Abstract:

Background: Upsurge of multidrug resistance tuberculosis is an emerging public health problem in developing countries, associated with poor compliance with anti-tuberculosis therapy (Am. Directly observed treatment-short course strategy (DOTS) has been widely reported to improve the compliance and treatment outcome among the patients reported in all level of health care system. Current study was conducted with objective to evaluate treatment outcome among tuberculosis patients registered under DOTS.

Methodology: A descriptive study was conducted in DOTS center of private teaching hospital, District Mirpurkhas, province Sindh from January - December, 2012. All registered patients were followed-up during their course of treatment to assess treatment outcome in accordance of World Health Organization (WHO) guideline as: cure, treatment completed, default, treatment failure, death or other. Data were analyzed by using EpiInfo version 3.2.

Results: Among 641 patients, n=542 (84.5%) had pulmonary and n=99 (15.4%) had extra pulmonary tuberculosis, mean age was 27.7 years (range: 7-80), n=343 (53.5%) were male. Persons aged 25-34 years were highly affected n=174 (27.1 %). Of all patients, treatment outcome was classified as treatment success (cure and treatment completed) in n=396 (61.7%), defaulted n=166 (25.8 %), treatment failed n=24 (3.7%) and transferred out n=51 (7.8%), death n=4 (0.6%) patients. Females n=93 (14.5%) and rural population n=98 (15.2%) were more likely to experience default than males n=73 (11.3 %) and urban population n=68 (10.6%).

Conclusion: Treatment success rate among tuberculosis patients was fairly satisfactorily with high defaulter rate, which may be corrected by enhance supervision, improved counseling activities and implementation of default tracing and home visit by health worker.

Keywords: Tuberculosis, Treatment, directly observed treatment-short course

Introduction:
Tuberculosis (TB) is a major public health problem, attributed to huge burden of morbidities and mortalities worldwide. In 2013, an estimated 9 million incident cases with 1.5 million deaths (1,140,000 in HIV-negative and 360,000 in HIV-positive peoples) reported from the mycobacterium tuberculosis1. Geographically, more than 95% of new TB cases and deaths occur in low and middle income countries2. The 83% of total incident cases were reported from the three regions i.e. South-East, Western Pacific and African region, among them the highest rates of incident cases and deaths per capita were reported from the African region3. The case fatality rate has exceeded 50% in some African countries where HIV prevalence rate are high. 4 Pakistan ranks fifth amongst TB high-burden countries imposing 61% of the TB burden in the Eastern Mediterranean Region. Approximately 273,097 new TB cases emerge every year with incidence rate of 410/100,000 and mortality rate 0.66/100,000. Possible cause of this high numbers are rapid increase in number of peoples living below the poverty line, overcrowding, poor living conditions, malnutrition. war, inadequate availability of anti-tuberculosis therapy (Am in health care setting, poor compliance with ATI, underfunding of National Tuberculosis control Programes (NTCPs), and non-adherence to program policies.6 The National TB Control Program of Pakistan is accountable for developing national guidelines, outlining the policies and engendering resources for execution of TB control measures at Provincial and district level.

For the early diagnosis and adequate treatment of TB infectious Directly Observed Treatment Short Course strategy (DOTS) strategy was adopted as National Strategy in 2000 and expanded to all level of health care system? In DOTS strategy at least the 2 initial months of treatment, patients take drugs directly under the observation of health care providers, as guided by international tuberculosis authorities8-9, which ensure high successful treatment rate (from 86% to 96.5%)10, major reductions in drug resistance, and relapse11. Jasmer et al observed that DOTS strategy was significantly associated with a higher treatment success rate than self-administered therapy (97.8% VS. 88.6%) and a low-
The prevalence of tuberculosis-related mortality rate (0% VS. 5.5%)12. Despite the availability of free anti-tuberculosis drugs in all level of health care setting, many patients are not successfully treated13, resulted in an extended period of infection, resistance to drugs, increase morbidity and mortality14. Ideally, treatment outcome in all patients should be routinely monitored by the epidemiological surveillance system, which serves as a proxy indicator for the quality of TB treatment15. So far, very few studies have documented the treatment outcomes of DOTS in Pakistan16-17,18, but never conducted in this setting. To fill the existing gap of the knowledge current study was conducted with objective to evaluate the treatment outcome of TB patients enrolled in DOTS clinic of a private teaching hospital located in rural area of Sindh.

Methods:
A cross sectional descriptive study was conducted among 641 TB patients registered from 1st January to 31st December 2013 in DOTS clinic of Muhammad Medical Teaching Hospital, Mirpurkhas. It is an only tertiary hospital providing health services to 1.5 million population of rural Sindh. All registered patients were followed up periodically until completion of their medication with objective to evaluate the treatment outcome. Information on age, sex, address, education, socioeconomic status and type of tuberculosis were collected from each patient by face to face interview. Disease related information including form of tuberculosis (pulmonary or extra pulmonary tuberculosis), type of tuberculosis (smear positive or smear negative), type one category of tuberculosis (new cases) and type 2 category (defaulter, failure, relapse) and treatment outcome were evaluated by World Health Organization (WHO) guideline19. We used following definition Cured: A pulmonary TB patient who was sputum smear-positive at the beginning of treatment and become sputum smear-negative in the last month of treatment and on at least one previous occasion.

Completed Treatment:
A pulmonary 1extra pulmonary TB patient who completed treatment but did not meet the criteria of failure or cure (negative sputum smear or culture results in the last month of treatment and on at least one previous occasion)

Defaulted:
A patient whose treatment was interrupted for two consecutive months or more for any reason

Treatment Failure:
A TB patient who was initially sputum smear/ culture positive and remained smear positive at month 5 or later during treatment

Died:
A TB patient who dies for any reason during the course of treatment

Transferred out:
A Category IV patient who has been transferred to another reporting and recording unit and whose treatment outcome is unknown

Successfully Treated:
A TB patient who cured or completed treatment

Unsuccessful Treatment:
A TB patients whose treatments were interrupted, transferred out or failed on treatment.

All collected data collected were entered and analyzed by using SPSS version 16 after cleaning. Validity of data ensure through random checks and double entry. In descriptive statistics frequency tables and charts were generated. Cross tabulations of variables was done to find out association between variables. A p-value of less than 0.05 was considered as statistically significant.

Ethical Considerations:
Ethical clearance for the current study was obtained from the Research Ethics Review Committee of Muhammad Medical College with registration number of MMC/ RERCn13. An informed consent was obtained from each patient before collection of relevant information. In order to ensure confidentiality, names or identification numbers of TB patients were not included in the data sheet.

Results:
A total of 641 tuberculosis patients were registered at Muhammad Medical College Teaching hospital between January-December 2013. Of these, n::343(53.5%) were male and n::298 (46.5%) were female with the mean age of 27.7 years. N::405 (63%) of the patients were belongs to urban area. Among total n=537 (83.7%) were belong from low socio-economic status. Over half n=367 (57.2%) were illiterate while only n=35 (5.4%) had college education. Regarding occupational status, 392 patients (61%) were unskilled and 103 (16%) were skilled and the rest were semi-skilled workers.

(Table 1)
Among total n=542 (84.5%) patients had pulmonary tuberculosis and n=99 (15.4%) extra pulmonary tuberculosis (Table 2).

Table 1: Demographic characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency N=641</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-14</td>
<td>84</td>
<td>13%</td>
</tr>
<tr>
<td>14-24</td>
<td>117</td>
<td>18.2%</td>
</tr>
<tr>
<td>25-34</td>
<td>137</td>
<td>21.3%</td>
</tr>
<tr>
<td>35-44</td>
<td>174</td>
<td>27.1%</td>
</tr>
<tr>
<td>45-54</td>
<td>59</td>
<td>9.2%</td>
</tr>
<tr>
<td>55-64</td>
<td>32</td>
<td>4.9%</td>
</tr>
<tr>
<td>&gt;65</td>
<td>38</td>
<td>5.9%</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>367</td>
<td>57.2%</td>
</tr>
<tr>
<td>Primary</td>
<td>140</td>
<td>21.8%</td>
</tr>
<tr>
<td>Matric</td>
<td>99</td>
<td>15.4%</td>
</tr>
<tr>
<td>College</td>
<td>35</td>
<td>5.4%</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unskilled</td>
<td>392</td>
<td>61%</td>
</tr>
<tr>
<td>Skilled</td>
<td>103</td>
<td>16%</td>
</tr>
<tr>
<td>Semi-skilled</td>
<td>146</td>
<td>22.7%</td>
</tr>
</tbody>
</table>

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Pulmonary tuberculosis patients, n=397 (73%) were smear positive patients and n=145 (26.7%) were smear negative. Most of the patients n=583 (91%) were belongs to category one (new cases) and remaining n=58 (9%) were fall in category two including relapse n=14 (2.1%), return after defaulter n=29 (4.5%) and treatment failure cases n=15 (2.3%) (Table 2).

A detailed summary of treatment outcomes of the TB patients is presented in Table 3 & Table 4. A total of 641 tuberculosis patients were analyzed: n=71 (11%) cured, n=321 (50%) completed treatment, n=168 (26.2%) defaulted.

Table 2: Form & Type of TB

<table>
<thead>
<tr>
<th>Types of TB</th>
<th>Male: N=343</th>
<th>Female: N=298</th>
<th>Total: N=641</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>301</td>
<td>241</td>
<td>542</td>
</tr>
<tr>
<td>Extra-pulmonary</td>
<td>42</td>
<td>57</td>
<td>99</td>
</tr>
</tbody>
</table>

Table 3: Outcome of Tuberculosis Treatment

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>N=641</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cured 71 11%</td>
<td>Treatment 321.50% Complete</td>
<td>Treatment Failure 253.9%</td>
</tr>
<tr>
<td>Dead 4 0.6</td>
<td>Defaulted 168 26.2%</td>
<td>Transferred out 52 8.1%</td>
</tr>
</tbody>
</table>

Table 4: Treatment outcome by sex, age group, patient category and TB type

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cured: N=71</th>
<th>Defaulter: N=121</th>
<th>Failure: N=25</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Male</td>
<td>49 (69.2%)</td>
<td>15 (12.6%)</td>
<td>7 (9.9%)</td>
<td>61</td>
</tr>
<tr>
<td>Female</td>
<td>22 (30.8%)</td>
<td>106 (87.4%)</td>
<td>8 (11.1%)</td>
<td>136</td>
</tr>
<tr>
<td>Age Group</td>
<td>Urban</td>
<td>Rural</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>59 (83.1%)</td>
<td>12 (9.9%)</td>
<td>7 (9.9%)</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>60 (85.7%)</td>
<td>13 (18.6%)</td>
<td>73</td>
</tr>
</tbody>
</table>

Discussion:
In Low and Middle countries Tuberculosis is consider as a one of the leading causes of morbidities and mortalities among infectious diseases. For effective control of tuberculosis infection, it is a pre-requisite to detect the cases as early as possible, ensure complete treatment with good compliance and get cured. To achieve this objective DOTS strategy has been welcome as an effective method. In current study tuberculosis was observed more in male as compared to females. Similar results were reported in studies conducted in Nigeria, Zimbabwe, Ethiopia, India, 21 and Pakistan. While Mir Azam Khan et al, reported equal number of cases in both sex. Most of the tuberculosis cases occur in population of age group 15-59 years, which coincidently are the most productive age in term of economic and reproduction. Similar trend was observed in the current study more than 80% of the cases were belongs to age less than 60 years. This is in line with local and international. Studies 27-28-29 Current study shows that pulmonary TB accounted for 542 cases (84.5%) of the total burden of the disease in the study population, while the extra-pulmonary tuberculosis attributed to 99 (15.4%) cases. This is at variance with the finding of studies conducted in Ethiopia where extra-pulmonary TB was found in 56.2% and 22% of respondents.
patients by Menke et al observed 76.1% success rate. High treatment success rate 80.3% was also reported by Diel et al in 518 cultures positive TB patients. In line of this observation Chennaveerappa et al noted 84.2% success rate among 181 patients. The difference in success rate may be due to increase default and transfer out rate among current study population patients.

In agreement with the studies carried out at national and international level, the study reported the higher treatment success rate among male TB patients as compared to female TB patients, increase number of defaulter and deaths were also observed among male patients. However, the proportion of female patients enrolled for AU were relatively low compared to male patients, which may be due to cultural and religious barriers.

In this study the treatment success rate was higher in patients living in urban area than in rural living patients (54% vs. 43%), which may be due to poor access to health facilities, or non-availability of health care facility, drugs and staff in the rural settings. These findings are same line the study carried out in three districts in Burkina Paso where geographical distance was observed as a major challenge for rural patients in access to health facilities.

The default rate in this study was high 26% as compare to study conducted in Nigeria and India, which may be due to low poor access to health facility or lack of motivation. Our study suggests that there is a need to take urgent action to low the default rates in our TB control programs. Intervention like, counseling, home visits and motivation, and health education supposed to be strengthened and implemented in our health care setting to reduce default rates in tuberculosis patients. The TB treatment failure rate of this study was 3.9%, which was higher from the study conducted in India reported 1.6% treatment failure rate. On the contrary side study from Nigeria and Ethiopia reported 8.3% and 18.6% respectively. First limitation of this study is that no attempt was made to visit the defaulted patients to find out reason. Second limitations is that information on co-infection with HIV was not collected and current study only conducted in one teaching hospital which might affect its generalizability. Finally, inadequate financial resources constraints played a limiting role in extending this study beyond one hospital.

**Conclusion:**
The treatment success rate was unsatisfactorily i.e. 60.4% among pulmonary and 64.6% in extra-pulmonary tuberculosis patients. It was also lower in patients of rural area 43% and in female population 55.9%. A high proportion of patients defaulted (26.2%) transferred out 8.1% and treatment failed 3.9%, which is a serious public health problem that needs to be addressed urgently. To improve treatment success rate of tuberculosis patients we recommend constant supportive follow-up and supervision of TB patients by health workers and family during intensive and continuous phase of therapy, for defaulter and motivation of defaulter patients (defaulter tracing) health education to reduce treatment interruption, and community mobilization for early detection and treatment of TB cases.

**Conflict of Interest:**
The author(s) declare that they have no conflict of interest.

**Authors Contributions:**
MA was the primary researcher, conceived the study, designed, participated in data collection, conducted data analysis and drafted the manuscript for publication. MR and MNS assisted in data collection and preparation of first draft of manuscript. All authors interpreted the results, and reviewed the initial and final drafts of the manuscript.

**Acknowledgements:**
Authors would like to thank all the staff members of DOTS clinic, Muhammad Medical College for the proper documentation of patient's information and their genuine assistance during data collection.

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