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SOCIO-DEMOGRAPHIC AND CO-MORBIDITY STUDY OF TB PATIENTS FROM SELECTED AREAS OF PUNJAB PAKISTAN

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ABSTRACT: The study was carried out to investigate the socio-demographic characteristics and co-morbidity of patients suffering from tuberculosis from selected hospitals of Faisalabad and Lahore, Pakistan. A total of 366 patients were included in the study. The ZN microscopy was carried out along with PCR. The socio-demographic characteristics of each patient were recorded along with any comorbidity. All the patients under study were found positive by ZN staining, while, 258 (70.5%) were found positive by PCR. Of these 258 patients, 52% were females and 48% were males. The 36.8% patients were between 16-30 years, 40% had a body weight between 41-50 Kg, 75.6% were married, 51.9% were uneducated, while 41.8% had education up to ten grades, and 38% were housewives. Tuberculosis alone was present in 36.8% cases, while 63.2% patients had other disease conditions as well. Out of 63.2%, 24% had diabetes, 17.8% had hepatitis virus infection, 11.2% had diabetes and hepatitis (HCV) together, 4.2% had HIV infection, 12.3% had both HIV and HCV infections together and 3.4% had myocardial infarction. Among TB patients 52% were females, 75.6% were married and 51.9% uneducated. The 63.2% patients had comorbidity of which 24% had diabetes, 17.8% viral hepatitis, 4.2% HIV and 3.4% myocardial infarction.

KEYWORDS: Tuberculosis, comorbidity, socio-demography, ZN, PCR.

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1. INTRODUCTION

The tuberculosis is chronic disorder as old as the human history and the Mycobacterium tuberculosis is recovered from Egyptian mummies [1]. WHO reported that Pakistan is ranked 5th among highest tuberculosis burden countries [2] The occurrence of tuberculosis in Pakistan is 181/100,000 populations per year [3].Pakistan is under developing country. The poverty, malnutrition and illness is directly related to each other due to economical constrain [4]. Malnutrition in early ages decreases the immunity that render the undernourished individual and those are more susceptible to infection [5]. Tuberculosis is more linked with congested areas with low income group, low literacy rate and an inadequate health care facilities. So suspects of tuberculosis often remain undiagnosed under such circumstances [6]. The death rate in TB patients also depends on co-morbidity. It is established that occurrence of other diseases in TB patients is cardiac diseases, cancer, diabetes, various infections and toxicity of the drugs [7]. Diabetic patients are more prone to infections, because the high blood glucose levels compromise the immune system [8, 9]. Up to 2% of TB patients can develop cardiovascular diseases [10]. More than 8.6 million (4.8% of the population) Pakistani population are infected with Hepatitis C [11]. Population infected with hepatitis C virus [HCV] have a high incidence of latent to TB infection [12]. Occurrence of Tuberculosis with human immunodeficiency virus (HIV) infections is the main cause of death. The Population of Punjab carrying 57% of the TB burden of Pakistan as Punjab is the largest province of country [13]. Keeping in view, it was an attempt to investigate the socio-demographic facts regarding the magnitude of TB patients and co-morbidities of other disorders in selected pockets of central Punjab, Pakistan.

2. MATERIALS AND METHODS

The study was approved formally by the ethical /synopsis scrutiny committee and finally approved by the Directorate of graduate studies and research board (GSRB) University of Agriculture Faisalabad. The patients coming for diagnosis of tuberculosis in TB hospitals of Faisalabad, DHQ hospital Faisalabad, Gulab Devi Chest Hospital Lahore, DHQ hospital Gojra and District prison Faisalabad were included in the study. The sputum samples were collected then confirmed by ZN staining and PCR. The information about patients was recorded on a specially designed case history performa. All the patients were told about the study and their verbal consent was sought to be included in the study. The Zeihl Nelsen staining was done following the method as described previously [14]. The PCR was performed on sputum samples which were digested and decontaminated using 4% Sodium hydroxide method. DNA extraction was done by Phenol Chloroform method. Direct PCR was performed by

using set of oligonucleotide primers [TB-1F [5' GAACAATCCGGAGTTGACAA 3'; TB-1R [5' AGCACGCTGTCAATCATGTA 3'] which were specific to MPB70 sequence for identification of *M. tuberculosis* complex [15]. The data obtained were analyzed by applying the Chi-Square test by using SAS software [SAS, 2007].

3. RESULTS AND DISCUSSION

Socio-demography of TB patients:

The results of sociodemograpy of patients are presented in Table 1. All the 366 samples collected from suspected TB patients were found positive by ZN staining microscopy (Figure 1), while 258 (70.5%) were found positive by PCR (Figure 2). One hundred and thirty four were females, while 124 were male. TB was significantly higher in patients of age between 16-30 years (36.8%) and patients having the body weight between 41-50Kg (40%). The disease was new in 68.9%, while relapse was reported by 17.4% patients. The results suggest that 9.9 time's higher chances of tuberculosis in married than unmarried. Of the TB patients, 76% had family members between 5 to 10 and 31.8% had a family history of TB. The majority of patients were uneducated (51.9%) or had only education to high school level (41.8%) and had a monthly income between 5000 to 10000 rupees (75.6%). The results showed that house wives (38%) and labourer (24.4%) were in majority followed by students (9.3%). It was further noted that 27.1% patients belonged Rajput clan, 14.7% Jat and the third being the Sheikhs (15.9%) (Table 1).

Co-morbidity: The results revealed that TB alone was present in 36.8% cases and 24% had diabetes also, 17.8% had HCV, diabetes + HCV together was in 11.24% cases, HIV was in 4.2%, HIV+ HCV in 2.3% cases and myocardial infarction was in 3.4% as co-morbidity [Table 2].

DISCUSSION

Ziehl Neelsen's (ZN) staining of sputum smear is the most widely used diagnostic technique for *M. tuberculosis* in developing countries, but it has limitation of the presence of minimum 1000 bacili/ mL of sputum sample [16]. The culture isolation technique is the gold standard method for tuberculosis diagnosis is, but require longer time duration for growth of *M.tuberculosis* isolates [17]. It has been reported by Riaz *et al*. that detection of MTB complex by PCR of clinical sample is most acceptable technique for the early tuberculosis and must be used before starting anti-tuberculus therapy with expensive and toxic drugs [18]. Therefore, in the present study, ZN positive samples were confirmed through PCR. In the present study, PCR analysis showed that 70.5% were found positive by PCR. This study reveals socio-demography of the TB patients and the extent of co-morbidities in two major cities of Pakistan. The result showed no difference in distribution of disease in male and female. Saqib *et al.* reported same proportion of male and female (49.6 and 50.4%, respectively) in Rawalpindi and Islamabad [19]. However, Bates *et al.* and Khattak *et al*. reported more number of males from India and Pakistan because females remained in houses, while the male spend most of times outside and have more chances of contracting the disease [20, 21].

Cadmus *et al*. Filho *et al.* and Towhidi *et al*. found higher tuberculosis rate in people of productive years (20-40) of age [22-24]. However, Al-Kadhimi and Dawood reported that majority of patients were of 60 year of age [25]. The significantly higher number of patients had body weight 41-50 Kg which is lower than normal weight, may be due to TB infection as TNFα effect the appetite in TB patients. The 32.1% patients were diagnosed within 60-90 days after the onset of symptoms, 21.3% were diagnosed within 90 to 180 days and 11.6% within 30 days. Jagodzinski *et al*. obsrved that 31.3% patients were hospitalized within 30 days and 28.3% up to 60 days after the onset of symptoms of TB [26].Frequency percentage of married patients was 75.6% (195/258) compared with the unmarried (24.4%; 63/258). These findings are in agreement with those of Ali *et al*. who reported that and 64.6% were married, respectively [27]. The number of family members also influence the disease distribution as majority of patients had 5-10 family members Sami-ul-Haq *et al*. reported higher TB prevalence in families having 7 to 14 members in Sindh, Pakistan [28]. During present study 31.8% of patients had family history of tuberculosis and higher proportion of patients were uneducated (51.7%). Similarly, Jethani *et al*. also repoted that 95% of patients had family history of disease and found higher number of cases in un-educated (40.8%) [29]. Munsab *et al.* also reported higher number of cases (57.3%) in people with upto primary school education, and less in graduates (3.7%) [30]. The present results showed that 75.6% had medium income (Rs. 5000-10000), 12.4% lower income (Rs. <5000) and 3.1% belonged to the higher income group (Rs. >20000). It has been reported that poverty is linked with disease because of malnourishment, unhygienic lifestyle along with the lack of healthcare facilities, even if diagnosed they afraid to disclose themselves as a TB patient [31].The results showed that 38% were house wives, 24.4% laborers and 9.3% were students. Gupta *et al*. reported higher prevalence of TB patients among labourers (44%), working in offices (27.0%), retired and unemployed (6.3%), household (12%) and students (11%) [32]. In Pakistan, because of its agricultural practices and the use of biomass fuel early marriages, consecutive pregnancies, lactation and malnutrition weaken immunity resulting in higher susceptibility to tuberculosis [33-34]. Furthermore, Munsab *et al*. reported that unskilled workers (36.6%) are more infected than skilled workers (17.06%) [30].The most significant infected ethnic group was Rajput 27.1%, Sheikh and Ansari (15.9%) and Jat (14.7%). The majority of the families of Rajput and Jat belong to land and cattle farming in rural areas with inbreeing may be harbouring suscuptible genes for tuberculosis while, Sheikh and ansari belong to shopkeeping and power looms. The role of genetics need to be explored further to find the link in the occurrence of disease in some ethnic groups.Tuberculosis alone was present in 36.8% cases, while 63.2% cases showed comorbidity with other diseases and 24% cases had diabetes as co-morbidity. These results indicate that tuberculosis alone is rare, most of the time it has some comorbidity. Gldhaber-Fiebert *et al*. and Veswanathan *et al*. also reported a positive association between tuberculosis and diabetes [35, 36]. Jabbar *et al*. also reported a ten time increase in tuberculosis in patients with diabetes in Pakistan

[37]. The results showed that 17.8% patients had HCV as co-morbidity. Richards *et al*. and Sami-ul-Haq *et al*. reported equal number (22%) of TB patients infected with HCV in Georgia and Rahim Yar Khan, Pakistan, respectively [38, 28]. The results of the present study revealed that 4.2% cases had HIV comorbidity. The present results, however, suggest that HIV is not a serious issue in Pakistan because of the social setup of the country. It was observed that 3.4% cases had comorbidity as myocardial infarction. Myocardial infarction is on the increase all over the world and also in Pakistan. Fowler reported that only 1-2% of TB patients showed cardiovascular involvement [39]. Rajesh *et al*. reported 24% occurrence of cardiovascular involvement in TB patients in India [40].

4.CONCLUSIONS

The socio demographic aspects are fundamental and standard tools in population those provide the foundation and to manage the eradication, prevention and control various disease outbreaks. It has been concluded that lower socioeconomic and edu-cultural status, lack of awareness and ignorance of health care systems in urban and rural areas and also the co-morbidities (including diabetes, hepatitis C, HIV and MI) are the basic cause of spread of tuberculosis and noncompliance of anti-tuberculosis treatment. PCR is the most reliable technique should be used for the diagnosis before starting anti-tuberculosis drugs.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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SUPPLEMENTARY FILES

Figure 1; ZN stained smear from the sputum sample, pink colored rods of bacteria against blue back ground.

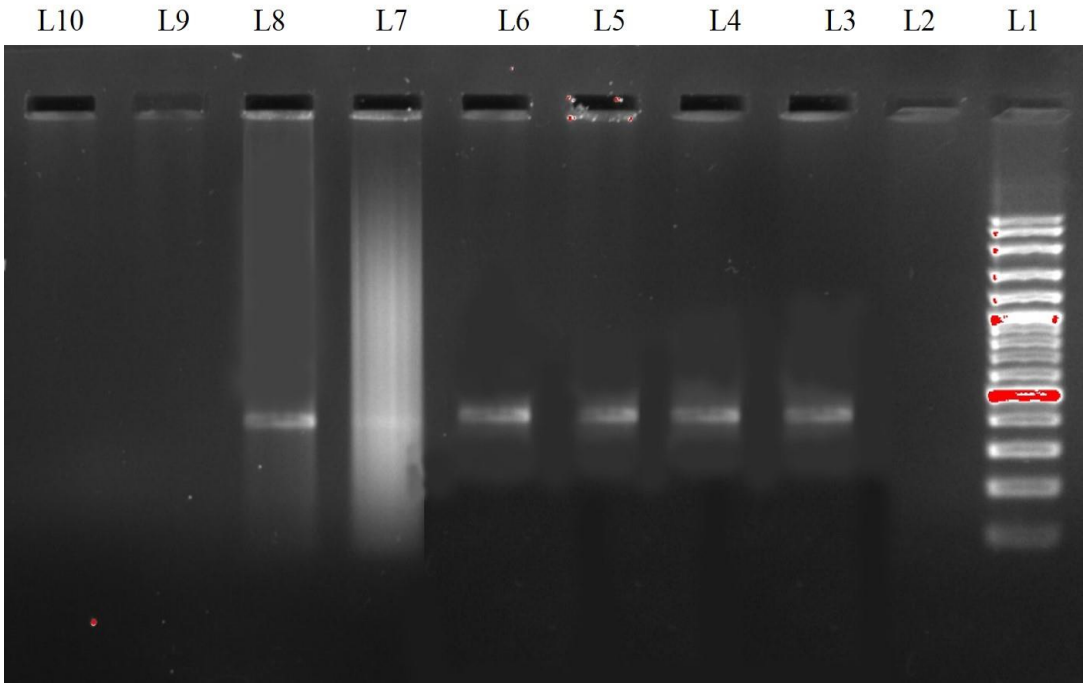

Figure 2: PCR product of *Mycobacterium tuberculosis* complex.

From right to left Lane 1, DNA Ladder; lane 2;Negative control Lane 3 - 8, Positive PCR product; Lane 9,10, Negative PCR product.

Table 1: The results on socio-demographic factors of TB patients

Parameters	No of Cases (N)	Frequency Percentage (%)	95% CI Lower Limit	Upper Limit
PCR				
Negative	108	29.5	25.00	34.34
Positive	258	70.5	65.66	75.00
	Odds Ratio = 0.18; reciprocal = 5.71; P <0.0001			
Gender				
Female	134	52	45.84	58.00
Male	124	48	42.00	54.16
	Odds Ratio = 1.17; reciprocal= 0.86			
Age				
<15 years	8	3.1	1.45	5.80
16-30 years	95	36.8	31.10	42.84
31-45 years	61	23.7	18.76	29.12
46-60 years	61	23.7	18.76	29.12
>60 years	33	12.8	9.12	17.29
	P <0.0001			
Weight (Kg)				
< 20 Kg	6	2.3	0.95	4.77
21-30 Kg	22	8.5	5.56	12.42
31-40 Kg	53	20.5	15.94	25.80
41-50 Kg	103	40	34.07	46.00
51-60 Kg	52	20.2	15.59	25.38
>60 Kg	22	8.5	5.56	12.42
	P <0.0001			
Duration				
< 30 days	30	11.6	8.13	15.98
30-60 days	21	8.13	5.25	11.97
60-90 days	83	32.1	26.68	38.06
90-180 days	55	21.3	16.64	26.63
180-365 days	21	6.2	3.71	9.67
365-730 days	9	3.4	1.71	6.30

>730 days	9	3.4	1.71	6.30
Unknown	35	13.6	9.79	18.16
	P < 0.0001			
Relapse /New				
New	178	68.9	63.15	74.41
Relapse	45	17.4	13.17	22.44
Unknown	35	13.5	979	18.16
	P <0.0001			
Marital Status				
Unmarried	63	24.4	19.47	29.94
Married	195	75.6	70.06	80.53
	Odds Ratio = 0.10; reciprocal = 9.58; P <0.0001			
Family members				
≤5	22	8.5	5.56	12.42
5-10	196	76	70.47	80.89
10-15	27	10.5	7.15	14.66
≥15	13	5.0	2.83	8.25
	P < 0.0001			
Family History of TB				
No Family TB	162	62.7	56.76	68.53
Family TB	82	31.8	26.32	37.66
Unknown	14	5.4	3.12	8.73
	P <0.0001			
Kind of Blood Relation				
Close Relative	69	84.2	75.03	90.89
Life partner	6	7.32	3.02	14.60
Others	7	8.5	3.81	16.16
	P <0.0001			
Education				
Uneducated	134	51.9	45.84	58.00
High School	108	41.8	35.95	47.96
More than High School	9	3.5	1.71	6.30
Professional education	7	2.7	1.19	5.29
	P < 0.0001			
Monthly Income (Rupees)				

≤5000	32	12.4	8.79	16.86
5000-10000	195	75.6	70.06	80.53
11000-20000	23	8.9	5.87	12.87
≥20000	8	3.1	1.45	5.80
	P <0.0001			
Occupation/Profession				
Labor	63	24.4	19.47	29.94
Driver	9	3.4	1.71	6.30
House Wives	99	38	32.21	44.03
Livestock holders	10	3.8	1.99	6.80
Electrician	8	3.1	1.45	5.80
Tailor	12	4.6	2.54	7.77
Student	24	9.3	6.19	13.32
Farmer	11	4.2	2.26	7.29
Beautician	3	1.2	0.30	3.13
Teacher	3	1.2	0.30	3.13
Medical rep	4	1.6	0.49	3.70
Professional	5	1.9	0.71	4.24
No work	4	1.6	0.49	3.70
Shopkeeper	3	1.2	0.30	3.13
	P < 0.0001			
CAST				
Arain	11	4.3	2.26	7.29
Baloch	3	1.4	0.49	3.70
Bari	4	1.6	0.49	3.70
Balore	2	0.78	0.13	2.54
Chris	4	1.6	0.49	3.70
Dogar	8	3.1	1.45	5.80
Gill	15	5.5	3.12	8.73
Gujar	5	1.9	0.71	4.24
Jat	38	14.7	10.79	19.45
Lali	3	1.4	0.49	3.70
Malik	6	2.3	0.95	4.77
Mughal	18	7	4.32	10.60
Pathan	7	2.7	1.19	5.29
Rajpot	70	27.1	21.97	32.80

Rawal	2	0.78	0.13	2.54
Shah	12	4.7	2.54	7.77
Sayed	9	3.5	1.71	6.30
Sheikh	41	15.9	11.81	20.74
	P < 0.0001			

Table 2: The results of comorbid conditions

Parameters	**No of cases (N)**	**Frequency Percentage (%)**	**95% CI Lower Limit**	**Upper Limit**
TB alone	95	36.8	31.10	42.84
TB+Diabetic	62	24.0	19.11	29.53
TB+HCV	46	17.8	13.52	22.86
TB+Diabetes+ HCV	29	11.24	7.80	15.54
TB+ HIV	11	4.2	2.26	7.29
TB+HCV+HIV	6	2.3	0.95	4.77
TB +MI	9	3.4	1.71	6.30