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Comparison of Anti-Tuberculosis Treatment Outcomes of Pulmonary Tuberculosis in Current, Ex and Non Smokers

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Authors' contributions

This work was carried out in collaboration among all authors. Author SKT designed the study and collected the data. Authors MK and AA wrote the protocol and wrote the draft of the manuscript. Authors NAJ and KCL managed the literature searches. Author IAM managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Objective: To detect treatment outcomes in current smokers, ex - smokers and nonsmokers, in newly diagnosed pulmonary TB patients.
Methodology: This cohort prospective study was conducted in the department of Microbiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi, with the collaboration of different (DOTS) centers of Pathology Karachi Medical and Dental College, Karachi. All newly diagnosed pulmonary TB patients registered for treatment either of gender were included. The patients were divided into three groups. Group-A: Current smokers, Group-B: Ex-smokers, Group-C: Non-smokers. Patients were followed for 6 months. Outcome was assessed in

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terms of cured or failure. All the information was enrolled in pre-designed proforma. Data was analyzed by using SPSS version 20.

Results: In current study mean age of non-smokers was 44.20±17.73, ex-smokers 43.13±15.67 years mean age of smokers was 38.07±15.67 years. Males were in majority in all study groups as in ex-smokers group, males were 98.75%, non-smoker males were 90.0% and in smoker group males were 92.50%. At starting of treatment, mean weight of smoker patients was 55.50±5.41 kg, ex-smoker's 48.91±9.00 kg and mean weight of non-smokers 48.71±7.04 kg. P-0.001. At starting of treatment, the mean ESR of non-smokers was 89.31±10.02, ex-smoker's was 82.62±12.18 and smokers ESR average was 80.61±15.83. P-0.001. After 6 month treatment, cured rate was (96.25%) in non-smokers, (90%) in smokers and (93.75%) in ex–smokers.

Conclusion: This study concluded that cured rate was high in non-smokers. Smoking status in individuals greatly affects the tuberculosis treatment outcome with enhance failure rate.

Keywords: Tuberculosis; treatment; smokers; ex-smokers; non-smokers.

1. INTRODUCTION

Tuberculosis (TB) is an ancient disease that has evolved along-with mankind for many centuries, it is a major global health problem and proved to be the second most common cause of death from an infectious disease, after HIV [1]. It is transmitted through inhalation of air droplets from coughing or sneezing of infected person. Tuberculosis primarily involves the lungs but can affect other parts of conducting airways that includes larynx, trachea and bronchus [2]. Various strains of Mycobacteria are found to be causative agents of this deadly disease [3]. Global prevalence of TB reached to about 8.7 million newly diagnosed cases and 1.4 million deaths in 2012 [4]. Developing countries of South Asia are severely affected with increasing disease burden of TB. Prevalence of TB in Pakistan is around 181 cases per 100,000 population and with each passing year the number is increasing [2]. Tuberculosis is also the third most common cause of morbidity and mortality with poor nutritional status in the mothers of reproductive age. Newly infected individuals may present in one of the two forms, either symptomatic infectious state, called active TB, or an asymptomatic, noninfectious state called latent TB infection (LTBI). Majority of the population has LTBI, although it is a symptomless state but it can transform into active state at any time. Furthermore, active TB can either affect the lungs only causing pulmonary TB or can spread to other organs leading to development of extra pulmonary TB [1]. Around 90% of cases are affected by pulmonary tuberculosis. However, 15-20% of cases of active pulmonary TB progress into extra pulmonary TB. Young children and immunocompromised individuals are more prone to develop extra pulmonary TB [5]. Prevalence of extra pulmonary tuberculosis ranges between 15-20% in Pakistan [2]. Traditionally, tuberculosis can also be divided into primary or post primary disease, Primary tuberculosis occurs on the first contact between host and tubercle bacillus, this mostly occurs in childhood but can develop at any age in those who are not previously exposed to tuberculosis. Post primary tuberculosis mostly developed in an adult who have normal immune response. It usually occurs due to reactivation of primary infection after several years of dormancy. Post primary tuberculosis usually affects lungs especially upper lobe with cavitations and damage of lung tissue but usually does not affect regional lymph nodes or any other organ [6]. After the exposure to infection the development of acute pulmonary tuberculosis follow any of the two stages. Either it rapidly progress to active disease or remain dormant to be reactivated by some risk factors. Both stages are controlled by two types of risk factors. These may be exogenous or endogenous. The exogenous risk factors include proximity to infected individual, indoor air pollution, social and behavioral risk factors like alcohol and smoking. The healthcare workers and household contacts are more prone to get *Mycobacterium tuberculosis* (MTB) infection due to close contact [7]. Poor housing, food insecurities, financial difficulties and illiteracy are some other exogenous risk factors which also contribute to the occurrence of TB [8]. The endogenous risk factors are host related that increases the progression of infection. Among them immunosuppressive states like Diabetes mellitus, chronic renal failure, malnutrition and also co-morbid infections like HIV, Hepatitis C virus are well established factors, also children and old age individuals, are more likely to be infected with pulmonary tuberculosis [9]. The causative organisms of tuberculosis include various members of *Mycobacteria tuberculosis*

complex (MTBC). This complex includes a group of species and subspecies that comprises the human and animal pathogens [10]. The important member of MTBC is the *Mycobacterium* tuberculosis, which is the most common cause of TB in humans. Mycobacterium tuberculosis is an obligate aerobe and facultative parasite, pathogenic to human being, which resides intracellularly in alveolar macrophages [11]. Pulmonary TB is diagnosed by various methods which either may be clinical, radiological, immune-serological (both antigen and antibody detection) or microbiological. The bacteriological diagnosis may be by direct or indirect method. Direct methods are more reliable and accurate than indirect, and these include smear microscopy, histological examination, culture isolation and molecular methods. Indirect methods include Monteux test and interferon gamma release assay (IGRA) [12]. According to WHO suggestions for TB, prevention, control, routine surveillance and direct observed treatment short course (DOTs) is mandatory for its eradication. Regarding the treatment of TB, the aim of the TB programme is to successfully treat all patients started on its treatment. This can only be achieved by ensuring good compliance to treatment. TB is curable if patients take a complete and uninterrupted course of the appropriate drug therapy along with the preventive measures. Patient related factors which cause treatment failure include depression, poor knowledge about TB and efficacy of treatment, smoking and alcohol intake. Other factors such as aspects of poor or unknown medicine quality, inadequate drug therapy, shortage of availability of drugs with interrupted supplies, inadequate patients follow-up, poverty, malnutrition, lack of social mobilization have all contributed to the emergence of drug resistant strain of mycobacteria. Regarding the role of smoking in TB development and its effects on TB treatment outcomes has been a major public health problem throughout the world, it is estimated that people who smoke have approximately twice the risk of both Mycobacterium tuberculosis infection and active tuberculosis [13]. It has long been suggested that smoking works as a major factor which affect rates of TB morbidity and mortality. However, data on the role of smoking on treatment outcomes among patients with tuberculosis is inadequate [14]. This study has been conducted to assess treatment outcomes in current smokers, ex - smokers and nonsmokers, in newly diagnosed pulmonary TB patients.

2. MATERIALS AND METHODS

2.1 Place of Study

This cohort prospective study was conducted in the department of Microbiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi, with the collaboration of different DOTs centers and chest ward of JPMC, Karachi Medical and Dental College, Karachi during one year from 2018 to 2019. All the newly diagnosed pulmonary TB patients registered for treatment in the above mentioned centers, age more than 15 years and either of genders was included. All the diabetic patients and having other sever and chronic co-morbidities including those, who did not want to participate in the study were excluded. After taking informed consent all the patients were divided into three groups.

Group-A: Current smokers (n=80)
Group-B: Ex-smokers (n=80)
Group-C: Non-smokers (n=80)

Initial base line details of the patients such as age, sex, Sputum smear, *Mycobacterium* tuberculosis status, chest x-ray findings and other relevant details pertaining to TB was recorded. After informed consent data will be obtained, from all patients, those who are confirmed diagnosed case of pulmonary tuberculosis.

2.2 Self-Reported Status of Patient (Questioner)

- Self-reported current smoking status? Yes / No
- Self-reported previous smoking status? Yes / No
- Number of cigarettes smoked per day.
- When started or quit smoking.

3. RESULTS

In current study mean age of non-smokers was 44.20±17.73 years, followed by ex-smoker's mean age was 43.13±15.67 years and smoker's mean age was 38.07±15.67 years. Males were commonest in all study groups as (98.75%) males were in ex-smokers group, (90.0%) males were in non-smokers group and (92.50%) males were in smokers group. However most of (10.0%) females were found smokers, (7.50%) females were non-smokers and only (1.25%) females were ex-smokers (Table 1).

At starting of treatment, average weight of smokers was high 55.50±5.41 kg in contrast to ex-smokers as 48.91±9.00 kg and non-smokers as 48.71±7.04 kg (p=0.001). At starting of treatment, the mean ESR of 89.31±10.02 was found most high in non-smokers group, while ex-smokers its average was found 82.62±12.18 and in smokers was 80.61±15.83 (p=0.001) (Table 2).

At starting of treatment, 1+ was found in 35 cases of non-smokers, 14 ex-smokers and 05 cases smokers, while 2+ was seen in 25 cases of non-smokers, 10 smokers and 28 ex-smokers. However, 3+ was seen highest among 65 smokers, followed by 20-non-smokers and 38 ex-smokers. At starting of treatment, cavitation was most common among ex-smokers 26.25% as compare to 25.0% smokers and 17.50% non-smokers. While infiltration was most common among 63(78.7%) non-smokers as compare to 57(71.2%) ex-smokers and 56(3.7%) smokers. However, P/effusion was found 5.0% in smokers, 1.25% in non-smokers and 2.5% among ex-smokers (p=0.001) (Table 3).

According to outcome comparison after 6 month treatment, Cured rate was 77 (96.25%) in nonsmokers, 72(90%) in smokers and 75(93.75%) in ex –smokers. Failure rate were 3(3.75%) non-smokers, smokers 8(10 %) and 5(6.25%) ex–smokers (Table 4).

Table 1. Cases distribution according to age and gender at starting of treatment n=240

Variables	Non-smokers	Smokers	Ex-smokers	P-value
Age				
(Mean±SD)	44.20±17.73	38.07±15.67	43.13±15.02	0.040
Gender				
Female	20(25%)	8(10%)	6(7.5%)	0.076
Male	60(75%)	72(90%)	74(92.5%)	
Total	80(100%)	80(100%)	80(100%)	

Table 2. Mean weight and ESR comparison among study groups at starting of treatment n=240

Variables	Non-smokers	Smokers	Ex-smokers	P-value
Weight Kg	55.50+7.04	48.71+5.41	48.91+9.00	0.001
ESR	60.31+10.02	82.61+15.83	81.62 +12.18	0.001

Table 3. Sputum-AFB and X-ray comparison among study groups at starting of treatment n=240

Variables	Study group			P-value
	Non-smokers	Smokers	Ex-smokers	
Sputum-AFB				
1+	35(43.75%)	5(6.25%)	14(17.5%)	
2+	25(31.25%)	10(12.5%)	28(35%)	0.012
3+	20(25 %)	65(81.25%)	38(47.5%)	
Total	80(100%)	80(100%)	80(100%)	
CXR				
Cavitation	14(17.5%)	20(25%)	21(26.25%)	
Infiltration	63(81.25 %)	56(70%)	57(71.25%)	0.001
P/effusion	3(03.75%)	4(5%)	2(2.5%)	
Total	80(100%)	80(100%)	80(100%)	

Table 4. Outcome comparison among study groups after 6 months treatment n=240

Outcome	Study group			P-value
	Non-smokers	Current smokers	Ex-smokers	
Cured	77(96.25%)	72(90%)	75(93.75%)	0.001
Failure	03(3.75%)	08(10%)	05(06.25%)	

4. DISCUSSION

On global perspective among many other diseases, tuberculosis is the leading cause of morbidity and mortality. Tobacco smoking is affecting one fifth of the world's population with higher prevalence in TB affected regions [15]. Multiple reports show that smoking is not only a well-known risk factor for development of TB but is also found to be affect TB therapy by increasing Infectivity and delayed sputum conversion. In this study, the weight of the patients after two months of anti TB treatment was found to increase from the weight at the start of treatment as; approximate weight gain of 2 kg in non-smoker 57.16%, current smokers 49.5% 1.9 kg and 50.38% 2 kg in ex-smokers. This finding is covered by a study done by Aziza R et al. [16] as according clinical assessment there was 91.1% patients of TB (non-smokers) showed weight gain between 2 to 5 kg in contrast to in 35.3% of smokers. After 6 months of treatment, the nonsmoker group experienced more weight gain (63.83±6.92 6 kg than smokers and ex-smokers (mean 5 kg weight gain (55.47±5.19 5 kg, 54.10±7.67 6 kg respectively), indicating more positive outcome of anti TB treatment in nonsmoker group of this study.

In this study we found that at starting of treatment, sputum positivity of 3+ was higher in smoker group 65 subjects (81.25%) as compared to ex-smokers 38(47.5%) and nonsmokers 20(25%). Furthermore, after 2 and 6 months of treatment, frequency of 3+ sputum positivity was still higher in smokers as compared to other groups, indicating the adverse effects of smoking on patient's condition and also on treatment effectiveness. In accordance with our finding, Leung et al. [17] also reported that sputum was found to remain positive after 2 months of treatment in smokers and ex-smokers as compared to non-smokers. Regarding the findings of CXR, cavitation and infiltration was seen mostly in smokers and ex-smokers in comparison to nonsmokers at the initiation of treatment. These lesions healed significantly in nonsmokers (93.75%) after 2-6 months of treatment but only 75% smokers and 88.75% ex-smokers showed healed scars. Aziza R et al. [16] in their study also concluded that the smoker subjects had more generalized lesions as compared to nonsmokers who had only one type of lung lesion after 2-6 months of treatment. We performed Gene Xpert method for diagnosis of TB in our 3 groups of 80 Subjects each. We found that gene expert was able to detect TB in all the patients (100%) of each group. On the contrary, microscopy showed Sputum 3+ positivity in only 65(63%) smokers, 38(47.5%) ex-smokers and 20(25%) nonsmoker per 80 subjects. Hence, the aptitude of gene Xpert for diagnosing tuberculosis came out to be higher than microscopy. Our findings have been confirmed by a study conducted by Shah W et al. [18] who observed that GeneXpert is more accurate and reliable than sputum smear microscopy in predicting pulmonary as TB sensitivity of gene expert around 97.83% as compared to only 68.48% of sputum microscopy.

In this study the treatment success rate was found to be 77(96.25%) in our nonsmoking group after 6 months of anti-tuberculosis treatment while 72(90%) in smoker and 75(93.75%) in the ex-smoker group were cured. Hence, the treatment failure rate was highest in smokers with 8(10%) followed by ex-smokers 5(6.25%) and in nonsmokers 3(3.75%) with a significant p-value of 0.001. on other hand Chaung H et al. [19] reported the higher failure rate of TB treatment around (33%) and there was most severe pulmonary lesions seen chest X-ray. Khan AH et al. [20] also observed that the smoking had a strong influence on the tuberculosis and a significant barrier towards treatment success. Aguilar JP et al. [21] found in their study that treatment failure risk was 2.1 times more among smokers. In the light of these observations it can rationally be speculated that relation of smoking with treatment failure could be due to the chemical contents of smoke which have deleterious effects on defense mechanisms of host. The host immunity is required to control the multiplication of TB bacilli by production of nitric oxide by alveolar macrophages [13]. Other mechanisms which are disturbed due to nicotine content of smoke include TNF-alpha production [22], reduced IFN-γ production by T cells [23] and reduced pulmonary surfactant protein production, hence decreasing host immunity against Mycobacterium TB. However Altet N et al. [24] also observed the link between tobacco smoking and tuberculosis due to a weakened IFN-γ response due to the direct tobacco smoking.

5. CONCLUSION

This study concluded that smoking status in individuals greatly affects the tuberculosis treatment out come with enhance failure rate. Also, decreases incidence of failure in ex-smokers indicating the improved immunological

conditions of these individuals. Therefore, it is recommended that increased number of smoking cessation program can play imperative role in reducing generalized tobacco use among individuals. Furthermore, in a low resource country like; Pakistan, integration of smoking cessation interventional program along with the TB control programs at national level would support and enhance the effectiveness of both TB eradication without extra finical burden on the community and country. Male smokers should be given distinctive consideration, as they constitute a major part of total TB patients and smokers globally.

CONSENT

Written informed consent was taken from all participants to carry out the study.

ETHICAL APPROVAL

This study will be carried out after the approval from the hospital ethical committee, JPMC Karachi.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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