ORIGINAL ARTICLE

Glycemic Control and Clinical Outcomes of Diabetic Pulmonary Tuberculosis Patients

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ABSTRACT

Aim: To investigate the role of glycemic control in clinical outcome of smear positive pulmonary tuberculosis patients who also had diabetes.

Methods: This prospective multicenter study was conducted in Pulmonology Department of Sheikh Zayed Hospital, Rahim Yar Khan, Services Hospital, Lahore and Bahawal Victoria Hospital, Bahawalpur. From July 2014 to June 2016 after taking approval from ethical committee of the Hospital. Total 280 patients who also had diabetes were enrolled in study by non-probability consecutive sampling. They were divided in two groups. One group having good glycemic control (HbA1C<7%) and second group having poor glycemic control (HbA1C>7%). Written permission was signed by each patient recruited in study. Quantitative variables like age, body mass index, smoking pack years, blood glucose level, glycosylated hemoglobin level and hemoglobin were statistically measured and analyzed in mean and standard deviation and t-test was applied to check the significance. Qualitative variables like gender, income, smoking status and glycemic control were statistically measured and analyzed in frequency and percentage and chi-square test was applied to check the significance.

Results: Among total 280 patients on radiographic examination, cavitary lesions were noted in 136(78.6%) and 43(40.2%) patients for PGC and OCG groups respectively. It was found that, cavitary lesions were more frequently occurred in patients with PGC. Therefore, the difference was statistically significant. (χ^2 =42.33, p=0.000). At the end of the intensive phase of therapy, majority of the patients i.e., 87(50.3%) with PGC remained smear-positive compared to OGC patients i.e. 13(12.1%). This difference was statistically significant (χ^2 =41.88, p=0.000). As far as treatment outcome; 120(69.4%) and 100(93.5%) patients were observed as cured in PGC and OCG groups respectively. This difference was also statistically significant. (χ^2 =22.79, p=0.000).

Conclusion: Poor glycemic control before treatment of pulmonary tuberculosis can be associated with poor clinical outcome in the form of lung cavitations and delayed sputum smear conversion. It is also associated with more relapse in tuberculosis.

Keywords: Diabetes mellitus, Pulmonary tuberculosis, Glycemic control

INTRODUCTION

Diabetes mellitus is accelerating pandemic disease[1]. It is a metabolic disorder. Insulin deficiency and insulin resistance are main pathology in diabetes mellitus. It had been estimated that approximately 230 million people of the world are suffering from diabetes that can increase up to 552 million people until 2030[2]. A total expenditure of 471 billion US dollars was recorded in 2012[3]. It is one of the bigger socio economic burden for the developing countries. This is an alarming situation that in last two decades, prevalence of diabetes has risen. Prevalence of diabetes in Pakistan was ranging from 7.6% to 11% and it can reach up to 15% (14 million) until 2030[4]. On basis of diabetes prevalence, Pakistan is number 7 in list and it is expected that it will be number 4 in the list in prevalence of diabetes in urban population is 22.04% and 17.15% in rural population in Pakistan[5]. Health care system of Pakistan is under resourced and overburdened in dealing with this situation. A national effort is required in not only treating but more on preventing the diabetes mellitus. Diabetes is associated with many complications. Like cardiovascular disease due to diabetes is main cause of deaths and premature illness[6]. Main cause of blindness and renal failure is also diabetes. It is also associated with amputations due to diabetic foot development.

World Health Organization has reported that eight highest burden countries of diabetes also have highest burden of tuberculosis[7]. Patients suffering from pulmonary tuberculosis usually present with complaints of fever, loss of appetite, weight loss, cough and hemoptysis. Diabetes mellitus is well known risk factor for tuberculosis[8]. Developing countries like Pakistan, India, Bangladesh and Brazil, burden of diabetes and tuberculosis and interaction

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between them will be more concerning. World Health Organization has declared diabetes and tuberculosis global epidemic[9]. To deal with this situation, World Health Organization and International Union against Tuberculosis and Lung disease have proposed a framework to control and care diabetes and tuberculosis[10].

This study was planned to investigate the role of glycemic control on clinical outcome of pulmonary tuberculosis patients suffering from diabetes. It is great challenge across the world to treat and prevent both diabetes and tuberculosis. It is very important to understand the association between these two diseases so that any information can be used to control and prevent these diseases locally. So this study will help to establish the facts locally and will educate and encourage further research. Study done by Chen Yuan Chiang et al. was taken as reference study[11].

MATERIALS AND METHODS

This prospective multicenter study was conducted in Pulmonology Department of Sheikh Zayed Hospital, Rahim Yar Khan, Services Hospital, Lahore and Bahawal Victoria Hospital, Bahawalpur from July 2014 to June 2016 after taking approval from ethical committee of the Hospital. Total 280 patients who also had diabetes were enrolled in study by non-probability consecutive sampling. They were divided in two groups. One group having good glycemic control (HbA1C<7%) and second group having poor glycemic control (HbA1C≥7%). Written permission was signed by each patient recruited in study. Exclusion criteria of study were following: 1) patients who had taken anti tuberculosis drugs previously, 2) patients with HIV infection, 3) patients with history of connective tissue disorders, 4) patients with renal failure, 5) patients with history of liver disease, 6) patients with pregnancy, 7) patients with any malignancy, 8) patients with history of taking any steroids or cytotoxic drugs, 9) patients with clinical and radiological suspicion of tuberculosis but sputum smear were negative and 10) patients who were chronic alcoholics. For the study sample size was calculated by using a reference study done by ChenYuanChiang et al. for which confidence interval was taken as 95%, study strength 80, and odd ratio for unfavorable outcomes 3.38 in patients with poor glycemic control[11].

Patients in this study were recruited from outpatient department. All the patients who were known diabetics and presented in outdoor with compatible history of tuberculosis like cough, fever, weight loss, hemoptysis, loss of appetite and dyspnea were advised for sputum smear examination. Patients with one or more sputum smear positive for acid fast bacilli were enrolled in study. Detailed clinical history was taken regarding, duration of diabetes, duration of symptoms, their association and any history of drug or pervious hospital admission was recorded. Clinical examination was conducted in each patient to check the complications of diabetes and tuberculosis, also to check any sign of other systemic disease. Vitals were recorded at the time of diagnosis. Personal information like age, gender, body mass index, any drug history, smoking status, history of alcohol, living area and income were recorded by filling the Performa.

Venous sample was taken from each patient in sitting position and hemoglobin, blood sugar level and glycosylated hemoglobin level were evaluated. All patients with smear positive tuberculosis and diabetes were advised chest radiography. X ray lesions were classified according to American Thoracic Society criteria by one pulmonologist and one radiologist into mild, moderate, advanced and very advanced lesion. Each symptom such as fever, cough, weight loss, loss of appetite, dyspnea and hemoptysis was given one score each. Total 0-6 score was calculated in each patient depending upon the presence of symptoms. Patients with score ≥4 were considered as having high symptomatic disease. All the patients were followed for 2 years after initiation of treatment. At the end of treatment, clinical, radiological features, sputum conversion after 2 months, relapse rates and cure rates were compared between patients with good glycemic control and patients with poor glycemic control.

Data was statistically analyzed by using SPSS volume 23. Quantitative variables like age, body mass index, smoking pack years, blood glucose level, glycosylated hemoglobin level and hemoglobin were statistically measured and analyzed in mean and standard deviation and t-test was applied to check the significance. Qualitative variables like gender, income, smoking status and glycemic control were statistically measured and analyzed in frequency and percentage and chi-square test was applied to check the significance. p value ≤0.05 was kept as significant.

RESULTS

Overall, 280(100%) patients were included, in this study. There were 173(62%) patients had HBA1c (poor glycemic control, PGC) level≥7% and 107(38%) patients had HBA1c (optimal glycemic control, OGC) level<7%. The Mean±S.D age and BMI of the patients of PGC group was 51.26±2.32 years and 22.03±2.38 kg/m^2 respectively. While, the Mean±S.D

age and BMI of the patients of OCG group was 47.81±3.27 years and 19.88±3.12kg/m^2 respectively. Gender distribution, in PGC group, was observed as 112(64.7%) males and 61(35.3%) females, while, in OGC group, there were 71(66.4%) males and 36(33.6%) females. There were 57(32.9%) and 20(18.7%) smokers in PGC and OGC group respectively. Diabetic status of PGC group was observed as 48(27.7%) new and 125(72.3%) old. However, in OGC group, there were 44(41.1%) new and 63(58.9%) old. The differences were statistically significant between age (p=0.000), BMI (p=0.000), diabetic status (p=0.021) smoking status (p=0.009) except gender (p=0.783), in groups (Table 1).

On radiographic examination, cavitary lesions were noted in 136(78.6%) and 43(40.2%) patients for PGC and OCG groups respectively. Noted that, cavitary lesions more frequently occurred in patients with PGC. Therefore, the difference was statistically significant. (χ^2 =42.33, p=0.000). (Table.2).

At the end of the intensive phase of therapy, majority of the patients i.e., 87(50.3%) with PGC remained smear-positive compared to OGC patients i.e., 13(12.1%). This difference was statistically significant (χ^2 =41.88, p=0.000) (Table 3).

As far as treatment outcome; 120(69.4%) and 100(93.5%) patients was observed as cured in PGC and OCG groups respectively. This difference was also statistically significant. (χ^2 =22.79, p=0.000) (Table 4).

Table 1: Demographic characteristics of PTB patients in both the optimal and poor control groups

Characteristics	PGC* (n=173)	OCG* (n=107)	Test of Sig.
Age	51.26±2.32 years	47.81±3.27 years	t=10.31, p=0.000
BMI*	22.03±2.38 kg/m^2	19.88±3.12 kg/m^2	t=6.49, p=0.000
Gender	M=64.7%, F=35.3%	M=66.4%, F=33.6%	χ^2 =0.076,p =0.783
Smoking Status	Smokers=32.9 %	Smokers=18.7 %	χ^2 =6.74,p= 0.009
Diabetic Status	New=27.7%,Old=72.3%	New=41.1%,Old=58.9%	χ^2 =5.36,p= 0.021

*PGC: Poor glycemic control; *OGC: Optimal glycemic control: body mass index

Table 2: Types of lesions on CXR

Types of lesions	PGC*	OCG*	Total	P-value
Cavitary	136(78.6%)	43(40.2%)	179	0.000
Noncavitary	37(21.4%)	64(59.8%)	101	
Total	173(100%)	107(100%)	280	

*PGC: Poor glycemic control; *OGC: Optimal glycemic control

Table 3: Sputum conversion at 2 months

Sputum at 2 months	PGC*	OCG*	Total	P-value
Positive	87(50.3%)	13(12.1%)	100	0.000
Negative	86(49.7%)	94(87.9%)	180	
Total	173(100%)	107(100%)	280	

*PGC: Poor glycemic control; *OGC: Optimal glycemic control

Table 4: Treatment Outcome (cured or failure)

Outcome	PGC*	OCG*	Total	P-value
Cured	120(69.4%)	100(3.5%)	220	0.000
Failure	53(30.6%)	7(6.5%)	60	
Total	173(100%)	107(100%)	280	

*PGC: Poor glycemic control; *OGC: Optimal glycemic control

DISCUSSION

Results of this study had shown that poor glycemic control HbA1C ≥7% in diabetic patients were higher in percentage with symptoms and positive smear. Best of our information, this is first study in South Punjab of Pakistan, which demonstrated that clinical outcomes of pulmonary tuberculosis are associated with pre-treatment HbA1C in patients who had also diabetes mellitus. Results of study also reported that diabetes mellitus had its influence on the final outcome of pulmonary tuberculosis treatment and it was related to HbA1C level before treatment. The results of this study are almost equivocal to another study done by Chiang et al[11]. They reported that diabetic patients with poor glycemic control had higher percentage of patients with any complaint like cough, weight loss, hemoptysis and dyspnea. And these patients with poor glycemic control had more chance of to remain smear positive after completion of intensive phase of anti-tuberculosis therapy.

Similarly, another study done by Leung et al[12]. Reported that diabetic patients were more likely to be sputum culture positive after two months' therapy as compared to non-diabetic patients, and this was associated significantly with level of hba1c. Our study extends and compliments the findings of recently published study by Vinay Mahishale et al[1]. They concluded that poor glycemic control is associated with more relapse rates in pulmonary tuberculosis patients. They also found that risk of advance and more sever pulmonary tuberculosis in the form slower smear conversion, lung cavitations and positive sputum smear. Study done by María Eugenia Jiménez-Corona et al. also supports finding of this investigation[13]. They published that prevalence of diabetes mellitus among tuberculosis patients was 29.63% and diabetic patients with pulmonary

tuberculosis had sever clinical manifestations in form of high rate of treatment failure, delayed sputum conversion and higher rate of relapse and recurrence. Study by Park et al. reported equivocal results[14]. It is important to mention the very interesting analysis of Webb et al[15] in tuberculosis patients with diabetes who had higher level of mean HbA1C in comparison to diabetic patients without tuberculosis. They reported that among diabetic patients with poor glycemic control, contact with tuberculosis source along with per unit increase in HbA1c level was associated with more prevalence of tuberculosis. This study also supports the results of study by Chiang et al[16].

With these results many studies have recommended screening of diabetes mellitus in all pulmonary tuberculosis patients on all health facilities[17]. World Health Organization global tuberculosis report in 2013 have published that in spite of progress in many aspects of controlling tuberculosis, the speed is too slow with only 2% decrease in tuberculosis per year[18,19].

The relationship between diabetes mellitus and sputum culture remaining positive even after treatment of tuberculosis for two to three months had been investigated previously but results were inconsistent[20]. Strength of this study was that study design was prospective and also HbA1C levels of all diabetic patients were available which facilitate to draw a clear relationship between pulmonary tuberculosis clinical outcome and poor glycemic control.

There were limitations of this study. First, it was single centre study and its results cannot be generalized. Second, it did not investigate the probable relationship between poor glycemic control and multi drug resistant tuberculosis.

CONCLUSION

Poor glycemic control before treatment of pulmonary tuberculosis can be associated with poor clinical outcome in the form of lung cavitations and delayed sputum smear conversion. It is also associated with more relapse in tuberculosis. So optimal glycemic control is necessary to achieve good clinical outcomes in pulmonary tuberculosis.

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