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Risk Profile of Developing Multi-drug Resistant Tuberculosis in Pulmonary Tuberculosis Patients at Narsingdi, Bangladesh.

Dr. Sujan Saha, MBBS, MPH[(1)]
Dr. Shaikh Abdus Salam MBBS MPH[(2)]
Dr. Abdul Sadeque MBBS MPH DrPH[(2)]
Dr. Mita Saha, MBBS, DCH[(1)]
Dr. Md. Akhter Hossain PhD[(3)]

Abstract:
Tuberculosis is till now an important causes of mortality and morbidity in Bangladesh, a part of South East Asian region caused by Mycobecterium tuberculosis. The disease primarily affects the lungs to cause pulmonary tuberculosis. Multidrug-resistant TB (MDR-TB) is caused by the same bacteria but that are resistant to both isoniazid and rifampicin, the most effective anti-TB drugs, which increases the morbidity of the patient as well as the cost management causing an important impact upon national health economy. To prevent or to control this the 'risk score' obtained from this study could be applied at the high risk community level for early suspicion and can refer to them for further DST and thus the economical load will be lessen of treating MDR-TB. A descriptive cross-sectional study was done over a peroid of 6 months taking a sample of 145 pulmonary tuberculosis patients by convenient sampling in the DOTS Corner of Sadar Hospital, Narsingdi, Bangladesh a semi-urban area which is 53 kms away from Dhaka, Capital of Bangladesh to get a socio-demographic variation. A semi-structured questionnaire was developed in English and then translated into Bangla. The questionnaire was developed using the selected variables according to the specific objectives. Pre-testing was done before the onset of data collection on 5% subjects. The investigation reports (sputum microscopy, chest radiograph findings, category of the patients etc.) were collected from the case history file. Descriptive statistics including means, medians, standard deviations and ranges for continuous data and frequencies and proportion for categorical data will be calculated. Data will be presented in appropriate tables and graphs. For inferential statistics mainly t-test, and $\chi 2$-test was used. All the tests will be two tailed and $p<0.05$ was considered to be statistically significant. Both univariate and bivariate analysis were done. In order to find out association between the dependent and independent variables; Logistic regression and Chi2 tests at 5% significance level was done. For better view of the study population, some tables, graphs and charts was used. The statistical analysis of the data was carried out by using software program SPSS version 17. The study implicated the socio-demographic analysis, cross sectional risk factor analysis was done and also implicated the use of Risk Score for early detection of MDR-TB which was statistically significant for identifying the patients of pulmonary tuberculosis who are at risk of MDR-TB.
Keywords: Tuberculosis; MDR-TB; DOTS Corner; Risk Profile; Sputum Microscopy

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1. Introduction

Tuberculosis (TB) is an infectious bacterial disease caused by *Mycobecterium tuberculosis*. The disease primarily affects the lungs to cause pulmonary tuberculosis. It also infects the intestine, meninges, bones and joints, lymph nodes, glands, skin and other tissues of the body.[1] The disease is usually chronic with varying clinical manifestations according to the site of infection. Multi-drug resistant tuberculosis (MDR-TB) is one of the hard to treat form of this TB, emerging worldwide in recent times.[2] Multidrug-resistant TB (MDR-TB) is caused by the same bacteria but that are resistant to both isoniazid and rifampicin, the most effective anti-TB drugs. MDR-TB results from either primary infection by the resistant bacteria or may develop in the course of patient's treatment.[1]Data from drug resistance surveys and continuous surveillance among notified TB cases suggest that 3.6% of newly diagnosed TB cases in 2013 and 20% of those previously treated for TB had MDR-TB.[2] The highest levels of MDR-TB are found in eastern Europe and central Asia, where in some countries more than 20% of new TB cases and more than 50% of those previously treated for TB have MDR-TB[2].Based on drug resistance information from 114 countries and 2 special administrative regions (SARs) of China, the proportion of MDR among new, previously treated and combined cases was estimated for countries with no survey information available. It is estimated that 489,139 (95% CI, 455,093-614,215) cases emerged in 2006,

and the global proportion of resistance among all cases is 4.8% (95% CI, 4.6-6.0)[3]. China, India, and the Russian Federation are estimated to carry the highest number of MDR cases. China and India carry approximately 50% of the global burden.[3] There is no MDR-TB prevalence data available for Bangladesh based on socio-economic, demographic and geographic similarity we expect this will yield a different result from other areas of country in this context.

The treatment outcomes for MDR and XDR TB are poor compared with that for drug-susceptible TB. The necessary second line of drugs (SLDs) are more potent but toxic and more expensive. Many SLDs are not available in resource-limited settings, and treatment regimens for drug-resistant TB with or without HIV co-infection are based on case series and expert consensus. Specific medication regimens for the treatment of MDR and XDR TB should be tailored based on DST results, if available. However, in most settings, DST is not accessible for individual patients and standard regimens are used, preferably from population-based DST data. If MDR or XDR TB is suspected while awaiting DST, empiric therapy may be initiated with four or five oral SLDs usually including a fluoroquinolone and an injectable agent, though embarking on a second-line regimen without prior proof of drug resistance may not be recommended in most settings.[7,8] The addition of a single injectable agent, such as streptomycin, to a failing first-line regimen should be strictly avoided. Oral SLDs include ethionomide, prothionomide, cycloserine, terizidone, para-aminosalicylic acid (PAS) and the fluoroquinolones. Despite significant heterogeneity among reported treatment trials for MDR-TB, a recent meta-analysis suggests three characteristics associated with clinical success: regimens including five or more drugs, a longer duration of treatment (at least 18–24 months) and employment of the DOTS-plus strategy. Additionally, surgical resection can be beneficial in a carefully selected population of patients with pulmonary drug-resistant TB but the adjunctive procedure is of unclear benefit in HIV positive patients who are more likely to have primary drug resistance and harbor disseminated disease.[9]

In most central and western European countries where TB, particularly drug resistant forms of TB, are imported, absolute numbers as well as proportions of MDR-TB among all cases are relatively stable but in south east Asia the MDR-TB trends are gradually increasing.[10]Seven countries have reported data on drug resistance since 2002, namely, Bangladesh, India, Indonesia, Myanmar, Nepal, Sri Lanka, and Thailand. India reported data from three districts and one state, while Indonesia reported data from one district only. Orissa in India, Sri Lanka, and Thailand reported less than 2% MDR-TB among new cases. Districts surveyed in the states of Kerala, West Bengal and Gujarat in India as well as Mimika district of Papua province in Indonesia, and Nepal reported between 2-3% MDR-TB among new cases. New data from Gujarat State, are the first reliable source of data on previously treated cases in India and show 17.2% MDR-TB among this group. Myanmar reported a higher level of 3.9% (2.6%-5.7%) MDR-TB among new cases. While a few tertiary-care facilities have reported levels of multi-drug resistance as high as 60% among previously treated cases, these are not representative of the situation in the community.[10,11]

With a population of 150 million, Bangladesh ranks sixth among countries with a high TB burden. The estimated prevalence and incidence rates of all forms of tuberculosis are respectively 387 and 223 per 100 000 population, in 2007[12]. TB control activities are further expanded by increasing the number of peripheral laboratories, sputum collection or smearing centers so that access to TB diagnostic services improves. The case-detection rate increased to 73% in 2007. The reported treatment success rate has increased to 92% for the cohort of patients registered in 2006. The National TB Guidelines are updated bringing national policies in line with more recent international recommendations. A nationwide disease prevalence survey is being conducted to establish more accurate estimates of the prevalence of tuberculosis and to assess the trend of the epidemic in the country.[3]

It was highlighted that recording and reporting of contribution to MDR-TB case detection by different types of providers and place of all previous treatments has not yet become standardized. Therefore, information about the role of private practitioners in previous treatments and referrals of MDR-TB suspects is currently not well known. Furthermore, there are no standard mechanisms for feedback of clinical information to referring units nor is there follow-up of cases lost during the referral process[13].Few other institutions have laboratories able to perform drug-susceptibility tests (DST) for TB. One military hospital has DST facilities but reported that, so far, no MDR-TB cases were identified. Two large private hospitals also have DST facilities. According to the MDR-TB focal point in NIDCH, they refer all their identified MDR-TB cases to NIDCH. None of these laboratories are part of the national quality assurance system. The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) also has a DST laboratory only for research purpose.[14]

More than 80% of all patients identified with MDR-TB were previously treated by the Damien Foundation while the other patients were treated by other providers linked to NTP. No MDR-TB suspects were referred by private practitioners during the past two years.[6,11] Only 17% of diagnosed MDR-TB cases reported having been treated in the private sector (unpublished Damien Foundation data). It is not clear if this is due to the low (and declining) number of TB patients being treated in the private sector (and little MDR-TB emerging there) or unwillingness among private providers to refer their MDR-TB suspects.[14]

The inability to rapidly confirm TB diagnosis and determine subsequent drug susceptibility remains one of the greatest hindrances to successful TB control. Sputum microscopy detects only 50% of pulmonary TB cases compared with standard culture under ideal conditions and is even less sensitive in immune-compromised hosts.[14] Furthermore, diagnosis of drug-resistant TB by solid or liquid culture and indirect DST by the proportional method still may require 2–3 months.[15] Unfortunately, such tests are lengthy, costly, and not universally available in resource-limited settings, which bear the major burden of MDR- and XDR-TB. WHO estimates that up to 96% of patients with MDR-TB are not being diagnosed and treated according to international guidelines[4,6]. Therefore, it is imperative to develop new methodologies for faster and affordable DST, as well as low-cost techniques, for easier identification of patients at risk for MDR-TB.[16]

Clinical prediction rules (CPR) are simple, standardized clinical tools that utilize components of history, physical examination and basic testing to stratify risk of developing MDR-TB, help make a diagnosis, or predict an outcome.[7-9]In tuberculosis, CPR were developed to focus on infection control decisions, the diagnosis of smear-negative pulmonary TB,and prognosis.[15-19] In a recent retrospective study, a CPR was developed to predict the presence of drug-resistant TB in a high HIV prevalent area – Thailand. In this cross-sectional study a clinical prediction rule might be developed to stratify risk for MDR-TB among patients with pulmonary tuberculosis.[20]

Now assessment of risk of pulmonary TB patients in developing MDR-TB is essential. Early interventions are be required for those TB patients who are at risk of developing MDR-TB. Stratification of the patients into different risk group can facilitate to take such appropriate interventions easily' This study was done to assess the risk profile of developing MDR-TB in pulmonary tuberculosis patients at Narsingdi and at the same time to assess level of risk of developing MDR-TB among the pulmonary TB patientsin relation to age, gender, socio-economic status and life-style and to develop an algorithm/tool for MDR-TB risk assessment among the pulmonary TB patients in that district of Bangladesh.

2.Materials and Methods

To assess the Risk Profile of developing MDR-TB in pulmonary tuberculosis Patients we did an observational cross-sectional study which was conducted. The study was conducted study was conducted at DOTS corner, Sadar Hospital in Narsingdi, 53 kilometers away from Dhaka city for period of 06 months (July 2014 to December 2014). PTB patients were included attending DOTS corner, Sadar Hospital in Narsingdi who gave consent and were willing to participate our study. But patients, who already developed MDR-TBas they have already developed the outcome of interest by sputum culture sensitivity and drug susceptibility testing (Xpert MTB/RIF), and patients who did not give consent for the study were not included in the study.

2.1 Data Source and Analysis

The study was conducted at a single point in time.Convenient sampling was followed. The sample size estimated using the following formula:

$$n = \frac{z^2pq}{d^2}$$

Here,

n = Sample size

z = Standard normal deviate set at 1.96 which is corresponding to 95% CI

p = Prevalence of MDR-TB = 20% (According to global tuberculosis report, 2013)

q = Prevalence of non-MDR = 80%

d = Degree of precision = 5%

Therefore, n = 245.86~246 (approximately)

Calculated sample size n = 246.But 145 samples could be included within the data collection period.

A semi-structured questionnaire was developed in English and then translated into Bangla. The questionnaire was developed using the selected variables according to the specific objectives. Pre-testing was done before the onset of data collection on 5% subjects. After pre-testing, necessary modifications are done and questionnaire is finalized. A check list was used to record the disease related data. The data was collected through face to face interview and recorded on the questionnaire. The investigation reports (sputum microscopy, chest radiograph findings, category of the patients etc.) will be collected from the case history file. Then physical assessment including chest examination and anthropometric measurement including height and weight will be done. Height was measured by measuring tape while patient on standing and on bare foot. Weight was measured by bath-room scale with minimum clothing and then BMI was calculated.

For risk factor of MDR-TB, type of TB, contact history, abnormal lung findings, chest radiograph were categorized into different scores. On the basis of CPR, score for history of default/relapse given as '3'; for prior contact with MDR or TB patients '2'; cavitary chest radiograph '1'; abnormal breath sound (crackles) '-1' and other than these findings, all are given '0'.Predictive scores were derived from statistically significant factors at

the cut-off point of the receiver-operating curve that yielded the best area under the curve. This CPR canprovide a decisional guide for the clinician on whether to send a patient's respiratory specimen for sputum culture and drug susceptibility testing.

For data entry, processing and analysis Statistical Package for Social Sciences (SPSS) version17 was used. Data was checked, cleaned, coded and edited properly before analysis. The analytical plan of the study included description of the study population by their socio-demographic characteristics first. Descriptive statistics including means, medians, standard deviations and ranges for continuous data and frequencies and proportion for categorical data was calculated. Data was presented in appropriate tables and graphs. For inferential statistics mainly t-test, and χ^2-test will be used. All the tests were two tailed and $p<0.05$ was considered to be statistically significant. Both univariate and bivariate analysis were done. In order to find out association between the dependent and independent variables; Logistic regression and Chi^2 tests at 5% significance level was done. For better view of the study population, some tables, graphs and charts were used.

2.2 Ethical Considerations

The participants were informed in details about the nature of the study. They were not exposed to any physical, psychological and social risk. Only the individuals willing to participate in the study were included. Informed written consent was taken from the participants. Every participant enjoyed his/her right to participate or refuse to participate and to withdraw participation at any time. The confidentiality of the information obtained from the participants was maintained by the principal investigator. Data were intended to be used solely for this study.

3. Results

3.1 Socio-demographic characteristics of the patients

3.1.1 ***Age:***

The age of the study sample varied between 18 and 50 years with a mean of 30.79 ± 7.74 years. One-fourth of them were less than 25 years of age followed by 25 to 29 years (22.1%).

Table 1: Distribution of Patients by Age

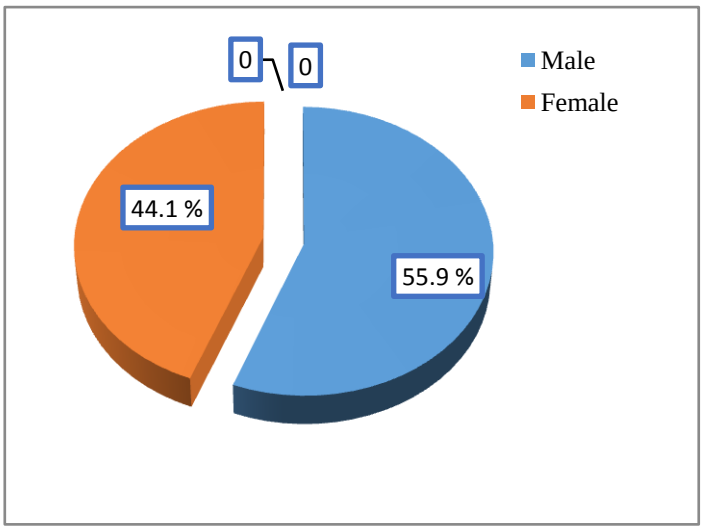
Age in years	**Frequency**	**Percent**
<25	36	24.8
25–29	32	22.1
30–34	28	19.3
35–39	22	15.2
≥40	27	18.6
Total	145	100.0

3.1.2 *Sex:*

Among 145 TB patients, 81 (55.9%) were males and rest of them were females.

Figure 1 Distribution of Patients according to Sex

n = 145

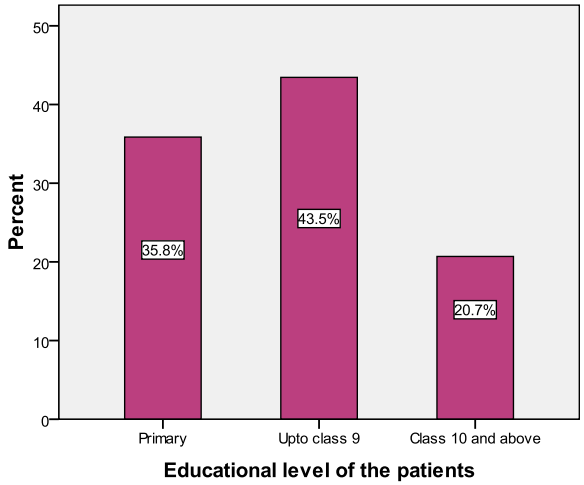


3.1.3 *Education:*

One-third of the patients completed primary level of education whereas one-fifth completed class ten and above.

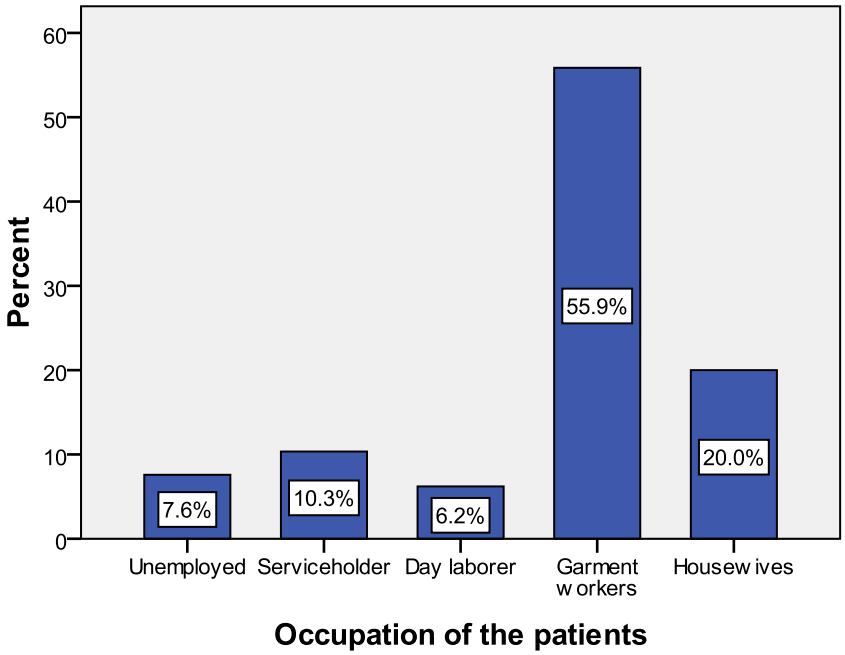
Figure 2: Distribution of Patients according to Educational Status

n =145



3.1.4 ***Occupation:***
Majority (55.9%) of them were garment workers and one-fifth were housewives.

Figure 3: Distribution of Patients by Occupation
n = 145

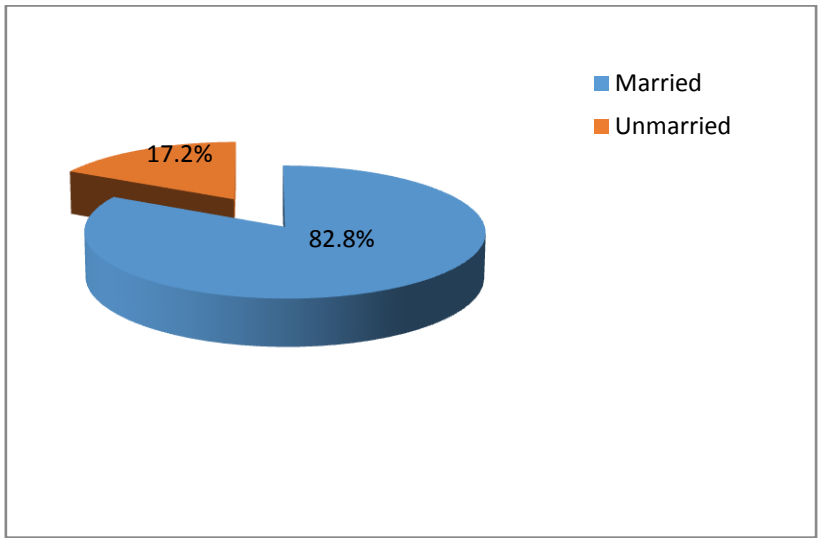


3.1.5 ***Religion:***
All Patients under study were practicing muslim.

3.1.6 ***Marital status:***Four-fifth of the patients were married.

Figure 4: Patients distribution by Marital Status

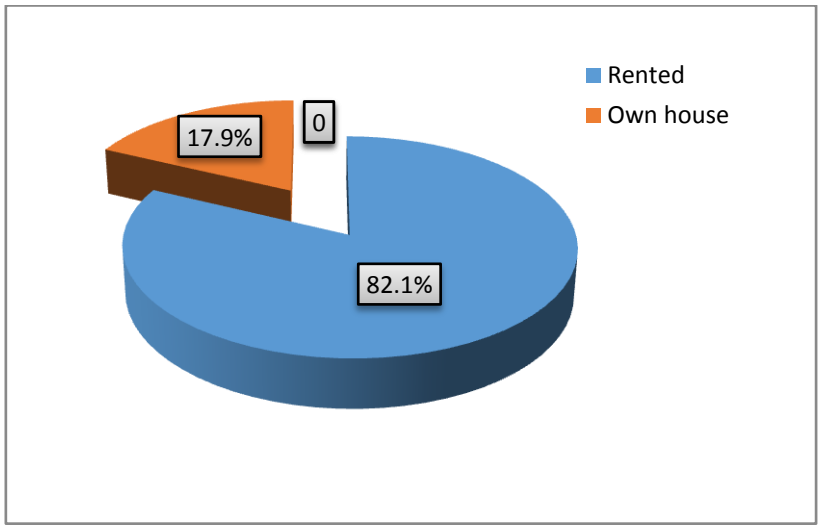
n = 145



3.1.7 ***Usual place of residence:***
All of the patients resided in urban area of them 6.9% were in urban slum.

3.1.8 ***Ownership of residence:***
Only one-fifth of the patients had ownership of their houses, rests were to pay rent.

Figure 5: Distribution of Patients by Ownership of Residence
n =145



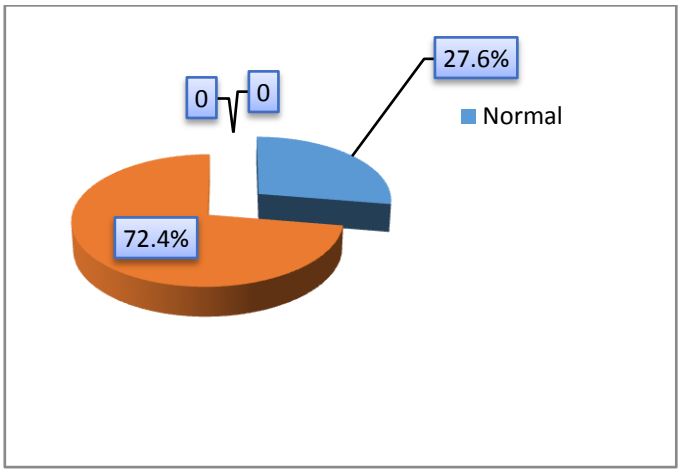
3.1.9 ***Housing condition:***
Roofs of the most houses were made of tin, walls and floors were of concrete.

Table 2: Distribution of Patients according to Housing Condition

House		Frequency	Percent
Roof	Tin	143	98.6
	Concrete	2	1.4
Wall	Tin	22	15.2
	Concrete	123	84.8
Floor	Mud	13	9.0
	Concrete	132	91.0

3.1.10 ***Crowding index:***
For normal environment, maximum of 2 persons could be resided in a single room of 110 sq. feet and of 3 persons in double room of 220 sq. feet. Persons residing more than those of mentioned above will be considered as overcrowding. Three-fourth of the patients were living in overcrowding.

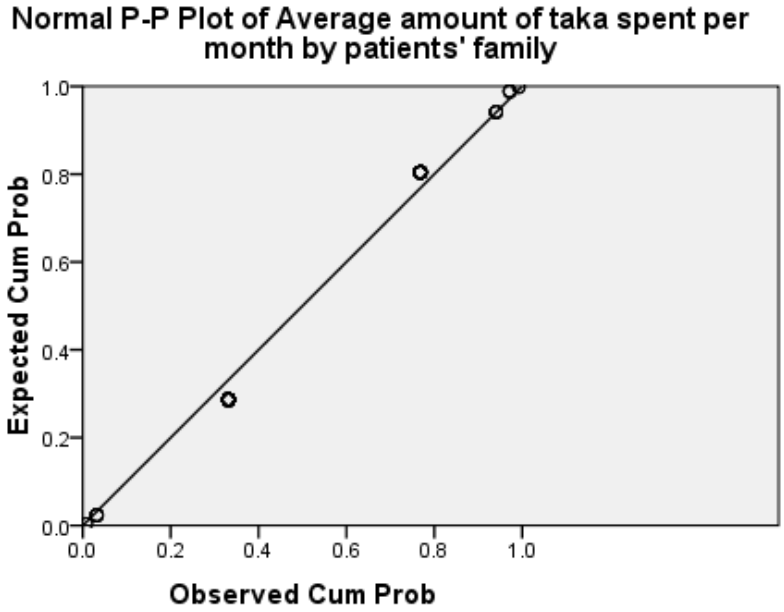
Figure 4.1.6: Distribution of Patients Household by Crowding Index
n =145



3.1.11 ***Family expenditure:***

Average monthly family expenditure of the study sample varied between 7000 and 15000 taka with a mean of 10793.10 ± 1408.80 taka. Most of the patients' family spent 10000 taka (56.6%) per month followed by 12000 taka (31%).

Figure 7: Distribution of Patients according to Monthly Family Expenditure



3.2 Multi-drug resistant tuberculosis risk:

Data on history of default or relapse, prior contact with MDR-TB or TB patients, crackles, breath sound, cavitation in chest radiograph were taken to assess MDR-TB risk in this study.

3.2.1 ***Type of Tuberculosis:***

Most of the patients were newly diagnosed (98.6%). 93.1% were sputum positive.

Table 3: Distribution of Patients according to Type of TB

Type of TB	Frequency	Percent	
New smear negative	8	5.5	98.6
New smear positive	135	93.1	

Relapse	2	1.4
Total	145	100.0

3.2.2 ***Contact history:***
Four-fifth of the patients reported to have contact with TB patients, among them maximum were exposed to neighborhood patient before diagnosis. All of them did not know whether the contact persons were suffering from MDR-TB or not.

Table 4: Distribution of Patients according to Contact History

Contact history	**Frequency**	**Percent**
No	30	20.68
Yes	115	79.32
Relationship with contact		
Parents	1	0.87
Neighbors and colleagues	04	3.48
Colleagues	13	11.30
Neighbors	97	84.35

3.2.3 ***Chest radiograph findings:***
Three-fourth had no documents, cavitation was not found.

Table 5: Distribution of Patients according to X-ray report

X-ray findings	**Frequency**	**Percent**
Normal	31	21.4
Patchy opacity	8	5.5
Not available	106	73.1
Total	145	100.0

3.2.4 ***Grading of MDR-TB risk:***
Total score ranged from 0 to 5 with a mean of 1.63 ± 0.90.
More than three- fourth of the patients scored '2' indicating 'high risk', while one-fifth scored '0' represented as 'low risk group'.

Table 6: Proportion of the patients classified by the MDR-TB score

MDR-TB risk group	**Frequency**	**Percent**
Low (0 point)	30	20.7
High (≥2 points)	115	79.3

Total	145	100.0

3.3 Risk of MDR in relation to age and sex:

Age: Risk of MDR-TB differ significantly in age. This difference among risk group is highly significant (t= 2.97, p = 0.003).

Table 7: Age in different MDR risk

MDR risk group	Frequency	Age Mean ± SD	t	p
Low	30	34.43±8.76	2.97	0.003
High	115	29.83±7.20		

Sex:In this study sex difference among different risk group was not statistically significant (χ^2= 0.921, p > 0.05). In each risk group both sexes were almost in same proportion.

Table 8: Sex difference in different MDR risk

Gender	**MDR risk**		Total	χ^2	p
	Low (%)	High (%)	%		
Male	17 (20.99)	64 (79.01)	81(55.90)	0.01	0.921
Female	13 (20.31)	51 (79.69)	64(44.1)		

3.4 Socio-economic status with MDR-TB risk:

Educational status:Different educational status in different risk groups were statistically significant (χ^2=35.69, p=0.000). A patient with lower educational status belonged to higher risk group.

Occupation:Occupational variation was statistically significant (χ^2=31.1, p =0.000) in different risk group. Garment workers were in higher risk group followed by housewives.

Residential area:Significant association was found betweenplace of residence and MDR risk group (χ^2=5.62, p=0.018). Urban patients were relatively in higher risk group than of urban slum.

Ownership of house:Ownership of house played a significant role in MDR risk (p=0.003). Those patients who had own house were in lower risk group.

***Crowding index*:** There was no significant association between crowding index and MDR risk group (χ^2=0.016, p=0.89). Patients of both environment were almost in same proportion.

Table 9: Socioeconomic status of the patients and MDR-TB risk

Educational status	**MDR risk**		**Total N=145**	**χ^2**	**p**
	Low (%)	**High (%)**			
Primary	6 (11.54)	46 (88.46)	52	35.69	0.000
Up to class 9	6 (9.52)	57 (90.48)	63		
≥ class10	18 (60.0)	12 (40.0)	30		
Occupation					
Unemployed	5(45.45)	6(54.55)	11	31.11	0.000
Service	13 (54.17)	11 (45.83)	24		
Garment worker	5 (6.17)	76 (93.83)	81		
Housewives	7 (24.14)	22 (75.86)	29		
Residential area					
Urban	25 (18.52)	110 (81.48)	135	5.62	0.018
Urban slum	5 (50.0)	5 (50.0)	10		
Ownership of house					

Rented	19 (15.97)	100 (84.03)	119	9.02	0.003
Owner	11 (42.31)	15 (57.69)	26		
Crowding index					
Normal	8 (20.0)	32 (80.0)	40	0.016	0.89
Overcrowding	22 (20.95)	83 (79.05)	105		

Family expenditure:Variation of average monthly expenditure among different risk group was not statistically significant (t=1.27, p=0.210).

Table 10: Distribution of patients by family expenditure and MDR risk

MDR risk group	Frequency	Mean ± SD	t	p
Low	30	11133.33±1716.72	1.27	0.210
High	115	10704.35±1311.04		

3.5 Risk of MDR in relation to lifestyle of the patients

3.5.1 *Smoking:*

Among all the TB patients, 76 (55.9%) were smoker, and all were male patients. Smoking habit did not show any significant association with MDR-TB risk (χ^2=0.263, p =0.608).

Table 11: Patients distribution according to smoking habit

Smoking	**MDR risk group**		**Total (%)**	**χ^2**	**p**
	Low (%)	High (%)			
Yes	13 (22.22)	63 (77.78)	76(55.9)	0.263	0.608
No	14 (18.75)	55 (81.25)	69(44.1)		

Half of them smoked daily, majority 63 (82.9%) of them consumed more than 20 sticks per day.

Table 12: Patients distribution according to type of smoker

Type Smoker (sticks/day)	**Frequency**	**Percent**
Moderate (10-20)	13	17.1
Heavy (>20)	63	82.9

Out of 76 smokers 63(82.9%) consumed at least 25 sticks per day followed by 13 (17.1%) who consumed less than 20 sticks per day.

Table 13: Consumption number of sticks and MDR-TB risk

MDR risk group	Frequency n	Average no of sticks ± SD
Low	15	21.67±3.08
High	61	24.67±1.24

3.5.2 *Betel-leaf and jarda consumption:*

Majority of the patients (86.9%) consumed betel leaf as well as jarda (82%)

Betel leafconsumption status in different risk group wasnot significant (χ^2=0.987, p= 0.61). But regular betel leafconsumption was more common in high risk group.

Table 14: Association of risk with betel leaf consumption

Betel leaf consumption	**MDR risk group**		**Total (%)**	χ^2	p
	Low (%)	High (%)			
No	5(26.32)	14(73.68)	19(13.10)	0.987	0.61
Regular	10(16.95)	49(83.05)	59(40.69)		
Occasional	15(22.39)	52(77.61)	67(46.21)		

Significant association was not found for jarda consumption but it was reported that most betel leafconsumers were usually consuming jarda regularly.

3.6 MDR risk in relation to clinical characteristics of the patients

3.6.1 Duration of cough:

Almost half of the patients had cough for six weeks and rest half almost equally for four weeks and eight weeks before diagnosis.

Table15: Distribution showing duration of coughing before diagnosis of TB

Cough duration(in weeks)	**Frequency**	**Percent**
4-6	35	24.1
6-8	71	49.0
8+	39	26.9
Total	145	100.0

3.6.2 Sputum microscopy:

1st sample : Almost half of the slides shown bacillary load of '1+'
2nd and 3rd sample : Four-fifth of the total slides had shown AFB load of '1+' and '2+'.
Among 135 sputum positive patients, 8 patients were found to have at least one slide with AFB load '3+'

Table 16: Distribution of patients by sputum microscopy

AFB load	**Sputum sample**					
	First sample		**2nd sample**		**3rd sample**	
	Frequency	%	Frequency	%	Frequency	%
Negative (no bacilli)	15	10.3	10	6.9	10	6.9
Scanty	10	6.9	7	4.8	9	6.2
1+	73	50.3	82	56.6	110	75.9
2+	44	30.3	40	27.6	15	10.3
3+	3	2.1	6	4.1	1	.7
Total	145	100.0	145	100.0	145	100.0

3.6.3 Body mass index of the patient:

Two-third of the patients were in chronic energy deficiency type1 while one-fifth were normal. Statistically significant difference was not found between BMI of the patient and MDR-TB risk (χ^2=0.949, p=0.622)

Table 17 Distribution of patients' body mass index

BMI of the patients	**MDR risk group**		**Total (%)**	χ^2	**p**
	Low (%)	**High (%)**			
CED II	4(30.8)	9(69.2)	13(9)	0.949	0.622
CED I	20(19.2)	84(80.8)	104(71.7)		
Normal	6(21.4)	22(78.6)	28(19.3)		

4.Discussion

Multi drug resistant tuberculosis (MDR-TB) is now one of the major public health concerns in developing countries. Disease trends are gradually increasing; setting up as a threat for human health. This cross sectional study was conducted at DOTS corner in Narsingdi Sadar hospital with a view to stratify the risk of developing

MDR-TB among pulmonary TB patients. A total of 145 pulmonary tuberculosis patients were selected. Association with age was found and the population was predominantly young which reflects more exposure of physically active person to the disease. In different international study young age groups are found as dominating factor for developing MDR-TB[3,22]. Association of sex with MDR-TB was not found in this study. While males predominated among TB cases in the world, association of sex with MDR-TB has been controversial. Studies in South Africa, Australia, the Netherlands and the United States of America have reported slightly higher odds ratios among females than males, while other studies fail to find such associations[23]. In general, it appears that the overall risk of harboring MDR-TB strains is not influenced by gender. Level of education usually influences type of occupation and ultimately affects economic status; it suggests that person with lower educational status might not get better job with satisfactory salary to run his livelihood with standard. In different studies it is clearly seen that patients with low socioeconomic status are vulnerable group for MDR-TB[23,24]. In this study it was reflected that garment workers had not much more income and most of them (43%) did not complete SSC level, which indirectly reflected their socio-economic burden.Most of the patients (93%) resided in urban area could not maintain crowd less environment as well as air pollution; in addition, low socioeconomic status and malnutrition favored these patients to have higher risk to develop MDR-TB. In this study though there was no significant role of overcrowding for MDR-TB, but different surveys show that MDR-TB can spread from person to person[25].

Heavy smoker (consume ≥20 sticks per day) might have more chance to develop MDR-TB. Smoking habit acts as a precipitating factor for developing obstructive and as well as interstitial lung diseases; make the person low immunity status. A case control study shows that the increased risk for pulmonary tuberculosis is significant in men who have smoked for over 20 years[23].

Clinical characteristics of the patients were not found statistically significant in this study as all the patients complained to have all the major sign-symptoms of TB except hemoptysis. Cavitation as chest radiograph findings and abnormal breath sound (crackles) act as important contributing factor for MDR-TB risk in Thi and Peruvian study[20,26]. In our study no cavitation was found as well as abnormal breath sound. A case control study shows that malnutrition might invite MDR-TB in pulmonary TB patients[25]. But in this study two-third patients were of underweight, statistically did not play any significant role for developing MDR-TB; might be due to limited sample size.Low socio-economic condition, malnutrition, immune suppressing diseases (HIV, DM) might play as contributing factor for MDR-TB, but due to time and limited sample size all events were not focused possibly. Especially data related to HIV risk factor might not be collected adequately as existing socio-religious stigmata. Maximum did not give the history of their diabetic status as they did not know their glycemic status.Findings of this study were consistent with other studies describing independent risk factors for MDR-TB. Risk factors that had been associated with MDR-TB include: known TB contacts, age younger than 29 years, low socio-economic status and unhealthy lifestyle. Similar to other third world countries, the prevalence of HIV co-infection was low, thus assessing the association with MDR-TB was not possible[28]. These results might be explained by the low number of patients with these risk factors into the sample.

We should note another study performed in Thailand. Boonsarngsuk and colleagues found that chest radiograph features, relapse after previous treatment, and prior incomplete treatment were associated with an increased risk for either isoniazid or rifampin resistance; a cut-off score of greater than two had a sensitivity of 58% and a specificity of 68%[20]. However, the study was retrospective, had a small sample size (290 patients), patients were selected base on physicians' judgment, patients were treated in a referral hospital, and included microbiological results from invasive procedures (bronchoalveolar lavage fluid); the prevalence of MDR-TB was 2.4% (7 cases) and HIV was 16%[20,28].

In this study there were some limitations. First, the small sample size could not be generalized. Second, while all patients had chest radiographs, not all films were available for interpretations. Third, our findings might not be applied to areas with higher prevalence of HIV/TB co-infection. Finally, similar to other real-world operational settings, we only included pulmonary TB patients. We applied CPR based MDR-TB risk score on TB patients of selected urban area to assess MDR-TB risk as well as to stratify the patients from lower to higher risk group for further attention; which would be essential for prevention of MDR-TB. A cross sectional analytical study usually yields results of weak association; further cohort study might be required to cover those limitations.

5. CONCLUSION:

The study focuses that four-fifth of the pulmonary tuberculosis patients were high risk while one-fifth were low risk in developing multi-drug resistant tuberculosis (MDR-TB). Almost half of the patients were less than 29 years of age who belonged to higher risk group to develop MDR-TB. Males were predominant from gender point of view. Garment workers, mostly resided in urban area with low level of education were high risk for MDR-TB.

Heavy smoker, have previous contact history with TB patients and history of relapse were in higher risk group. Three-fourth of the patients were living with overcrowding environment. Most of the patients were newly diagnosed. Two-third of the patients were underweight while one-fifth were in normal. Positive health seeking behavior, avoiding pollution and unhealthy lifestyle, adequate nutritional support, strictly maintain DOTS strategy might play as the key factors to prevent and control MDR-TB.

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