzed for various parameters such as gender, age and type of TB.

Statistical analysis

For statitical analysis, Pearson Chi-square test was applied at 0.05 level of significance to ascertain the association of gender, age and TB type with the infection morbidity.

3. Results

Of the total suspects (6549), 34.21% (2241) were positive for TB infection. Gender wise, 46.98% (1053) were males while 53.01% (1188) were females (P < 0.0001). Age wise, age group ≥15 was found highly affected with 75.94% (1702) infected individuals followed by age group 4-15 with 16.64% (373) and age group 0-4 with 7.40% (166) (P < 0.0001). On the basis of TB type, greater cases comprised of pulmonary sputum smear positive cases with 36.09% (809) followed by EPTB cases with 33.28% (746) (P < 0.0001). The share of pulmonary sputum smear negative cases was 30.61% (686). Infection rate was partially higher in quarter II (37.36%) as compared to quarter I (31.05%). Among the previously treated cases (77), 77.92% (60) were relapse cases, 12.98% (10) were treatment failure cases while 9.09% (7) were treatment default cases.

Table 1. New TB cases reported in quarter I

TB Type	Age group (years)	Male	Female	Total
Pulmonary Sputum Smear Positive	0-4	0	1	1
	5-14	6	19	25
	≥ 15	159	200	359
Pulmonary Sputum Smear Negative	0-4	16	13	29
	5-14	27	32	59
	≥ 15	107	118	225
Extra Pulmonary	0-4	17	15	32
	5-14	33	34	67
	≥ 15	107	110	217
Overall		472	542	1014

Table 2. New TB cases reported in quarter II

TB Type	Age group (years)	Male	Female	Total
Pulmonary Sputum Smear Positive	0-4	2	1	3
	5-14	9	20	29
	≥15	179	213	392
Pulmonary Sputum Smear Negative	0-4	26	19	45
	5-14	40	45	85
	≥ 15	115	128	243
Extra Pulmonary	0-4	30	26	56
	5-14	53	55	108
	≥ 15	127	139	266
Overall		581	646	1227

Table 3. Previoulsy treated TB cases reported in quarter I

Type	Relapse	After Failure	After Default	Total
Pulmonary	27	3	2	32
Extra Pulmonay	1	1	1	3
Overall	28	4	3	35

Table 4. Previously treated TB cases reported in quarter II

Type	Relapse	After Failure	After Default	Total
Pulmonary	31	4	2	37
Extra Pulmonary	1	2	2	5
Overall	32	6	4	42

4. Discussion

TB is a major infectious disease in Pakistan that accounts for 5.1% of total national disease burden [3]. In Pakistan, the WHO recommended DOTS strategy was adopted by National TB Control Program (NTP) in 1995 [18]. In the year 2001, as a result of NTP revival, TB emergency was declared in the country [19]. Since then, strategies have been devised for the control of TB and the infection is a top priority of the national health policy.

In the current study, high infection rate (34.21%) was identified. This result is in line with the previous studies reporting high TB morbidity [20-22]. In developing countries where the living standard of most people is low, many individuals may ignore the symptoms of cough and fever, resulting in diagnosis delay that contribute to greater TB cases [23]. A recent study [24] revealed a delay (duration between on-set of cought and final diagnosis followed by start of treatment) of 8 weeks in the infected individuals. Similarly, as Pakistan is one of the leading countries in the Mediterranean Region with low case detection rate [25] thus, undiagnosed and untreated individuals are a potential source of TB transmission to other individuals [26] that contribute to spread of the disease.

Gender wise, females (P < 0.0001) were relatively more affected by TB infection (Table 1 and Table 2). This pattern has been observed in previous studies too [20, 27]. On the contrary, the worldwide situation indicated by the report of WHO revealed greater morbidity in males [28]. In a recent study, it was stated that due to gender based biological differences TB morbidity may vary in both sexes [29]. The sex based biological differences also includes variation in level of exposure to TB and immunological and physiological factors contributing to post-exposure susceptibility differences leading to disease development [30-33]. In a study conducted in Madagascar region, it was observed that the clustering rate was much higher in females as compared to males

[34], suggesting that the disease progression was predominantely greater in females of that region.

Age wise, results indicated age group ≥15 (P < 0.0001) to be the most commonly affected (Table 1 and Table 2). These finding are in accordance with the previous reports from various parts of the country [20, 35, 36] and world [37] indicating TB as an infection of adults. One possible reason for high morbidity of TB in adults is the association of infection with immune deficiencies [38]. In Africa, a great number of TB cases were observed in individuals co-infected with HIV [39]. Although, TB is not prevalent in children [37], and TB presence in them is mostly attributed to their contact with adults [40]. However, some reports have revealed substantial TB cases in children with birth associated primary immune deficiencies [38, 41], highlighting the role of immune deficiencies in housing MTB. Unfortunately, the current study lacks information about the HIV status of infected individuals, which is limitation of the study.

The previously treated individuals comprised of treatment failure, default and relapse cases (Table 3 and Table 4). A major reason in treatment failure is the lack of medication complaince in many patients due to problems in health care system as indicated by a meta-analysis [42]. Not only this, sometime patients may be diagnosis default [43] (do not initiate treatment upon diagnosis). Treatment failure or relapse may be also due to drug resistance [44]. A study by Ghafoor et al. indicated 58.4% MDR-TB while 1.8% XDR-TB among failures and relapse cases [45]. The treatment of MDR-TB requires about 20 months relative to drug susceptible TB where regimen duration is about 6-9 months [46]. In retreatment of previously treated patients the response is generally very poor [47]. Further, the cost of MDR-TB is many times greater than drug sensitive TB [46, 48]. Hence, the management of MDR-TB cases thus add additional contraints onto the health system of developing countries [49, 50]. On part of the health care personnel there is lack of appropriate knowledge about the disease [51]. In a study by Khan et al. [52], it

was determined that 56.5% health staff prescribed the four-drug anti-TB regimen in the initiation phase and 52% prescribed the two-drug combination in the continuation phase while 82% were unaware to mention a single component of DOTS strategy. Cumulatively, these factors contribute to mismanagement and mistreatment that eventually lead to spread of the disease.

Conclusion

In conclusion, high Tuberculosis morbidity was observed in the current study. Pulmonary TB (sputm smear positive and sputum smear negative) persists to be the predominant form. Along with the new cases, considerable number of TB cases were identified as previously treated patients. Overall, there is a need of effective revival of the National TB Control Program with special attention toward KP, to decline the TB cases to a minimum possible level which is not only a serious health concern but also menace for national economy.

Acknowledgements

Conflict of Interest

The authors declare that they have no competing interests.

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