OUTCOMES OF SPUTUM POSITIVE PULMONARY TUBERCULOSIS IN PATIENTS WITH DIABETES MELLITUS – A PROSPECTIVE OBSERVATIONAL COHORT STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF M.D. GENERAL MEDICINE BRANCH I EXAMINATION OF THE TAMIL NADU DR. M.G.R. UNIVERSITY, CHENNAI TO BE HELD IN MAY 2019

CERTIFICATION

This is to certify that the dissertation "Outcomes of sputum positive pulmonary tuberculosis in patients with diabetes mellitus – a prospective observational cohort study" is a bonafide work of Dr. John Titus George carried out under our guidance towards the M.D. Branch I (General Medicine) Examination of the Tamil Nadu Dr. M.G.R. University, Chennai to be held in May 2019.

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DECLARATION

This is to certify that the dissertation titled "Outcomes of sputum positive pulmonary tuberculosis in patients with diabetes mellitus – a prospective observational cohort study" which is submitted by me in partial fulfilment towards M.D. Branch I (General Medicine) Examination of the Tamil Nadu Dr. M.G.R. University, Chennai to be held in May, 2019 comprises my original research work and information taken from secondary sources have been given due acknowledgement and citation.

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Lastly, I would like to thank God, my family and friends for their support and help throughout the duration of the study.

John Titus George

October 2018

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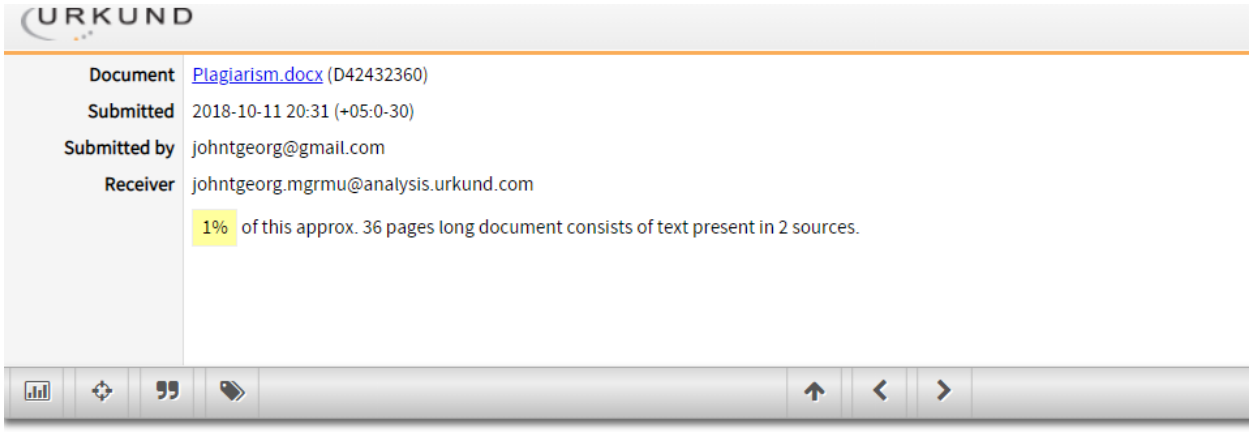
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ABSTRACT _____

Background: India is the diabetic capital of the world with 8.7% of the population having diabetes mellitus. (1). India also has a high burden of Tuberculosis (TB) and this amounts to significant mortality and morbidity. Diabetes mellitus (DM) has a negative impact on innate and adaptive immune responses which may impact treatment outcomes in patients with TB like cure rates, relapse rates and mortality. In this study we aim to study the clinical characteristics of diabetic patients diagnosed with tuberculosis, their sputum smear conversion rates and the treatment outcomes. We also wish to look at the relationship between glycaemic control and treatment outcomes of TB.

Methodology: In this prospective observational cohort study, 125 patients with sputum positive Tuberculosis were recruited. Among these, 68 patients (55 %) had diabetes mellitus and 56 patients (45%) were non-diabetics. They were followed up for a total duration of 6 months. Baseline anthropometric data was documented along with sputum AFB smear, AFB culture, Gene Xpert, glycosylated Haemoglobin and blood glucose levels. They were followed up at 2 months when sputum AFB smears and blood glucose levels were repeated. Those with sputum AFB smear positivity were followed up monthly till negative sputum smears were documented. At 6 months sputum AFB smear, AFB culture, Gene Xpert, glycosylated Haemoglobin and blood glucose levels were repeated. Treatment outcomes in terms of time to conversion of Sputum smears, mortality and cure rates were compared between the two groups. Results: We recruited 124 patients of which 68 were diabetic and 56 did not have diabetes. 11 patients (9%) of the patients were sputum positive at 2 months, among whom 6 were diabetics and 5 were non-diabetics. We demonstrated that smoking, Chronic Obstructive Pulmonary Disease, high bacillary load and the presence of fibrocavitatory lesions were associated delayed sputum conversion. We could not demonstrate an association between delayed sputum conversion and diabetes and poor glycaemic control. We also demonstrated a significant reduction in HbA1c after 6 months of Anti tuberculous therapy in the diabetic group [Mean difference – 1.76, 00195% CI of difference – (1.01 – 2.52) p value – 0.001]. There was no treatment failure recorded in our study. 57 % in the DM group and 50 % in the NDM group were

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India is the diabetic capital of the world with 8.7% of the population having diabetes mellitus.(1). India also has a high burden of Tuberculosis (TB) and this amounts to significant mortality and morbidity. Diabetes mellitus (DM) has a negative impact on innate and adaptive immune responses which may impact treatment outcomes in patients with TB like cure rates, relapse rates and mortality. In this study we aim to study the clinical characteristics of diabetic and non-diabetic patients diagnosed with tuberculosis their sputum smear conversion rates and the treatment outcomes. We also wish to look at the relationship between glycaemic control and treatment outcomes of TB.

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Conclusions: In this study, we demonstrated that Diabetes was not associated with poor outcomes in patients with pulmonary TB. There was also no association between DM and delayed sputum conversion. We also could not demonstrate any association between poor glycaemic control and delayed sputum conversion or mortality.

Keywords: Pulmonary Tuberculosis, Diabetes Mellitus, Outcomes

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacterium Mycobacterium tuberculosis. While it typically affects the lungs, it can affect virtually any part of the body. TB spreads from person to person by droplet method of transmission. (2)

TB is the leading cause of death due to an infective disease in the world(3). Active TB develops in hosts with impaired immunity and in people with increased exposure to patients with active tuberculosis.

Diabetes Mellitus (DM) is a chronic, non-communicable disease. Diabetes occurs when the body either cannot produce enough of the hormone insulin, or it is not able to use insulin effectively. Type 2 diabetes, is a condition where the body does not use insulin properly, resulting in elevated levels of glucose in the bloodstream. Diabetes mellitus has been shown to confer a threefold increased risk of developing TB.

The prevalence of diabetes is increasing, especially in the Asian countries, where the prevalence of TB is also on an upward trend. Globally, 70% of those with DM are in TB endemic regions. Diabetes mellitus has a negative impact on innate and adaptive immune responses which may impact treatment outcomes in patients with TB like cure rates, relapse rates and mortality. (7–12) This interplay between DM and TB is a complex one and if unchecked, could have disastrous consequences. In this study we aim to study the clinical characteristics of diabetic and non-diabetic patients diagnosed with tuberculosis their sputum smear conversion rates, treatment outcomes and the factors that affect them.

AIMS AND OBJECTIVES

Aim:

To study the outcomes of pulmonary tuberculosis among patients with diabetes mellitus.

Primary Objectives:

1. To study the cure rates of diabetic patients with pulmonary Tuberculosis
2. To assess sputum conversion rates among diabetic patients with pulmonary Tuberculosis and the time to clinical recovery
3. To identify the determinants of treatment outcomes of pulmonary Tuberculosis

Secondary Objectives:

1. To assess the effects of glycaemic control on treatment outcomes of sputum positive pulmonary tuberculosis

REVIEW OF LITERATURE

Introduction

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* (M.tb). While it typically affects the lungs, it can affect virtually any part of the body. TB spreads from person to person by droplet method of transmission. (2) Active TB develops in hosts with impaired immunity secondary to diseases like Diabetes Mellitus (DM), Human Immunodeficiency Virus (HIV) infection, patients on immunosuppressants etc; and in people with increased exposure to patients with active tuberculosis.

Diabetes Mellitus (DM) is a chronic, non-communicable disease. Diabetes occurs when the body either cannot produce enough of the hormone insulin, or it is not able to use insulin effectively. Type 2 diabetes, is a condition where the body does not use insulin properly, resulting in elevated levels of glucose in the bloodstream. It is associated with a number of microvascular and macrovascular complications and is associated with an increased susceptibility to infections like tuberculosis(4). The prevalence of diabetes is increasing, especially in the Asian countries, where the prevalence of TB is also on an upward trend. The interplay between DM and TB is a complex one and if unchecked, could have disastrous consequences.

Globally, 70% of those with DM are in TB endemic regions. In countries with the highest burden of TB, the prevalence of DM ranges from 2% to 9% (5). Also eight of the ten countries with the highest incidence of DM have been classified as high burden countries for TB by the World Health Organization (WHO) (6)

Burden of pulmonary tuberculosis

Globally in 2015, there were an estimated 10.4 million incident cases of TB equivalent to 142 cases per 100,000 population. According to the WHO in 2015, there were 2.2 million cases of TB in India out of a global incidence of 9.6 million. According to the WHO, around one-third of those developing active TB disease remain undiagnosed or are not notified to the public health authorities. This proportion of patients could account to close to 3.6 million individuals.

The estimated TB prevalence figure for 2015 is given as 2.5 million. Around 40 % of the Indian population is estimated to be infected with TB bacteria and the vast majority have latent rather than active TB. (13)

According to the TB India 2016 Revised National TB Control Programme Annual Status Report, New Delhi, 902,732 people were diagnosed to have sputum positive tuberculosis. The cure rate for new sputum positive cases in 2014 was 83%. In Tamilnadu, 54,547 new sputum positive cases were diagnosed. The cure rate for sputum positive cases in 2014 was 80% in Tamilnadu. 9,132,306 cases were tested for AFB in sputum of which 902,732 were positive.(14) The prevalence of TB among DM patients ranges from 0.38% to 14% with the overall median global prevalence being 4.1% (15).

Burden of diabetes mellitus

According to the international Diabetes federation, 415 million people have diabetes. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. Diabetes prevalence has been rising more rapidly in middle- and low-income countries. Around 80% of patients with DM live in low income and developing countries(16). The prevalence of DM in south east Asia is 8.4% (17). India is the diabetic capital of the world with 69.2 million people living with diabetes amounting

to a prevalence of 8.7% as per national surveillance data from 2015 (1). The prevalence of DM among TB patients ranges from 1.9% to 45%, with the median global prevalence being 16%(15) . The prevalence of DM among TB patients was found to be 15.2 % in a study from south India (18). Systematic screening for tuberculosis in people with diabetes could improve early detection in settings with a high tuberculosis burden. The number needed to be screened to detect one previously undetected case of tuberculosis in countries with a high tuberculosis burden range from 17 to 776 (19–21)**.**

Natural history of tuberculosis infection

M. tb is manly a pathogen of the respiratory system, but it also can disseminate to the other organs and can cause extrapulmonary TB. This pathogen has airborne transmission and once a host is exposed to M. tb it may be eliminated or may persist in the host. Elimination of the bacilli may be by an innate immune response or by an adaptive immune response based on memory T cell response. If not eliminated it persists as a latent TB infection which may progress to develop a subclinical infection and later active TB. Progression from latent TB to active TB may be subtle and those with subclinical TB can also transmit M. tb.(22) A person once infected with TB, can infect 3-10 people per year but only a few of them develop active TB. (23) People with active TB, have an average duration of infectiousness of more than one year. Among those infected with M. tb, 5-15% will develop active TB over period of months or few years. The remainder carry a risk of developing active TB throughout their lifetime.(24) In the absence of treatment, 50 % of those developing active TB succumb to the illness(25).

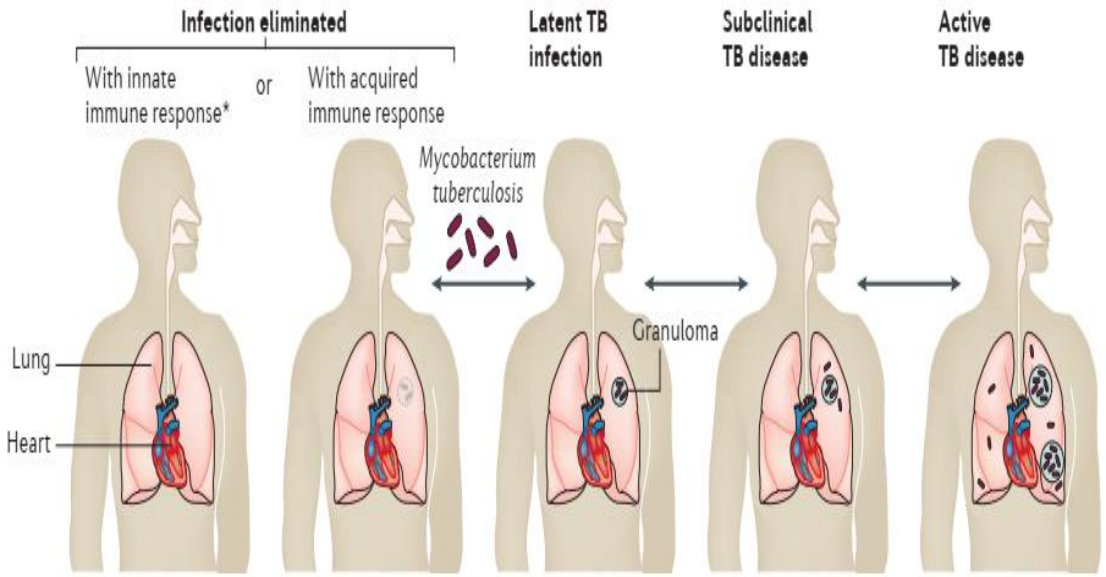


Figure 1. Spectrum of Tuberculosis.

Adapted from Pai M, et al. Tuberculosis. Nat Rev Dis Primer. 2016 Oct 27;2:16076.

Immunology of tuberculosis

M. tb enters the human body through the respiratory tract. After inhalation, it is translocated to the lower respiratory tract where it is phagocytosed by alveolar macrophages. The bacilli then blocks fusion of the phagosome with the lysosome. Then the bacilli through its specialised secretion system - ESX-1 secretion system, which is encoded by Region of difference – 1 (RD1) region in its genome; disrupts the phagosomal membrane thereby leading to the release of mycobacterial DNA and other products into the cytoplasm of the macrophage. This ESX-1 secretion system contributes significantly to the virulence of M.tb.(22,26).

If the macrophages fail to eliminate the bacilli, it then gains access to the pulmonary interstitium either through the infected macrophages that migrate to the lung parenchyma or by direct infection of the alveolar epithelial cells. Once in the parenchyma, a multi cellular host response is mounted and a granuloma is formed. M. tb is then transported to

the lymph nodes for T – cell priming by the dendritic cells or the inflammatory monocytes.(27) Additionally, M.tb can delay the initial priming of T-cells and the trafficking of T-cells into the lungs. Granuloma formation is a multicellular host response to wall of the TB bacilli, preventing spread to different tissues in the body. However M. tb can replicate within these cells and if the granuloma is unable to contain these bacilli, it can disseminate to other tissues.(22)

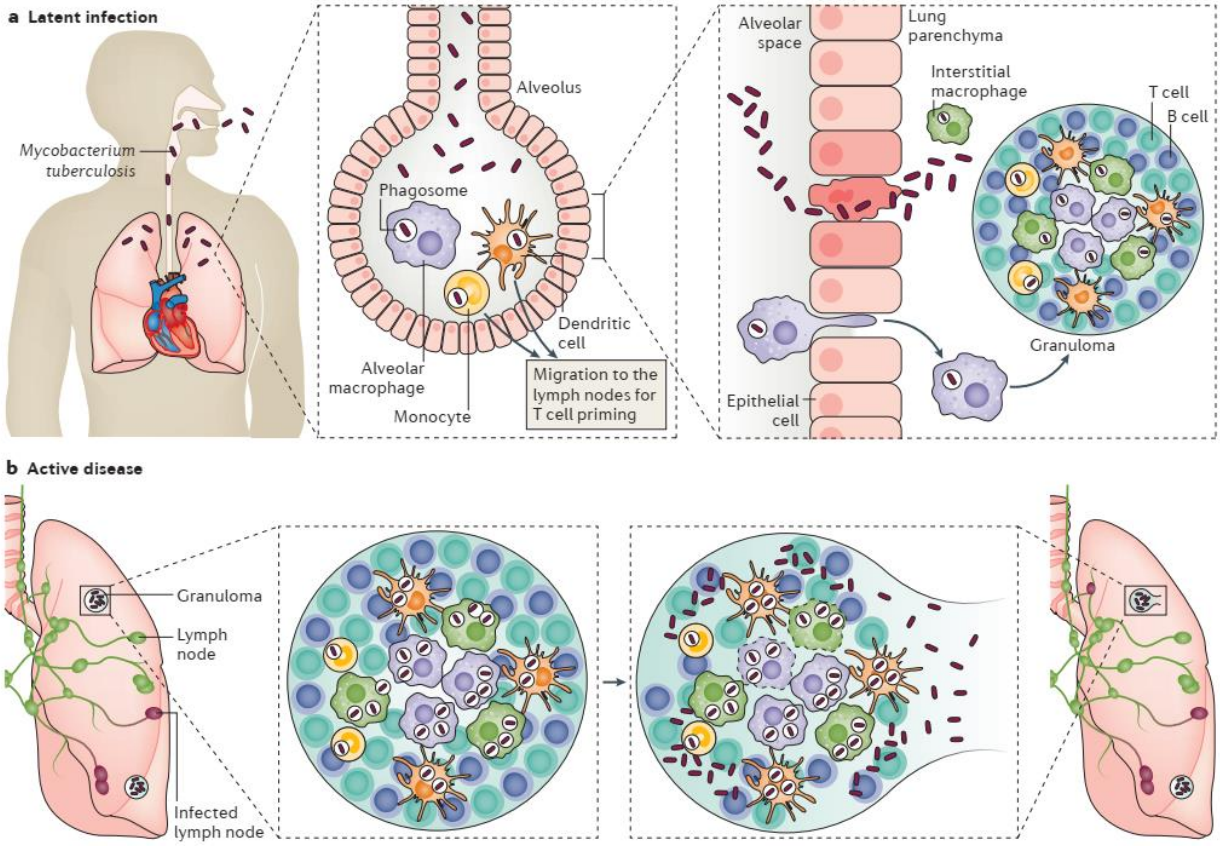


Figure 2. Mycobacterium tuberculosis infection

Adapted from Pai M, et al. Tuberculosis. Nat Rev Dis Primer. 2016 Oct 27;2:16076.

Pathogenesis of tuberculosis in diabetes mellitus

Diabetes increases the risk of active tuberculosis by about three times, principally by impairing the host-defences and thereby increasing the risk of progression from tuberculosis infection to active disease. (16,23–27).

A few animal studies have tried to elucidate the pathogenesis of increased susceptibility to TB in DM. Mice that have been infected with M. Tb have demonstrated higher bacterial loads of M. Tb compared to euglycemic mice, regardless of the route of inoculation of this pathogen. Diabetic mice have been shown to have significantly lower production of interferon gamma, interleukin -12 which are proinflammatory cytokines, playing a major role in the immune response to TB. Also fewer M. tuberculosis antigen (ESAT6) responsive T cells were demonstrated in a study in early M. tuberculosis infection suggestive of a diminished T helper 1 response(32,33).

In experimental studies, insulin has been shown to have an immunomodulatory effect. It reduces the Th1 to Th2 cell number ratio, thereby decreasing the Th1 immunity and the IFN-γ to IL4 secretion ratio. These are regarded as anti-inflammatory effects. It also downregulates the production of proinflammatory cytokines and acute phase proteins and up regulates the production of anti-inflammatory cytokines(7).

Diabetic patients without tuberculosis showed a strongly reduced non-specific IFN-γ production, which plays a role in inhibiting the initial growth of M.Tb. This reduced nonspecific immune response may be responsible for the increased risk of developing TB in patients with DM(8).

Another study showed that IFN-gamma and IL-12 levels in TB patients with DM were significantly lower than in those TB patients without DM. Also, IL-10 production was lower in patient with TB and DM as compared to patients with TB without DM. Production of IFN- γ a proinflammatory cytokine, playing a major role in the immune response to TB, was significantly lower in diabetics with TB with poor glycaemic control, as compared to those with good glycaemic control. The levels of IFN-γ were

negatively correlated with levels of HbA1c. This could explain the delayed sputum culture conversion seen in diabetics with TB (9).

A study evaluating leucocyte function in patients with DM demonstrated that polymorphonuclear neutrophil cell chemotaxis was significantly lower as compared to normal non-diabetic controls. Intracellular bactericidal activity has also demonstrated to be impaired in Diabetics. Chemotaxis and intracellular bactericidal activity were further impaired in the setting of poor glycaemic control in these studies(10,11).

All these studies support the hypothesis that DM directly impairs the innate and adaptive immune responses necessary to counter the proliferation of TB bacilli.(7–12)

Other factors that have been implicated in the increased susceptibility of diabetics to develop TB are alveolar macrophage dysfunction, pulmonary microangiopathy and micronutrient deficiencies. Studies have demonstrated the altered phagocytic function of alveolar macrophages in diabetics(34,35).

Another mechanism of the effects of DM on TB can be explained by lower plasma levels of ATT drugs, as evidenced by the lower plasma concentrations of rifampicin among those with DM and TB(34,36,37). In one study, patients with TB and DM had a 53% lower mean exposure to rifampin as compared to TB patients without DM in the continuation phase of therapy. Also, the maximum plasma concentration of rifampicin achieved was lower in diabetics with TB as opposed to those with TB without DM. A co-relation between plasma glucose concentration and exposure to Rifampicin was demonstrated in this study(38). Strangely, differences in the pharmacokinetics of rifampin, pyrazinamide, and ethambutol have not been detected in the intensive phase of ATT(39). Explanations suggested for this reduced exposure to rifampicin in the continuation phase of ATT among patients with TB and DM are the increase in body

weight from baseline in the continuation phase and possible differences in hepatic induction(39). A decrease in gastric acid secretion and impaired absorption of drugs also may contribute to this finding(37).

Association between diabetes mellitus and tuberculosis

Burden of disease

The most potent risk factor for TB is Human Immunodeficiency Virus (HIV) infection. However, due to the high prevalence of DM in the world, its effect on TB burden has been shown to be greater than HIV infection in studies(31). TB affects DM in many aspects. Jean et.al, performed a systematic review of literature and identified 13 observational studies that looked at the association of TB with DM. A total of 17,698 cases of TB were identified among 1,786,212 participants. This study showed that compared with people who do not have diabetes, people with diabetes have a 3.11-fold (95% CI 2.27–4.26) increased risk of developing active TB. This study also showed higher risks of developing TB in nations with a high background incidence of TB (12)

The estimated global cases of incident tuberculosis attributable to diabetes have increased substantially in the 22 countries accounting for 80% of the global tuberculosis burden, from 10% in 2010 (40) to 15% in 2013. A 52% incident rise was also seen in the estimated diabetes prevalence in these countries, from 5·4% in 2010, to 8·2% in 2013 (4). A meta-analysis showed that DM patients in low- or middle-income countries were at a higher risk of developing TB as compared to those in high income countries(41). More than 40% of diabetes-associated tuberculosis cases are in India and China (42). Studies have shown that, 12%–13% of patients with tuberculosis had diabetes(43–46). DM was diagnosed at the time of diagnosis of TB in more than 60 % of patients in 2 studies, showing that DM is under recognized (47,48). Given the increased risk of

tuberculosis among diabetics, active screening based on symptoms is recommended by the WHO(49)

A Mathematical modelling study on the incidence of DM and TB in India suggested that DM contributes to 15 % of the cases with pulmonary TB and 20 % of those with sputum positive pulmonary TB. It also showed that DM contributed to 80.5% and 86% of annual incident cases of pulmonary tuberculosis and sputum positive pulmonary TB respectively, among the diabetic population (50).

Epidemiology of tuberculosis in diabetes mellitus

TB is positively associated with reporting a diabetes diagnosis, longer duration of daily smoking and greater household crowding with additional persons per room. TB was negatively associated with more education, a home with good floors and walls or with a good toilet, an urban location and lesser number of people in the household (42).

Urbanization was found to increase the TB incidence in India because the annual risk of infection has been found to be 69% higher in urban than rural areas, which could be attributed to the increases in the prevalence of obesity and diabetes in urban areas, and increases in the prevalence of undernutrition in men who live in rural areas (51)

Among those with tuberculosis, DM was more commonly seen in those aged older than 35 years, patients with smear-positive pulmonary tuberculosis, current cigarette smokers, and those with recurrent tuberculosis (52–56). Among diabetics, tuberculosis was more commonly seen in those needing combined oral hypoglycaemic drugs and insulin, and those who had poorly controlled diabetes.(9,23,31).

In retrospective study done in Chile, looking at 1529 patients with DM over a period of 23 years, the 10-year risk of acquiring TB was 5.9 % among those with DM as compared

to the 0.8% among the general population. The 10 year risk of acquiring TB was 24.2 % among the patients with Diabetes on insulin as compared to 4.8 % among diabetics not requiring insulin (58).

A study conducted in Tanzania also showed higher risk of acquiring TB among diabetics with low Body Mass Index (BMI), younger age group and insulin use(59). A meta-analysis showed that insulin use increased the risk of developing TB by 2.5 - fold (41). Studies have demonstrated that TB patients with DM usually have a higher body weight prior to commencement of therapy, which generally increases after treatment. In a study from West Africa, obesity (Body Mass Index {BMI} > 30 kg⁄m2) was seen in 23% of diabetics with TB as compared to 3% in non-diabetics (60). Similarly in study conducted in Indonesia, 53% of TB patients with DM had a pre-treatment weight of more than 50 Kg, while only 16.5% of non-diabetic patients had a weight more than 50 Kg (47). In contrast a study from South India showed that patients with DM and pulmonary TB had a lower BMI.

A meta-analysis of 13 observational studies showed stronger associations between DM and TB in the those less than 40 years of age (12). However other studies have shown that TB patients with DM are 10-20 years older than those without TB(31), which could be due to the older age of presentation of Type 2 DM which is the most prevalent form of DM.

Patients with type 1 DM had a 3-5 fold risk of developing TB as compared to those with type 2 DM(59,61). Those with Type 1 DM were found to have more cavitatory lung lesions as compared to those without DM in a study(62) This was thought to be due to poor glucose control and longer duration of illness(63).

Clinical and laboratory characteristics of patients with diabetes mellitus and tuberculosis

In a study done in Taiwan it was found that diabetic patients were significantly more likely to have any symptom, cough, haemoptysis, tiredness, weight loss, positive smear and higher smear positivity grades as compared with non-diabetics. With maximum symptoms and smear positivity grades in patients with HbA1C>9%. (64)

A meta-analysis showed that DM patients with a glycosylated haemoglobin level (HbA1c) ≥ 6.5%, a Fasting Blood Glucose level ≥ 120 mg/dl, were at 1.87–fold and 3.30-fold increased risk of TB, respectively(41). A study conducted in South India showed that patients with DM and pulmonary TB had a greater likelihood of having a longer duration of DM and a poor glycaemic control(57).

After exposure to viable M.Tb bacilli, hosts who do not clear all the bacilli can develop latent TB infection (LTB) where they are asymptomatic and do not transmit the bacilli(65). Those with LTB have a life-time risk of 5%–15% to further progress into active tuberculosis(66). Progression to active TB depends on the immune function of the host. A meta-analysis of observational studies on LTB among diabetics showed that DM patients had a small but statistically significant odds of LTB (pooled OR, 1.18; 95% CI, 1.06–1.30) (67). A few studies have reported a higher frequency of TB among males with DM(31,68).

Diabetics have been shown to have lesser extrapulmonary manifestations as compared to non-diabetics(60,69).

There are conflicting findings on the rate of sputum positivity at the time of diagnosis of TB among diabetics. A study conducted in Saudi Arabia, showed that numerous Acid Fast Bacilli (AFB) was found in 65% of those with DM as compared to 54 % among

those without DM (68). Another study conducted in Turkey, showed higher sputum smear positivity among diabetics (70). A study conducted in Indonesia showed a lesser sputum mycobacterial load among diabetics as compared to no diabetics (71). In another study DM was shown to have no effect on sputum mycobacterial load (62). A study from South Korea demonstrated a higher sputum smear positivity among uncontrolled diabetics (defined as HbA1c > 7) as compared to well controlled DM and non-diabetics with TB(72).

A study done in Taiwan showed that 19% of Diabetics with TB had cavitatory lesions as compared to 10% among those without DM. This study also demonstrated the higher prevalence of nodular lesions on a chest X-ray among diabetics with TB(73). A study done in Saudi Arabia by Shaikh et.al, demonstrated higher prevalence of lung lesions in the lower lung fields in diabetics as compared to non-diabetics. This study also demonstrated that cavitatory lung lesions were more common among diabetics and that DM was an independent risk factor for lung lesions or cavities in the lower lung fields(74). Other studies have also shown that cavitatory lung lesions and lesions in atypical locations(70) are more common among Diabetics with TB (75–77). A study conducted in South Korea found that that uncontrolled DM (defined as HbA1c > 7) was associated with cavitatory lung lesions and reduced culture conversion at the end of 2 months(72). Patients with DM requiring insulin were found to have more cavitatory lesions as compared to non-diabetics (62).

Effects of diabetes mellitus on treatment outcomes of tuberculosis

There are varying reports on the effects of DM on the outcomes of TB. People with tuberculosis who have diabetes have a poorer response to treatment than do those without diabetes and are therefore at a higher risk of tuberculosis treatment failure, death, and

relapse after cure. Among those with active TB, TB treatment outcomes may be affected adversely by DM, by delaying the time to microbiological response, reducing the likelihood of a favourable outcome, and increasing the risk of relapse or death. The clinical presentation of TB in people with diabetes may be altered and change the sensitivity and specificity of conventional diagnostic algorithms (78). A few studies have showed no negative effects of DM on TB outcome like treatment failure, mortality and sputum culture conversion (68,72,79).

In a systematic review of literature by Baker et.al, the pooled relative risk of treatment failure and death among 12 studies which looked at the outcomes of DM on TB was 1.69 (95% CI, 1.36 to 2.12). Also the relative risk of death during treatment of TB was 1.89 (95% CI,1.52 to 2.36) in patients with DM as compared to those without DM (80). In a study conducted in Taiwan, it was found that patients with diabetes-related comorbidities had an increased risk of unfavourable outcome and one year mortality(64). Among patients with TB, DM was associated with a 5-fold risk of mortality in the first hundred days as compared with those not having DM. However DM did not affect long term mortality in this study(81). In TB patients higher treatment failure rates have been demonstrated among those with DM as compared without DM(82–84). Higher mortality rates among patients with TB and DM have been demonstrated as compared to those without DM (79,85,86). A meta-analysis and systemic review of the effects of DM on the outcomes of TB showed that among patients with TB, the risk of treatment failure or mortality was increased two-fold among those with DM as compared with those without DM (Odds ratio = 2.06, 95% CI: 1.68–2.53). Also, the Diabetics in this group had a higher risk of recurrence of TB as compared with the non – diabetics (Odds ratio =1.57, 95% CI: 1.38–1.79).

Among patients with TB there was no effect on sputum culture conversion at 2 months or 5 months among those with DM when compared to those without DM(81).

Among TB patients with DM, higher relapse rates have been shown in some studies(83,84,87) and a few other studies have not demonstrated any effect of DM on relapse rates of TB(68,88,89). Studies have shown that progression of TB is faster in those with DM when compared to those without DM. (12,30,50).

A study from South India showed that the adjusted odds ratios for successful treatment of TB among diabetics was significantly lower than that seen in those with TB without DM (18). Yet another Indian study demonstrated similar findings with the mean duration for sputum conversion being 64.2 (± 10.5) days in patients with TB and DM as compared to 61.5 (± 7.5) days in patients with TB without DM, which was statistically significant. Also the treatment failure rates were higher in the DM with TB group (4.2%) as compared to the TB without DM group (0.7%), which was also statistically significant(90).

One study reported 14.7% sputum smear positivity at the end of intensive phase of DOTS treatment among diabetics with TB and 3.6% sputum smear positivity in non-diabetics with TB (71). Other studies do not show any relation between DM and sputum conversion(17,68,79).

In a prospective study in Iran among patients with smear positive pulmonary TB and DM, those with poor glycaemic control (defined as HbA1c ≥ 7%) were more likely to have extensive lung disease, to have positive sputum smears and cavitatory lesions as compared to those with optimal glycaemic control (HbA1c < 7%)(91).

There is conflicting evidence regarding bacteriological conversion with DM in TB with some studies reporting slower conversion(36,82,92), with uncontrolled DM (HbA1c > 7) being a significant risk factor for positive sputum culture at 2 months(72).

A study in Peru also showed that sputum culture conversion was faster among TB patients with glycaemic control as compared to those without optimal glycaemic control(93). Those with poor glycaemic control were also more likely to have positive sputum smears after 2 months of therapy and have higher rates of treatment failure and relapse(91).

A systematic review on the effect of glycaemic control on poor outcomes in patients with TB and DM showed most of the studies had risk of bias but two studies which did not have the risk of bias showed that glycaemic control could have a favourable effect on TB treatment outcomes(94).

DM has to been shown to be an independent risk factor for the development of Drug induced Liver Injury(95). As most of the Antitubercular drugs are Hepatotoxic, the incidence of drug induced Liver injury may be higher in those with DM and TB(96).

Even though there is limited evidence on whether DM accelerates the emergence of drug resistant TB, especially multi drug resistant TB among those receiving TB treatment, it has been demonstrated in a few studies(97). However, a recently published systematic review and meta-analysis reported that diabetes was not associated with an increased risk of recurrent disease with drug-resistant TB (78).

Other factors affecting outcomes of pulmonary tuberculosis

Apart from Diabetes, other factors have been shown to affect the outcomes of pulmonary tuberculosis. A study conducted in China found that time to detection of M.tb on

automated liquid culture media, history of ever smoking, the presence of pulmonary cavitatory lesions and W-Beijing genotype were associated with delayed 2 month sputum culture conversion. (98)

A historical cohort study conducted in Japan among newly diagnosed patients with sputum positive pulmonary tuberculosis showed that a higher smear grading and a history of ever smoking were associated with delayed sputum culture conversion. This was postulated to be related to reduced Th1 cell immunity and innate immunity activation along with lung T cell recruitment associated with cigarette smoke exposure (99,100). The association of smoking with delayed sputum culture conversion at 2 months was also demonstrated in other prospective studies in Hong Kong and Brazil.(101–103). The study done in Brazil showing a dose response relationship between the number of cigarettes smoked daily and patients with positive sputum cultures after 2 months of treatment.(101)

Studies have shown that older age, male gender, and higher bacillary load are associated with delayed sputum smear conversion.(104,105) Also Bilateral radiological involvement and Diabetes mellitus have been associated delayed sputum culture conversion(104).

Effect of tuberculosis on diabetes mellitus

TB, similar to other infections, can worsen glycaemic control and complicate clinical management of diabetes(29). Also, TB medications may interfere with the treatment of diabetes through drug interactions, and diabetes may interfere with the activity of certain anti-TB medicines.

A study from China looking at the effects of TB on blood sugar levels, found that patients without DM did not develop uncontrolled sugars during TB treatment. However,

those newly diagnosed to have DM at the initiation of ATT, were likely to have higher blood sugar levels with TB treatment(106).

In patients with pulmonary TB, glucose intolerance has been demonstrated in 16.5% to 49% of the patients (34,44). A transient hyperglycemia has been demonstrated among patients with pulmonary TB. In study in Pakistan, 56% of patients on ATT who had glucose intolerance, which was demonstrated by an Oral glucose tolerance test (OGTT) had normal glucose tolerance after therapy and sputum conversion(107). Also achieving optimal glycaemic control has been shown to be more difficult during the active phase of TB, with some patients requiring insulin for the same (34,108).

Mechanism of hyperglycemia in tuberculosis

A variety of mechanisms have been thought to play a part in the hyperglycemia seen in TB infection. Inflammatory cytokines like Interleukin - 6 (IL-6) and TNF-α, by causing insulin resistance and reduced insulin production have been implicated in the pathogenesis of hyperglycemia in TB (34,109).

Drugs in the ATT regimen like Isoniazid, Rifampicin and Pyrazinamide have also been found to contribute to the hyperglycemia seen in TB(34,108,110–112).

Another major contributor to worsening glycaemic control in Diabetics with TB is the drug interactions between Oral Anti Diabetic (OADs) agents. Sulfonylureas and thiazolidinediones are metabolized by cytochrome P450 (CYP) enzymes in the liver. Rifampicin is a potent inducer of the cytochrome P450 (CYP) enzymes. Hence plasma levels of OADs are lower in Diabetics with TB on Rifampicin(31,113,114). This effect of Rifampicin is maximally seen in the first week after starting it and is normalized within two weeks of stopping it(114). Isoniazid is an inhibitor of some of these cytochrome P450 (CYP) enzymes. It has an inhibitory effect on CYP2C9 which is involved in the

metabolism of sulphonylureas. However the potent inducing effect of Rifampicin outweighs this inhibitory effect of Isoniazid and there is a net reduction in the plasma levels of sulphonylureas (115). This negative effect of Rifampicin on glycaemic control leads the need for higher doses of OADs like sulfonylureas and thiazolidinediones when used in diabetics on ATT. Also this emphasizes the need for monitoring of blood glucose levels in patients with DM once they are initiated on ATT(34).

Metformin which is a Biguanide is not subject to drug interactions with Rifampicin and hence is a safe and the ideal OAD to be used in those with DM and TB(116). However Metformin causes gastrointestinal side effects in 30 % of those on ATT(117). The other ideal medication for controlling DM in TB is Insulin, which is also devoid of the effects of rifampicin on its metabolism(34).

Current recommendations for the treatment of tuberculosis and diabetes mellitus

Studies have also shown that the time to sputum sterilization (indicated by sputum negativity at 2 or 3 months) is an important determinant of relapse (4–8).
The World Health Organization and the International Union Against Tuberculosis and Lung Disease have recently published a collaborative framework for care and control of TB and DM, to address the dual challenge of DM and TB (118).

Screening for diabetes mellitus in patients with tuberculosis

These guidelines recommend surveillance of diabetes among TB patients in all countries. Surveillance for diabetes among TB patients could be by a postprandial blood glucose measurement with glucometer 2 hours after a meal, which is the preferred method of screening for diabetes in primary healthcare settings. Fasting and random blood sugars have a lower sensitivity in diagnosing DM. Measurement of glycated haemoglobin

(HbA1c) or the oral glucose tolerance test is effective but expensive and time consuming but are useful in confirming a glucometer reading (119).

Screening for tuberculosis in patients with diabetes mellitus

These guidelines advocate TB surveillance among diabetes patients in settings with medium to high TB burden**.** According to these recommendations, patients newly diagnosed to have DM should be asked about the presence of cough (lasting more than 2 weeks) at the time of diagnosis and at each regular check-up for DM.

Diagnosis and Treatment of tuberculosis in patients with diabetes mellitus

The WHO guidelines advocate treatment and management of TB in people with diabetes according to the existing TB treatment guidelines and international standards. These guidelines also recommend the same TB treatment regimen to be prescribed to people with diabetes as for people without diabetes(118). The WHO now recommends daily dosing of ATT throughout the course of therapy in patients newly diagnosed to have TB. In populations known to or suspected to have high levels of isoniazid resistance, the WHO recommends using Isoniazid, Rifampicin and Ethambutol in the continuation phase as an acceptable alternative to Isoniazid and Rifampicin alone. The WHO also does not advocate extension of the intensive phase of ATT in TB patients who have received an ATT regimen containing Rifampicin throughout treatment, if a sputum smear is positive found at completion of the intensive phase.

Diagnosis of tuberculosis

For the diagnosis of TB, the WHO recommends the use of Nucleic acid amplification test - Xpert MTB/RIF as the initial diagnostic test rather than conventional microscopy, culture and Drug susceptibility testing in adults suspected of having multidrug resistant TB or HIV-associated TB. It also suggests that Xpert MTB/RIF may be used as the initial

diagnostic test in all adults suspected of having TB instead of conventional microscopy and culture in areas with adequate resources for the same. The WHO also recommends ‘using Xpert MTB/RIF as a follow-on test to microscopy in adults suspected of having TB but not at risk of MDR-TB or HIV-associated TB, especially when further testing of smear negative specimens is necessary ‘(120).

METHODOLOGY

Institutional review board

The institutional review board and ethics committee approved this study. The research funding was obtained from the fluid research grant of the institution. IRB number - 10518, approval date – 1.2.2017

Study design

This was a hospital based prospective observational cohort study.

Study setting

- This study was conducted in the Outpatient department and the inpatient wards of the Departments of General Medicine and Community health in Christian Medical College Hospital, a tertiary care centre in south India.
- Patients were recruited from March 2017 to December 2017
- The patients were followed up for a total duration of 6 months.

Participants

Inclusion Criteria

1) Adults >/= age of 18
2) Newly detected sputum positive Pulmonary Tuberculosis

3) Pre-existing/ newly detected Diabetic patients with sputum positive pulmonary TB

Exclusion criteria

1) Adults < age of 18
2) HIV positive individuals
3) Type I diabetes
4) Pregnancy
5) Multi drug resistant TB and Rifampin resistance on TB Xpert PCR

Case definitions

Tuberculosis case definitions

The following case definitions were used for this study as adapted from the WHO definitions and reporting framework for Tuberculosis(121)

Bacteriologically confirmed TB case:

'A case from whom a biological specimen is positive by smear microscopy, culture or WRD (such as Xpert MTB/RIF)'.

• *Clinically diagnosed TB case:*

'A case who does not fulfil the criteria for bacteriological confirmation but

has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases

diagnosed based on X-ray abnormalities or suggestive histology and extrapulmonary cases without laboratory confirmation'.

Classification based on anatomical site of disease:

Pulmonary tuberculosis:

'Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree'.

This definition also encompasses military TB as the lesions are in the lungs. Patients with pulmonary and extrapulmonary TB are classified as cases of pulmonary TB.

Extrapulmonary tuberculosis:

'Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges'. Patients with Tuberculous intra-thoracic lymphadenopathy or tuberculous pleural effusion, without radiographic abnormalities in the lungs are classified as cases of extrapulmonary TB.

Classification based on history of previous tuberculosis treatment:

New patient:

'A patient who has never been treated for TB or has taken anti – TB drugs for less than one month'.

Previously treated patient:

'A patient who has received 1 month or more of anti-TB drugs in the past'.

These patients can be further classified based on the outcomes of their most recent course of ATT as:

Relapse patients:

'Patients previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment and are now diagnosed with a recurrent episode of TB'.

Treatment after failure patients:

'Patients who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment'.

Treatment after loss to follow-up patients:

'Patients who have previously been treated for TB and were declared

lost to follow-up at the end of their most recent course of treatment.'

Other previously treated patients:

Patients who have previously been treated for TB but whose

outcome after their most recent course of treatment is unknown or undocumented.

<u>Classification based on drug resistance:</u>

Cases are classified based on M. tuberculosis drug susceptibility testing as follows -

Monoresistance:

'Resistance to one first-line anti-TB drug only'.

Polydrug resistance:

'Resistance to more than one first-line anti-TB drug (other than both isoniazid and

rifampicin)'.

Multidrug resistance:

'Resistance to at least both isoniazid and rifampicin'.

Extensive drug resistance:

'Resistance to any fluoroquinolone and to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance'.

Rifampicin resistance:

'Resistance to rifampicin detected using phenotypic or genotypic methods, with

or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether monoresistance, multidrug resistance, polydrug resistance or extensive drug resistance'.

<u>Treatment outcomes for tuberculosis patients:</u>

Treatment outcomes are separately defined for those with drug susceptible and drug resistant TB.

Cured:

'A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion'.

Treatment completed:

'A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least

one previous occasion were negative, either because tests were not done or because results are unavailable'.

Treatment failed:

'A TB patient whose sputum smear or culture is positive at month 5 or later during treatment'.

Died:

'A TB patient who dies for any reason before starting or during the course of treatment'.

Lost to follow-up:

'A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more'.

Not evaluated:

'A TB patient for whom no treatment outcome is assigned. This includes cases "transferred out" to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit'.

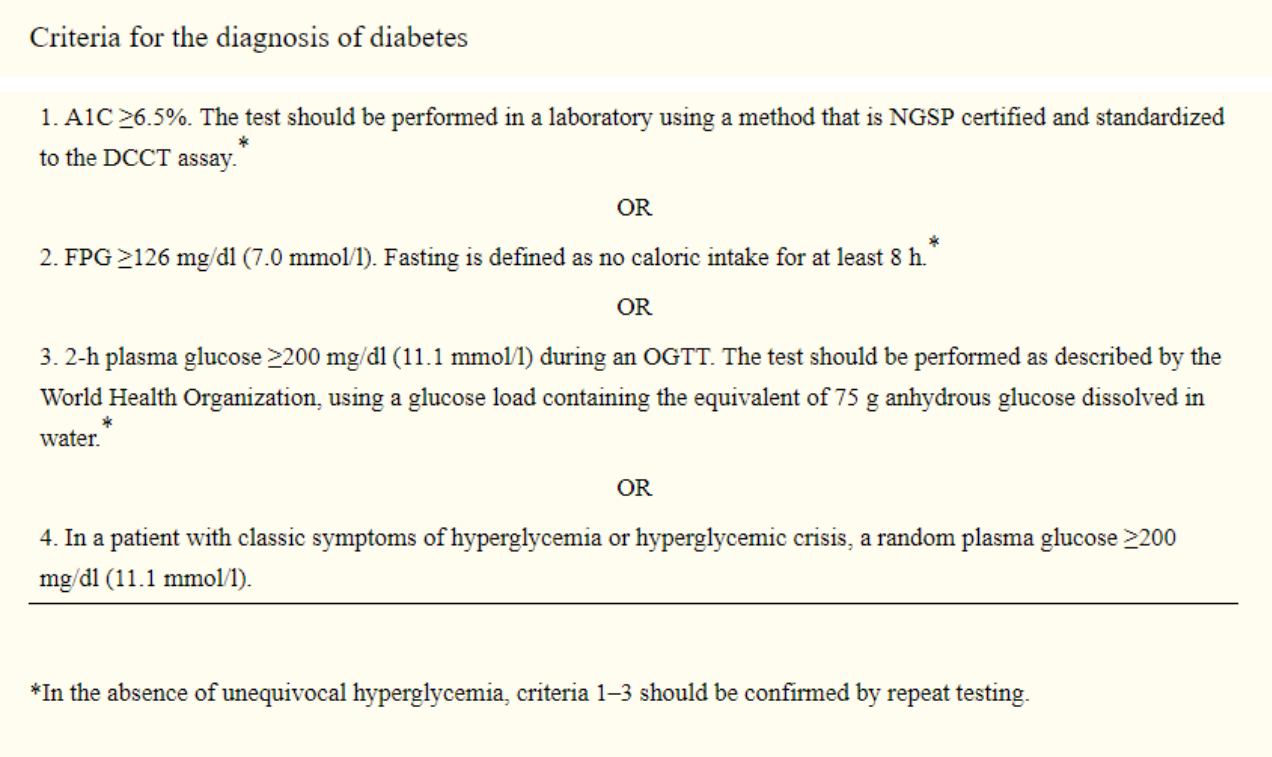
Treatment success:

'The sum of cured and treatment completed'.

<u>Diabetes mellitus case definitions</u>

The case definitions for Diabetes mellitus have been adapted from the American Diabetic association definitions. (122)

Diabetes Mellitus is diagnosed according to the following criteria:



Criteria for the diagnosis of diabetes

1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

2. FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.*

OR

3. 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l).

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.

Figure 3. Criteria for the diagnosis of diabetes mellitus. Adapted from Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2010 Jan;33(Suppl 1):S62–9.

Case ascertainment:

Patients were recruited from the outpatient department and the inpatient wards of the department of General Medicine and Community health. At initial assessment, basic history and examination was performed and a proforma was filled by the principal investigator. Patients were required to give a sputum sample for AFB smear and AFB culture, along with blood samples for glycosylated haemoglobin and fasting and post prandial blood glucose levels. Demographic data and anthropometric assessment were also performed at this point. Baseline investigations like haemoglobin, creatinine and

liver enzymes were also performed at this point. Patients were followed up at 2 months and if sputum AFB was negative, were followed up next at 6 months; while those with sputum AFB positivity at 2 monthly were followed up monthly till sputum AFB was negative and then at 6 months, as demonstrated in (Figure 4).

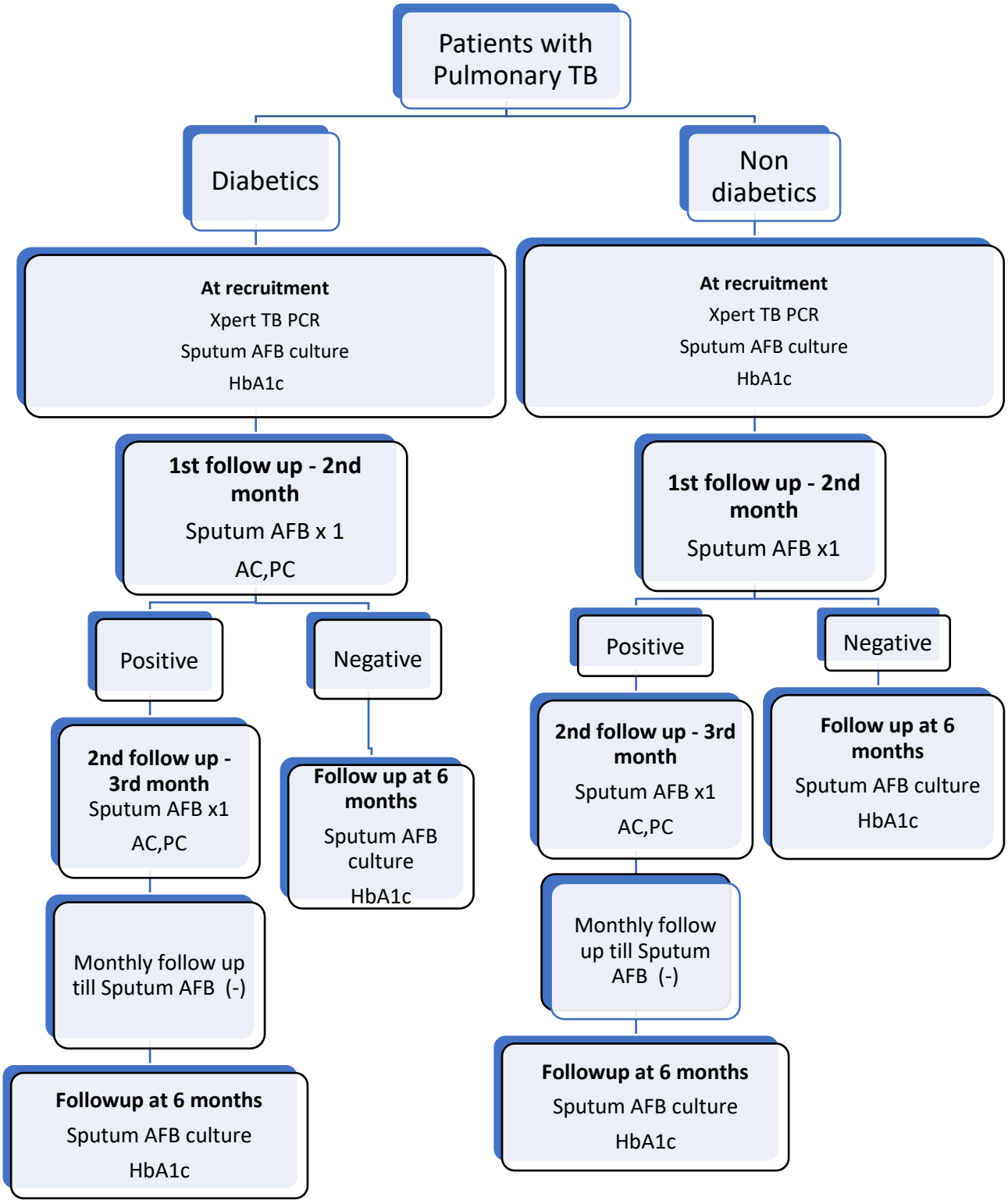


Figure 4. Detailed diagrammatic Algorithm of the study

Statistical analysis:

Sample size calculation:

For estimating sample size for comparison of treatment outcomes among TB patients with and without co-morbid diabetic status, we used the following formula,

$n = \{z\ 1\text{-}\alpha\sqrt{}\ [2P\ (1\text{-}P)] + z\ 1\text{-}\beta\sqrt{}\ [P\ 1\ (1\text{-}P\ 1\ ) + P\ 2\ (1\text{-}P\ 2\ )]\}\ 2\ /(P\ 1\ \text{-}P\ 2\ )\ 2$

where, $P = (P\ 1\ \text{-}P\ 2\ )/2$

Based on a recent study in South India(123), The treatment success rate among the non-diabetic TB patients (P 1) was assumed to be 90% (based on RNTCP accomplishments over the Years) The treatment success rate among the diabetic TB patients (P 2) was assumed to be 75%. With confidence level (α) of 95% and the power (1 - β) of 90%, the sample size needed to find difference between the two groups was estimated to be 109 in each group. Hence a total sample size of 220 will be recruited.

Data analysis:

Descriptive statistics were reported using Mean+/-SD. Frequency and percentage were reported for categorical variables. Chi square/Fisher's exact test were done to check the association between the categorical variables and the outcome variable.

Data entry was done using EpiData software version 3.1. Statistical analysis was done using SPSS version 23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). The treatment outcomes in the diabetic and the non-diabetic group were compared using students t test. P value <0.05 was considered as statistically significant.

RESULTS

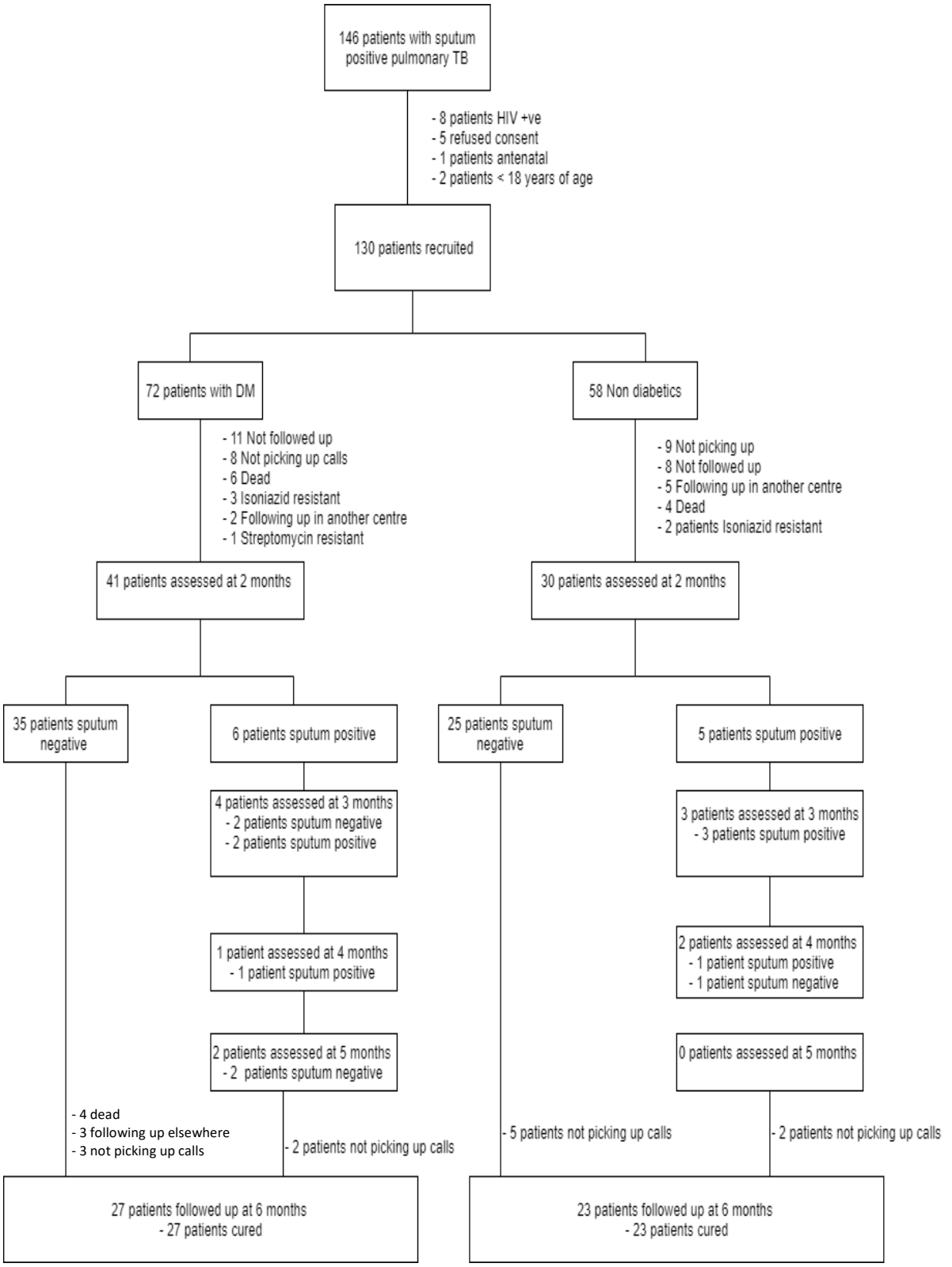


Figure 5 Consort statement

146 patients were detected to be sputum positive for AFB and were considered for recruitment. Among these, 16 patients were excluded for various reasons, according to the inclusion and exclusion criteria as shown in Figure 5. A total of 130 patients were recruited. Among them, 72 had DM and 58 did not have DM. Baseline characteristics and baseline investigations were performed for all these patients. Additionally, Sputum samples were sent for Xpert TB PCR, AFB culture and sensitivity – (LJ medium / MGIT). All patients were started on weight-based ATT, those with elevated transaminases, were started on hepatosafe regimens. These patients were then followed up at 2 months after initiation of ATT. 41 patients with DM and 30 non-diabetics were assessed at 2 months of therapy. 6 patients were excluded as they had resistance to at least one drug. 35 patients with DM and 25 patients without DM were sputum negative at 2 months. 6 diabetics and 5 non-diabetics were sputum positive at 2 months. These patients were followed up monthly till their sputum smears were negative. Among those with DM, 2 out of these 6 patients sputum converted at 3 months; 2 sputum converted at 5 months, one patient was lost to follow up and one patient who was positive at 3 months had not reviewed at 4 months or 5 months but was sputum negative at 6 months.

Among those without DM, who were sputum positive at 2 months, 1 patient was lost to follow up after 2 months. 3 patients were sputum positive at 3 months and one of these patients was lost to follow up after his 3-monthly evaluation. The other 2 patients were sputum negative after 4 months. One patient had not reviewed at 3 months but was sputum positive at 4 months. This patient did not follow up at 5 months but was sputum negative at 6 months of therapy.

At 6 months, 27 diabetics and 23 non-diabetics were assessed and all of them had sputum smears which were negative for AFB and were declared cured.

Demographics

Table 1. Baseline demographic characteristics

* Plus – minus values are means ± SD

Characteristics	Diabetics (N = 68)	Non-Diabetics (N = 56)	P value
Mean Age	51 ± 13	38 ± 17	0.001
Sex (%)			0.001
Male	56 (82)	31 (54)	
Female	12(18)	26 (46)	
Area of residence (%)			0.602
Urban	26 (38)	24 (42)	
Rural	42 (62)	33 (58)	
Average No. of people at home	5 ± 2	5.2 ± 2.4	0.364
Average No. of rooms	2.6 ± 1	2.6 ± 0.9	0.571
Socioeconomic status (%) (Modified Kuppuswamy scale)			0.504
Upper	5 (8)	9 (16)	
Upper Middle	28 (41)	21 (37)	
Lower Middle	28 (41)	19 (33)	
Upper Lower	7 (10)	8 (14)	
Lower	0	0	

Percentages in brackets

The Baseline demographic details were comparable among the diabetics and non-diabetics. The mean age in the DM group was 51 years with a standard deviation (SD) of 13. The mean age in the non-diabetic group was 31 with a SD of 17, which was significantly lower than the mean age in the DM group. 82 % of the diabetics were male while 54 % of the non-diabetics were male. 62 % of the diabetics and 58 % of the non-diabetics were residing in rural areas. The mean number of people residing at home was 5 with a SD of 2 in the DM group and 5.2 with a SD of 2.4 among the non-diabetics. The average number of rooms were 2.6 with a SD of 1 and 2.6 with a SD of 0.9 in those with and without DM respectively. 41 % and 37 % of diabetics and non-diabetics respectively belonged to the Upper middle Socioeconomic class. Lower middle class accounted for 41 % and 33% of the diabetics and non-diabetics respectively.

The average age was significantly higher in the DM group and had a significantly higher male preponderance.

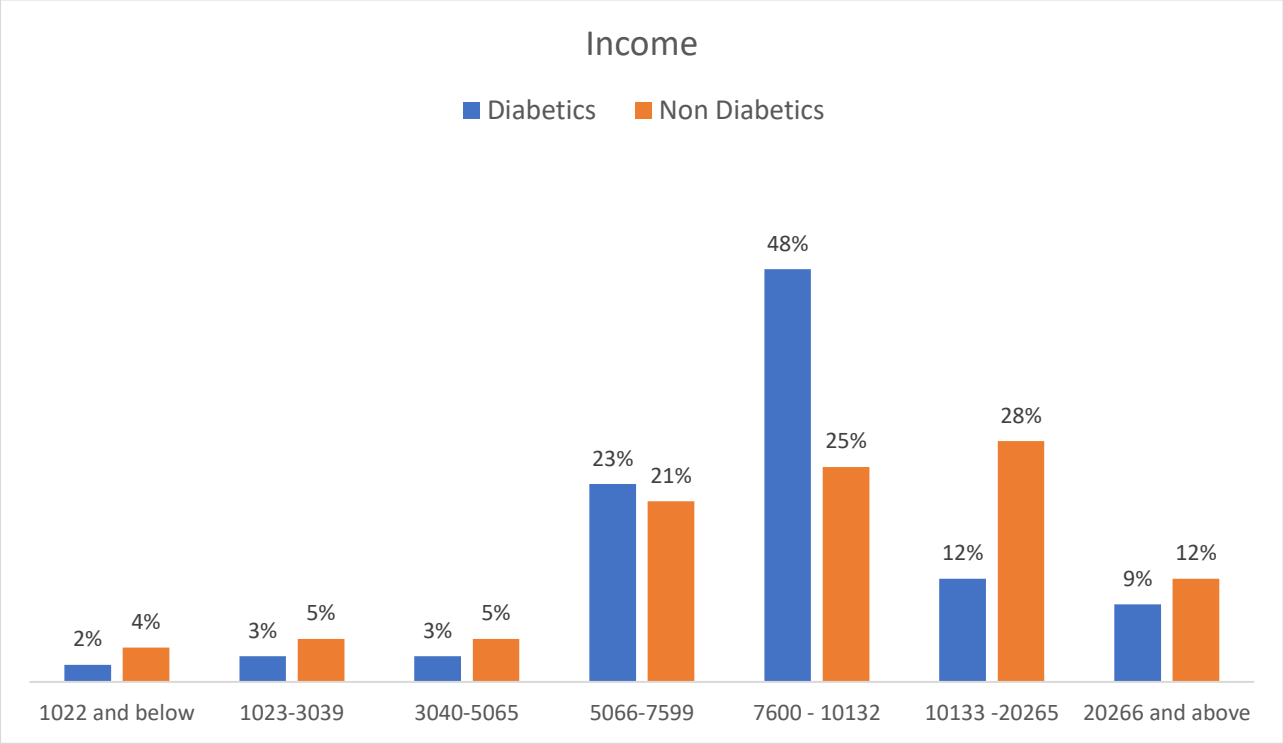


Figure 6. Income of patients

48 % of the diabetics had an income between Rs. 7600 and Rs. 10132. 28 % of the non-diabetics had an income between Rs. 10133 and Rs. 20, 265.

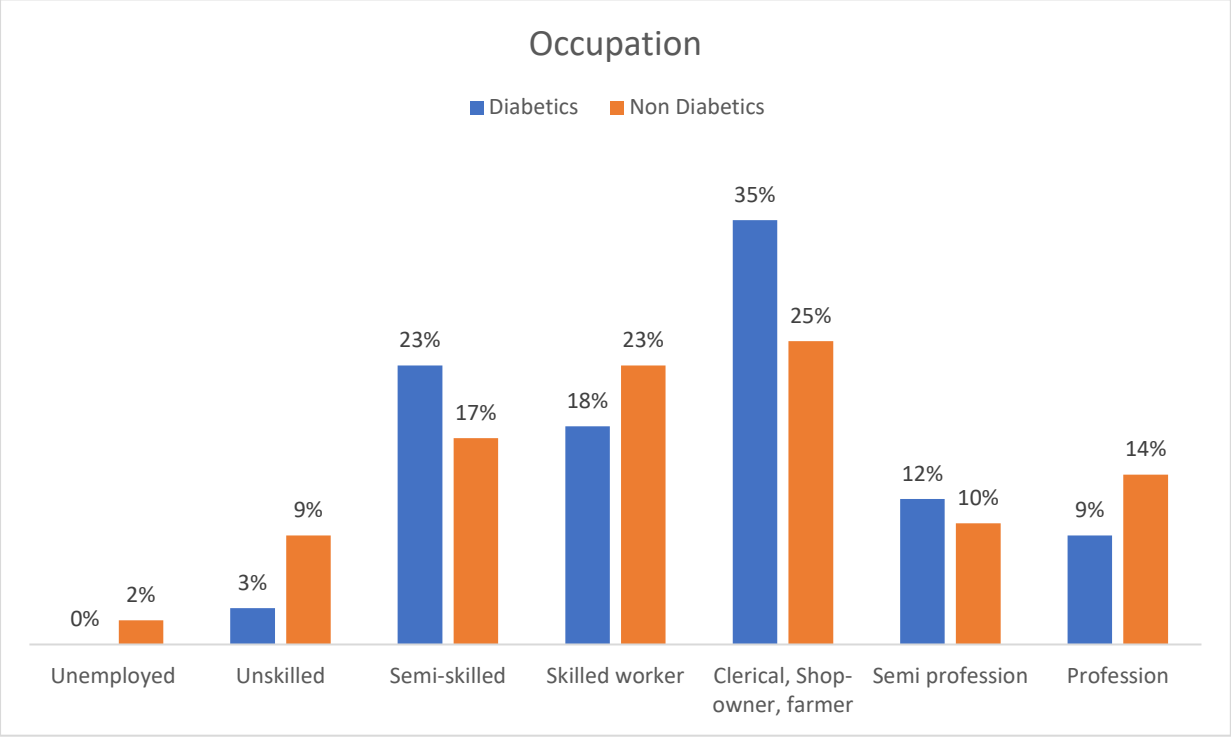


Figure 7. Occupation of patients

The most common occupation among those with DM was Clerical or owning a shop or farming - accounting to 35%. Clerical or owning a shop or farming was the occupation in 25 % of the non-diabetics. There was no significant difference between the occupational status of both groups (p value – 0.480).

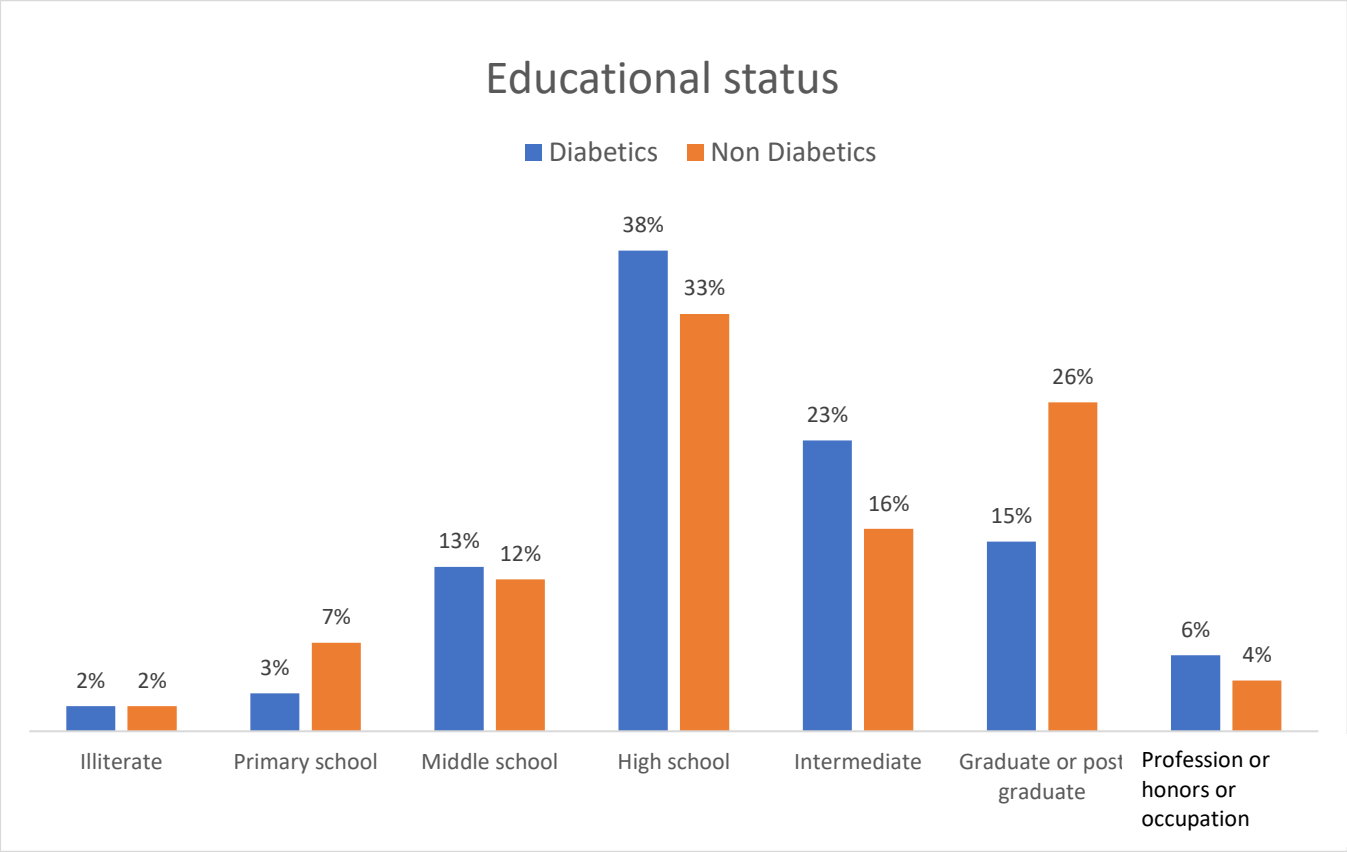


Figure 8. Educational status of patients

38 % and 33 % of diabetics and non-diabetics respectively had attended high school. 23 % of those DM had attended an intermediate school and 26 % of the non-diabetics had a graduate or post graduate degree. There was no significant difference in the educational status of both groups (p value – 0.649).

Clinical characteristics

Table 2. Clinical characteristics of patients (%)

Characteristics	**Diabetics (N = 68)**	**Non-Diabetics (N = 56)**	**P value**
Symptoms			
Fever	56 (82)	44 (77)	0.442
Cough	68 (100)	56 (98)	0.452
Expectoration	60 (88)	51 (90)	0.854
Haemoptysis	6 (9)	5 (9)	1.00
Chest Pain	3 (4)	2 (3)	1.00
Breathlessness	33 (49)	19 (33)	0.101
Loss of Appetite	58 (85)	59 (86)	0.947
Loss of Weight	52 (77)	39 (68)	0.286
Past TB	4 (6)	5 (9)	0.730
Outcomes of previous TB			0.524
Cured	2	4	
Treatment after failure patients	2	1	
Extrapulmonary TB			0.081
Sites of EPTB	6 (9)	11 (19)	
TB meningitis	6	5	
TB Lymphadenitis	1	4	
Abdominal TB	0	1	
Bone marrow TB	0	1	
Hypertension	26 (38)	7 (12)	**0.001**

*Percentages in brackets

Clinical characteristics of patients continued.

Characteristics	**Diabetics (N = 68)**	**Non-Diabetics (N = 56)**	**P value**
Hypothyroidism	3 (4)	4 (7)	0.700
Chronic liver disease	3 (4)	2 (4)	1.000
Chronic kidney disease	6 (9)	3 (6)	0.511
COPD	4 (6)	2 (4)	0.689
Smoking	28 (41)	13 (23)	**0.019**
No. of pack years	13	8.2	0.335
Ethanol consumption	21 (31)	5 (9)	**0.003**
Height	164.4 ±7.7	161 ± 9	0.21
Weight	55 ± 11.2	46 ± 11.7	**0.001**
BMI	20.4 ± 4	17.9 ± 3.7	**0.001**

*Percentages in brackets

Plus – minus values are means ± SD

Table 3. Clinical characteristics of Diabetics (%)

Characteristics	Frequencies
Duration	5.6
Newly diagnosed DM	6 (9)
Treatment modality for DM	
OHAs	50 (73)
Insulin	12(18)
Insulin and OHAs	4 (6)
Medical nutrition therapy	2 (3)
Complications of DM	
Neuropathy	20 (29)
Nephropathy	18 (26)
Retinopathy	12 (18)
IHD	5 (7)
CVA	3 (4)
PVD	2 (3)
Hba1c (initial)	9.5
Uncontrolled DM (HbA1c > 7)	50 (75)
AC	143 ± 19
PC	266 ± 33
Hba1c (6 months)	7.7

*Percentages in brackets

Plus – minus values are means ± SD

Most of the baseline characteristics were similar in both the groups. There was no significant difference in the symptoms at presentation like fever, cough, expectoration,

haemoptysis, chest pain, breathlessness, loss of appetite, loss of weight among the diabetics and the non-diabetics. 6 % of the diabetics and 9 % of the non-diabetics had a past history of having tuberculosis, which was not statistically significant. Those with a past history of TB were either cured or had failure of treatment and there was no difference in the frequencies of these among both the groups. Though the rates of extrapulmonary TB was more among the non – diabetics, this difference was not statistically significant. TB lymphadenitis was more common among the non – diabetics. In the DM group, 9% were newly diagnosed to have DM. Nearly 70 % of the diabetics were on oral diabetic agents and 18 % were on insulin. The most common microvascular complication was diabetic neuropathy which was seen in around 30% of the patients. Ischaemic heart disease was the most common macrovascular complication which was seen in 7% of the patients.

38 % of the diabetics had hypertension while only 12% of the non-diabetics had hypertension and this difference was statistically significant. There was no significant difference in the frequencies of other co morbidities like hypothyroidism, chronic liver disease, chronic kidney disease and chronic obstructive pulmonary disease among the diabetics and the non – diabetics.

Smoking frequency was more in the diabetics as compared with the non – diabetics and this was statistically significant. However, there was no significant difference in the mean number of pack years between the two groups. Ethanol consumption was also higher among the diabetics as compared to the non – diabetics and this difference was statistically significant. However, there was no significant difference between the mean duration of ethanol consumption between the groups. There was a significant difference in the weight and BMI of the patients with and without DM, with the non – diabetics

having lower weights and BMIs. The mean BMI among the non – diabetics was 17.9. 57 % of the non - diabetics were underweight while only 26 % were underweight among the diabetics. This difference was statistically significant.

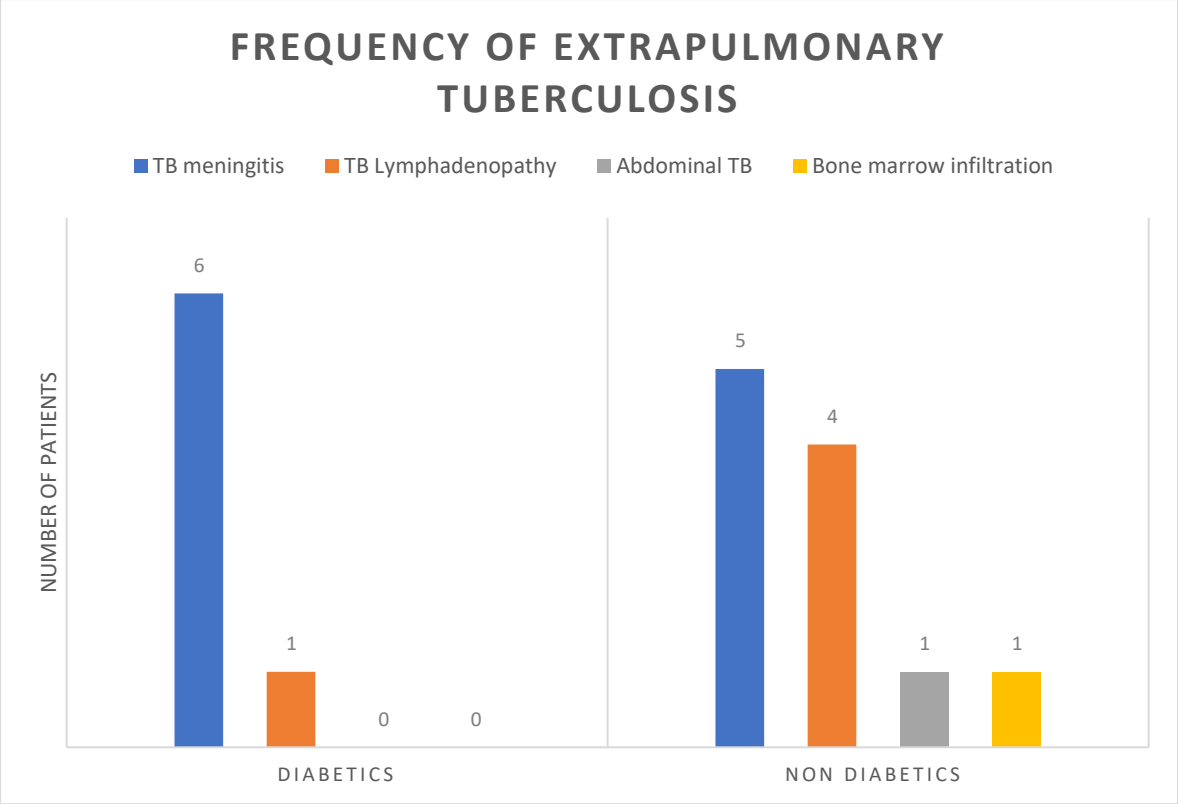


Figure 9. Frequency of Extrapulmonary Tuberculosis

6 patients (9%) and 11 patients (19%) of the patients had extrapulmonary TB along with pulmonary TB among those with and without DM respectively. Among the diabetics, 5 patients had TB meningitis and one patient had TB meningitis and TB lymphadenopathy. Among the Non-diabetics, 5 had TB meningitis, 4 had TB lymphadenitis, 1 patient had abdominal TB and 1 patient had bone marrow infiltration of TB.

Investigations

Table 4. Laboratory features of patients

Characteristics	**Diabetics (n = 68)**	**Non-Diabetics (n = 56)**	**P value**
Haemoglobin	11.8 ± 2.4	10.8 ± 2.5	**0.026**
Creatinine	1.0	0.8	0.134
Albumin	3.3 ± 0.7	3.0 ± 0.8	**0.038**
SGOT	32	38	0.466
SGPT	25	29	0.472
Hba1c	9.5 ± 2.5	5.3 ± 0.5	**0.001**
AC	143 ± 19	89 ± 8	**0.001**
PC	266 ± 33	127 ± 37	**0.002**
Sputum AFB			
Negative	10 (15)	15 (26)	
Scanty	6 (9)	5 (9)	
1+	25 (37)	9 (16)	
2+	18 (26)	11 (19)	
3+	9 (13)	17 (30)	**0.02**

*Percentages in brackets

Plus – minus values are means ± SD

Table 5. Chest X-ray findings (%)

Chest X-ray findings	Diabetics (n = 68)	Non-Diabetics (n = 56)
Normal	10 (15)	16 (29)
Consolidation	26 (38)	17 (30)
Milliary mottling	9 (13)	6 (12)
Fibrocavitatory changes	17 (25)	12 (22)
Reticulonodular opacities	6 (9)	4 (7)

*Percentages in brackets

Haemoglobin levels were significantly lower in the non-diabetics when compared with the diabetics. The mean albumin levels were lower than normal in both the groups (Normal albumin levels- 3.5- 5.5 in our institution) and the albumin levels were significantly lower in the non-diabetics. The mean HbA1c was 9.5 in the DM group and 5.3 in the NDM group.

The non – diabetics had a slightly higher percentage of patients with a normal chest X ray. Consolidation was the most common X ray finding in both the groups. There was no significant difference between the chest X ray findings in both the groups. 7% of patients with cavities were using insulin. However, there was no significant association between the two (p value – 0.49).

Sputum characteristics of patients

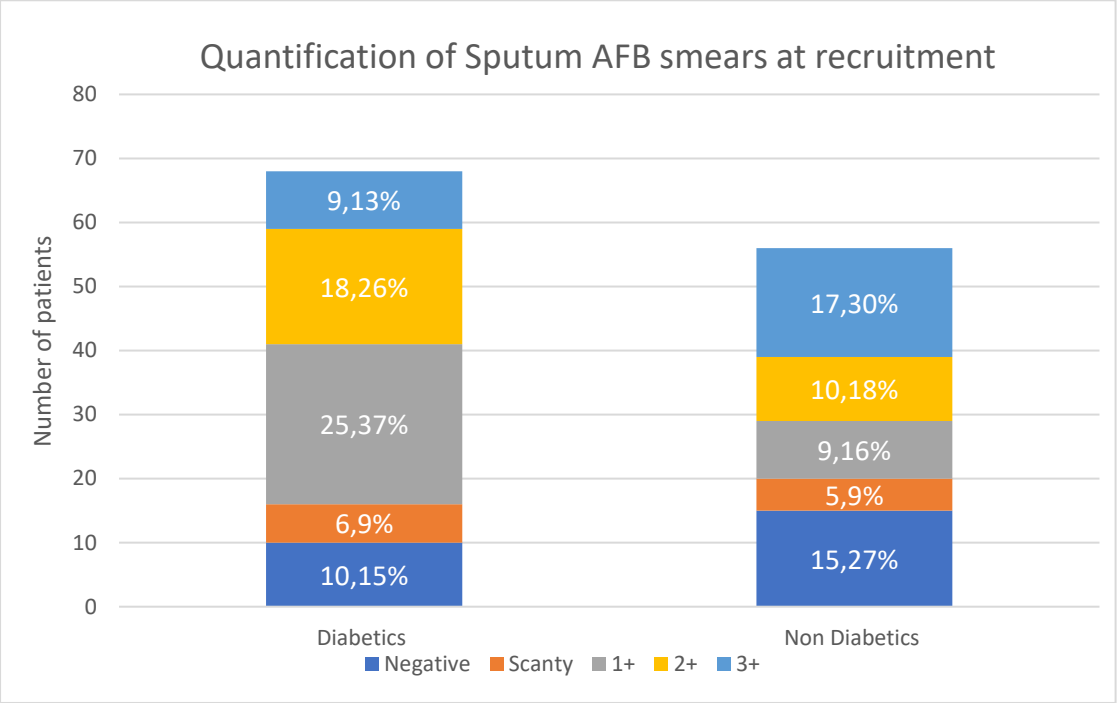


Figure 10. Quantification of Sputum AFB smears at recruitment

15 % of the diabetics had negative sputum smears while 27 % had negative smears among the non-diabetics. Scanty AFB was seen in 9% of the sputum smears in both diabetics and non-diabetics. 1+ AFB was seen in 37 % of the sputum smears of the diabetics whereas it was 16 % among the non – diabetics. 26% of the diabetics and 18% of the non- diabetics had 2+ AFB in sputum smears. The non – diabetics had a significantly higher bacillary load as compared with the diabetics. Among the 9 patients with a high bacillary load in the DM group, HbA1c levels were available for 8 of the patients and all of them had uncontrolled Dm (HbA1c > 7). There was no significant association between patients with HbA1c > 9 and high bacillary load (p value – 0.71)

90% (61) of the diabetics had given sputum for AFB culture while 82 % (46) of the non – diabetics had given sputum for AFB culture. 81 % of the sputum cultures of diabetics grew M. Tb, while in 9% sputum cultures did not show any growth and 10 % had not given samples for AFB culture.

61 % of the sputum cultures of the non - diabetics grew M. Tb, while in 21 % sputum cultures did not show any growth and 18 % had not given samples for AFB culture. Patients who had grown resistant strains or showed Rifampin resistance on Xpert Tb PCR were excluded from the study. Those patients who had neither given sputum samples for Xpert TB PCR or for AFB cultures were also excluded.

93% of the Diabetics gave sputum samples for Xpert TB PCR testing and among them, 100 % had a positive result.

95% of the non - diabetics had given sputum samples for Xpert TB PCR testing and among these, 91 % had a positive result while 4 % had a negative result and 5% of the patients had not given sputum samples.

Drug induced Liver injury

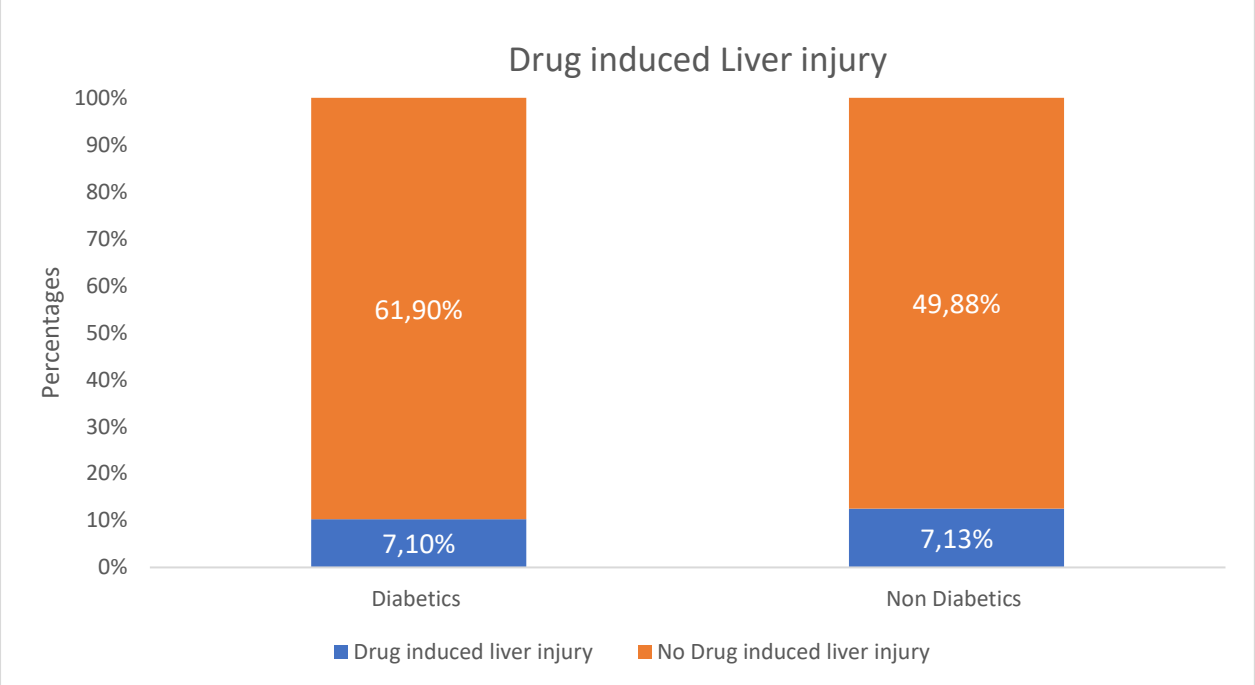


Figure 11. Dug Induced Liver injury in patients

Drug induced Liver injury (DILI) was slightly more common in the non-diabetic group. However, there was no statistically significant difference in the percentages of DILI in both the groups.

Effect of Treatment of TB on glycaemic control

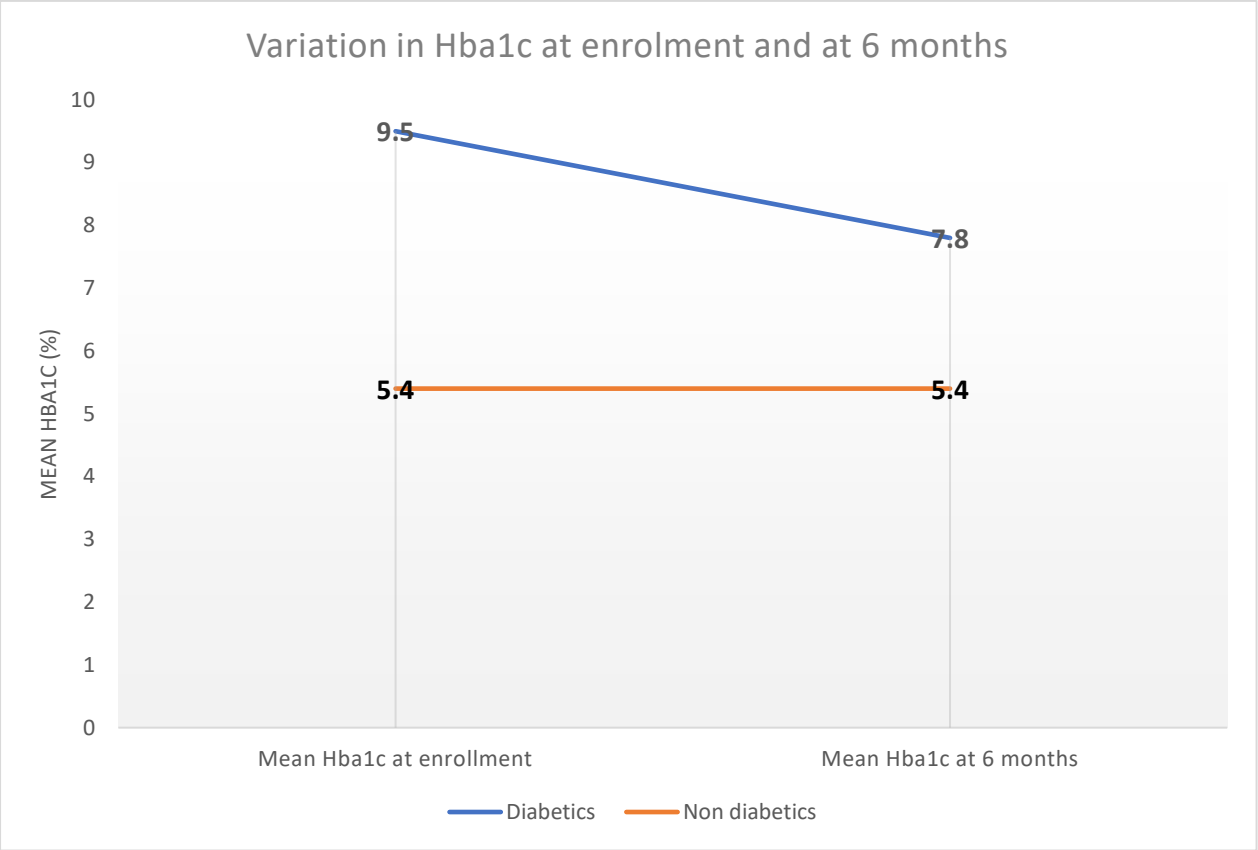


Figure 12. Variation in Hba1c at enrolment and at 6 months

The mean Hba1c at enrolment among those with DM was 9.5 %, which had reduced to 7.8 at 6 months. However only 27 patients with DM had followed up at 6 months. While, the mean Hba1c was 5.4 % at enrolment and at 6 months among those without DM, where 23 patients had followed up. The reduction in HbA1c in the DM group with the treatment of TB was significant [p value – 0.001, mean difference – 1.76, 95% CI of difference – (1.01 – 2.52)]

Delayed sputum conversion

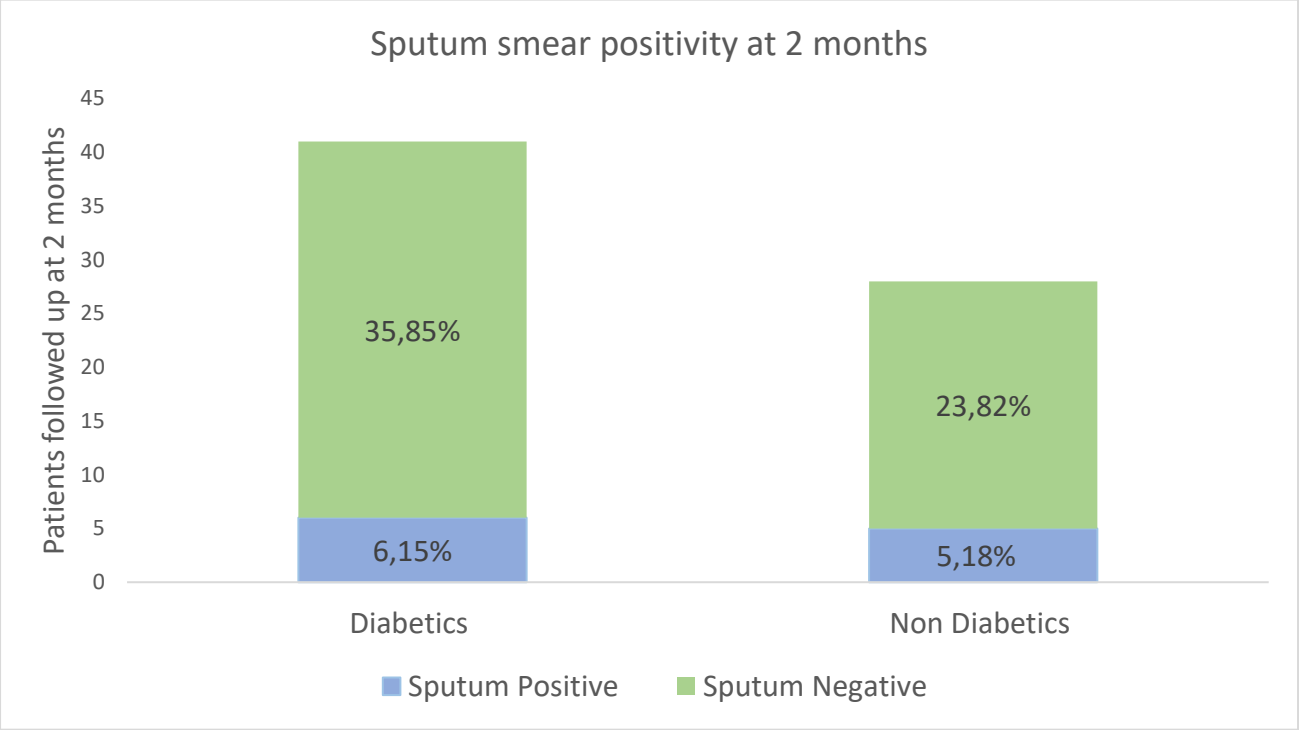


Figure 13. Sputum smear positivity at 2 months

41 patients with DM had followed up at 2 months and among them 6 patients (15%) were sputum positive. 28 non – diabetic patients had followed up at 2 months and among them 5 patients (18%) were sputum positive.

Table 6. Characteristics of delayed sputum convertors who were diabetics

Patient serial No.	1	2	3	4	5	6
Age	36	60	74	67	40	54
Sex	male	female	male	male	male	male
Prior TB	No	No	No	No	No	No
Duration of DM (in years)	1	10	15	10	6	3
Treatment of DM	OHA	OHA	OHA	OHA	OHA	OHA
Microvascular complications	No	Yes	Yes	Yes	No	No
Macrovascular complications	No	No	Yes	No	No	No
Extrapulmonary TB	No	No	No	No	No	No
Chronic Kidney Disease	No	No	No	No	No	No
Chronic Liver Disease	No	No	No	No	No	No
COPD	No	No	Yes	No	No	Yes
Hypothyroidism	No	No	No	Yes	No	No
Hypertension	No	No	Yes	Yes	No	No
Smoking	Yes	No	Yes	Yes	Yes	Yes
Packyears	2	NA	35	15	5	20
Ethanol consumption	No	No	Yes	Yes	Yes	No
Duration in years	NA	NA	15	10	10	NA

Characteristics of delayed sputum convertors who were diabetics continued

Patient serial No.	1	2	3	4	5	6
Weight (Kg)	43	65	68	49	44	50
BMI	15.8	27	25.00	21.50	18.00	22.20
Sputum smears	++	+++	++	+	+++	++
HbA1c	10.9	11.4	6.0	8.2	7.5	6.9
Haemoglobin	13.6	9.6	9.1	12.7	7.8	14.3
Creatinine	1.2	1.1	0.6	0.6	0.7	0.8
SGOT	26	24	17	33	75	NA
SGPT	16	24	14	40	46	NA
Albumin	3.0	3.4	3.10	3.10	2.70	4.60
AFB culture	Positive	Positive	Positive	Positive	NA	Positive
Sensitivity	Sensitive	Sensitive	Sensitive	Sensitive	NA	Sensitive
Xpert TB PCR	Positive	Positive	Positive	Positive	Positive	Positive
Rifampin resistance	No	No	No	No	No	No
Chest X ray findings	Fibro cavitatory changes	Consolidation	Fibro cavitatory changes	Fibro cavitatory changes	Milliary mottling	consolidation
Weight at 2 months	45	64	68	50	48	51
AFB smear - 2months	Scanty	+	Scanty	+	Scanty	Scanty
AC - 2months	159	437	118	113	157	111
PC - 2months	315	601	150	153	249	244
DILI*	No	No	No	No	No	No

*DILI – Drug induced Liver Injury

Characteristics of delayed sputum convertors who were diabetics continued

Patient serial No.	1	2	3	4	5	6
Assessment at 3 months	No	Yes	Yes	No	Yes	Yes
Weight at 3 months	NA	64	70	NA	49	52
AFB smear - 3 months	NA	++	+	NA	Negative	Negative
AC at 3 months	NA	272	NA	NA	120	NA
PC at 3 months	NA	241	NA	NA	180	NA
Hba1c at 3 months	NA	NA	6.1	NA	NA	7.0
Assessment at 4 months	No	No	No	Yes	No	No
Weight at 4 months	NA	NA	NA	52	NA	NA
AFB smear - 4 months	NA	NA	NA	++	NA	NA
AC - 4 months	NA	NA	NA	120	NA	NA
PC - 4 months	NA	NA	NA	170	NA	NA
Hba1c - 4 months	NA	NA	NA	NA	NA	NA
Assessment at 5 months	Yes	Yes	No	No	No	No
Weight at 5 months	46	65	NA	NA	NA	NA
AFB smear - 5 months	Negative	Negative	NA	NA	NA	NA
AC - 5 months	104	229	NA	NA	NA	NA
PC - 5 months	146	149	NA	NA	NA	NA

Characteristics of delayed sputum convertors who were diabetics continued

Patient serial No.	1	2	3	4	5	6
Assessment at 6 months	Yes	Yes	Yes	No	Yes	No
Weight at 6 months	48	66	66	NA	50	NA
AFB smear - 6 months	Negative	Negative	Negative	NA	Negative	NA
AFB culture at 6 months	NA	Negative	Negative	NA	Negative	NA
Treatment outcome	Cured	Cured	Cured	Not evaluated	Treatment completed	Treatment completed
Hba1c at 6 months	6.1	9.7	5.9	NA	7.0	NA

There were 6 patients with DM who were sputum positive at 2 months. Their characteristics have been described in (Table 6). The mean age of these patients was 55 years. The majority of these patients were male. 5 out of the 6 patients had a history of smoking. The mean weight of the patients was 53 Kgs and the mean BMI was 21.6 Kg/m^2. The mean Haemoglobin level was 11.2 g/dL in this group and the mean albumin was 3.3 g. The mean duration of DM was 7.5 years with a mean HbA1c of 8.5. 4 out of these 6 patients had followed up at 6 months. 3 of the 6 patients had microvascular complications of DM while only 1 patient had macrovascular complications.

Table 7. Characteristics of Delayed sputum convertors who were non-diabetics

Patient serial No.	1	2	3	4	5
Age	29	54	33	55	58
Sex	male	male	female	male	female
Prior TB	No	No	Yes - defaulted	No	No
Extrapulmonary TB	No	No	No	No	No
Chronic Kidney Disease	No	No	No	No	No
Chronic Liver Disease	No	No	No	No	No
Chronic Obstructive Pulmonary Disease	No	Yes	No	No	No
Hypothyroidism	No	No	No	No	No
Hypertension	No	No	No	No	No
Smoking	Yes	Yes	No	Yes	No
Packyears	8	15	NA	5	NA
Ethanol consumption	Yes	No	No	No	No
Duration in years	5.0	NA	NA	NA	NA
Weight (Kg)	40	55	38	64	50
BMI	15.2	20.4	15.60	23.10	21.10
Sputum smears	+++	+++	+++	+++	+++

Characteristics of delayed sputum convertors who were non - diabetics continued

Patient serial No.	1	2	3	4	5
HbA1c	5.3	5.9	5.4	5.4	NA
Haemoglobin	10.0	15.4	11.6	NA	12.1
Creatinine	0.8	1.2	0.7	0.9	0.6
SGOT	260	34	17	NA	20
SGPT	288	30	24	NA	9
Albumin	2.9	3.5	2.70	2.80	3.00
AFB culture	No growth*	Positive	Positive	Positive	NA
Sensitivity	NA	Sensitive	Sensitive	Sensitive	NA
Xpert TB PCR	Positive	Positive	Positive	Positive	Positive
Rifampin resistance	No	No	No	No	No
Chest X ray findings	Consolidation	Consolidation	Fibro cavitatory changes	Consolidation	Fibro cavitatory changes
Weight at 2 months	39	60	40	67	53
AFB smear – 2 months	4	4	1	4	4
DILI	Yes	No	No	No	No
Assessment at 3 months	No	No	Yes	Yes	Yes
Weight at 3 months	NA	NA	40	67	54
AFB smear - 3 months	NA	NA	+	Scanty	Scanty
Assessment at 4 months	Yes	No	No	No	No
Weight at 4 months	39	NA	NA	NA	NA
AFB smear - 4 months	++	NA	NA	NA	NA

*DILI – Drug Induced Liver Injury

Characteristics of delayed sputum convertors who were non - diabetics continued

Patient serial No.	1	2	3	4	5
Assessment at 5 months	No	No	No	No	No
Weight at 5 months	NA	NA	NA	NA	NA
AFB smear - 5 months	NA	NA	NA	NA	NA
Assessment at 6 months	Yes	No	No	Yes	Yes
Weight at 6 months	41	NA	NA	68	55
AFB smear - 6 months	Negative	NA	NA	Negative	Negative
AFB culture at 6 months	Negative	NA	NA	Negative	Negative
Treatment outcome	Treatment completed	Not evaluated	Not evaluated	Treatment completed	Treatment completed
Hba1c at 6 months	5.6	NA	NA	5.4	5.6

*Sputum sample for AFB culture was given 1 month after initiation of ATT.
Subsequent sputum smears were positive, but cultures were negative

There were 5 patients without DM who were sputum positive at 2 months. Their characteristics have been described in (Table 7). The mean age of these patients was 46 years. The majority of these patients were male. Only 1 out of the 6 patients had a history of smoking. The mean weight of the patients was 49 Kgs and the mean BMI was 19.1 Kg/m^2. The mean Haemoglobin level was 12.3 g/dL in this group and the mean albumin was 2.9 g. 3 out of these 6 patients had followed up at 6 months.

Table 8. Factors influencing delayed sputum conversion

Parameters	**Sputum positive at 2 months**	**Sputum negative at 2 months**	**p Value**	**Relative risk (95% CI)**
Diabetes			0.71	0.78 (0.21 to 2.89)
Diabetics	6	35		
Non-diabetics	5	28		
Sex			0.64	1.4 (0.34 to 5.89)
Male	8	38		
Female	3	20		
Past Tuberculosis			0.79	1.35 (0.14 to 13.36)
Yes	1	4		
No	10	54		
COPD			**0.001**	**21.3** 1.97 to 231.21)
Yes	3	1		
No	8	57		
Smoking			**0.0001**	**12.8** (2.89 to 56.89)
Yes	8	10		
No	3	48		
Ethanol consumption			0.15	2.74 (0.67 to 11.17)
Yes	4	10		
No	7	48		

Factors influencing delayed sputum conversion continued

Parameters	**Sputum positive at 2 months**	**Sputum negative at 2 months**	**p Value**	**Relative risk (95% CI)**
Underweight			0.53	0.7 (0.17 to 2.48)
Yes	4	27		
No	7	31		
Cavitatory lesions			**0.014**	**5.2** (1.29 to 21.16)
Yes	5	8		
No	6	50		
Anemia			0.84	1.15 (0.30 to 4.38)
Yes	7	35		
No	4	23		
Hypoalbuminemia			0.09	3.7 (0.74 to 19.04)
Yes	9	31		
No	2	26		

Factors influencing delayed sputum conversion continued

Parameters	**Sputum positive at 2 months**	**Sputum negative at 2 months**	**p Value**	**Relative risk (95% CI)**
High Bacillary load			**0.001**	**12.75** (2.96 to 54.93)
Yes	7	7		
No	4	51		
DILI			0.67	0.67 (0.07 to 5.57)
Yes	1	8		
No	10	50		
Uncontrolled DM			0.61	0.67 (0.09 to 4.01)
Yes	4	26		
No	2	8		

Table 9. Factors influencing delayed sputum conversion in diabetics and non-diabetics

Parameters	**p Value**	**Relative risk (95% CI)**
Male Sex		
Diabetics	0.87	0.8 (0.08 to 8.71)
Non-diabetics	0.30	2.81 (0.38 to 20.46)
Past Tuberculosis*		
Diabetics	NA	NA
Non-diabetics	0.21	5.5 (0.28 to 107.15)
COPD		
Diabetics	**0.001**	9.75 (3.85 to 24.67)
Non-diabetics	**0.21**	3.25 (0.28 to 107.15)
Smoking		
Diabetics	**0.002**	20 (2.01 to 199.73)
Non-diabetics	**0.02**	10 (1.15 to 86.87)
Ethanol consumption		
Diabetics	0.227	2.87 (0.49 to 16.97)
Non-diabetics	0.218	5.5 (0.28 to 107.15)
Underweight		
Diabetics	0.813	1.2 (0.19to 7.94)
Non-diabetics	0.141	0.23 (0.03 to 1.77)

Factors influencing sputum conversion in diabetics and non-diabetics continued

Cavitatory lesions		
Diabetics	**0.02**	7.7 (1.14 to 52.29)
Non-diabetics	0.264	3.2 (0.39 to 25.57)
Anemia		
Diabetics	0.413	2.1 (0.34 to 13.09)
Non-diabetics	0.393	0.4 (0.05 to 3.22)
Hypoalbuminemia		
Diabetics	0.13	5 (0.52 to 47.43)
Non-diabetics	0.418	2.6 (0.25 to 26.85)
DILI[#]		
Diabetics	NA	NA
Non-diabetics	0.89	1.15 (0.11 to 13.65)
High bacillary load[$]		
Diabetics	0.87	5.33 (0.67 to 42.2)
Non-diabetics	NA	NA

* No past history of Tb in diabetics; [#]No DILI in diabetics; [$]All non-diabetics had high bacillary load

COPD had a significant effect on delayed sputum smear conversion in patients with pulmonary TB and this effect was also demonstrated in the diabetic sub group. Smoking also had a significant effect on delayed sputum smear conversion in patients with pulmonary TB and this effect was also demonstrated in the diabetic and non-diabetic sub groups. The presence of fibrocavitatory lesions was associated with delayed sputum smear conversion in the entire group of patients and in the diabetic sub group. There was

a significant association between bacillary load and delayed sputum conversion in the entire study group and this was demonstrated in the NDM group as 100 % of the delayed convertors in the NDM group had a high bacillary load.

There was no significant association between DM and sputum smear conversion. Uncontrolled DM also did not have any significant effect on delayed sputum conversion.

There was no association which could be demonstrated between Ethanol consumption, past history of TB, being underweight, anemia, hypoalbuminemia, Drug induced Liver Injury and delayed sputum conversion.

Mortality

Table 10. Cause of death in patients with fatal outcomes

No.	Age	Cause	Day (From diagnosis)	Significant comorbidities
1.	22	Aspiration Pneumonia	29	TBM – MRC III Coma Vigil
2.	56	Diabetic Ketoacidosis (DKA) with septic shock	4	Klebsiella Pneumonia, DM
3.	52	Acute Liver Failure – ATT DILI, Refractory Hypotension	18	Renal Allograft recipient, Oliguric Renal Failure
4.	29	Type 1 DM with DKA, Hospital Acquired Pneumonia	NA (Died in another centre)	DILI, DM
5.	49	Hyperglycaemic Hyperosmolar State, Candidemia	20	Type 2 DM with poor glycaemic control
6.	71	Acute Coronary Syndrome	26	Aspiration Pneumonia, TBM – MRC III, DM
7.	59	DKA, Septic Shock	3	Invasive Rhino cerebral Mucormycosis, DM
8.	68	Acute Coronary Syndrome (ACS)	4	Rheumatoid Arthritis
9.	69	GNB Sepsis	20	Recent ACS, DM

Cause of death in patients with fatal outcomes continued

No.	Age	Cause	Day (From diagnosis)	Significant comorbidities
10.	65	Septic Shock with oliguric renal failure	7	T2DM
11.	56	NA	NA	Non-Hodgkin Lymphoma, DM
12.	54	Candidemia with Septic Shock	24	T2DM
13.	46	Hyperglycaemic Hyperosmolar state with septic Shock	3	Acute Respiratory Distress Syndrome, T2DM
14.	64	NA	NA	Hilar Cholangiocarcinoma

14 patients had fatal outcomes. 10 patients died during their hospital stay, 2 patients died during the intensive phase and 2 during the continuation phase of ATT. 10 were diabetics and 4 were non – diabetics. The associated co morbidities in the patients have been described in (Table 20).

Table 11. Characteristics of patients with fatal outcomes

Parameters	Patients with Fatal outcomes	Patients with non-fatal outcomes	p Value	Relative risk, (95% CI)
Diabetes			0.257	2.1 (0.68-7.58)
Yes	10	58		
No	4	52		
Prior TB			0.27	2.4 (0.45 – 13.17)
Yes	2	7		
No	12	103		
Extrapulmonary TB			0.1	2.9 (0.82 – 10.91
Yes	4	13		
No	10	97		
Smoking			0.13	2.3 (0.76 – 7.18)
Yes	7	33		
No	7	77		
Hypertension			0.06	3.4 (1.09 – 10.62)
Yes	7	25		
No	7	85		
CKD			**0.001**	**8.4** (1.99– 36.39)
Yes	4	5		
No	10	105		
IHD			**0.03**	**5.9** (1.19- 13.17)
Yes	2	3		
No	12	107		
COPD			0.08	4.4 (0.73 – 26.7)
Yes	2	4		
No	12	106		
Anemia			**0.02**	**7.7** (0.97 – 61.24)
Yes	13	69		
No	1	41		

Characteristics of patients with fatal outcomes continued

Parameters	Patients with Fatal outcomes	Patients with non-fatal outcomes	p Value	Relative risk, (95% CI)
Under weight			0.9	1.1 (0.39 – 3.21)
Yes	6	46		
No	8	64		
Uncontrolled DM			0.64	0.70 (0.16 – 3.12)
Yes	7	43		
No	3	13		
DILI			0.19	2.4 (0.59 – 10.16)
Yes	3	11		
No	11	99		
High Bacillary load			0.29	0.2 (0.04 – 2.09)
Yes	1	25		
No	13	85		
Mean Age	53.7 ± 17.2	44.3 ± 16.5	**0.04**	(7.68 – 18.81)[#]
Mean BMI	19.20 ± 4.3	19.27 ± 4.0	0.94	(1.11 – 3.87) [#]
Mean Weight	53.2 ± 12.6	50.8 ± 11.9	0.48	(4.52 – 12.59) [#]
Mean Albumin	2.6 ± 0.7	3.2 ± 0.7	**0.01**	(0.01 – 0.55) [#]
Mean Hba1c	8.3 ± 2.8	7.8 ± 2.8	0.54	(3.39 – 4.95) [#]
Mean Haemoglobin	10.4 ± 1.9	11.4 ± 2.5	0.14	(-2.39 – 0.36) [#]
Mean Creatinine	2.1 ± 2	0.8 ± 0.3	**0.001**	(-0.07 – 0.56) [#]

* Plus – minus values are means ± SD; [#]95% CI of difference of means

Table 12. Factors contributing to mortality in diabetics and non-diabetics

Parameters	p Value	Relative risk, (95% CI)
Prior TB		
Diabetics	0.1	7 (0.86 – 56.89)
Non-diabetics[@]	NA	NA
Extrapulmonary TB		
Diabetics	0.21	3.4 (0.53 – 21.52)
Non-diabetics	0.17	4.1 (0.65 – 25.9)
Smoking		
Diabetics	0.08	4.11 (0.96 – 17.61)
Non-diabetics*	NA	NA
Hypertension		
Diabetics	0.48	1.6 (0.45 – 6.78)
Non-diabetics	**0.05**	12 (1.31 – 109.33)
CKD		
Diabetics	**0.003**	7.8 (1.32 – 46.73)
Non-diabetics	0.20	5.9 (0.84 – 41.04)
IHD		
Diabetics	0.15	4.5 (0.67 – 31.78)
Non-diabetics[#]	NA	NA
COPD		
Diabetics	0.1	4 (0.86 – 56.89)
Non-diabetics[$]	NA	NA
Anemia		
Diabetics	**0.04**	7.3(0.87 – 61.52)
Non-diabetics[&]	NA	NA
Under weight		
Diabetics	0.46	1.7 (0.43 – 7.03)
Non-diabetics	0.77	0.7 (0.09 – 5.61)

Factors contributing to mortality in diabetics and non-diabetics continued

DILI		
Diabetics	0.27	2.6 (0.44 – 16.04)
Non-diabetics	0.43	2.5 (0.28 – 28.67)
Mean BMI		
Diabetics	0.52	(-3.57 – 1.84) ^
Non-diabetics	0.92	(-3.75 – 4.13) ^
Mean Weight		
Diabetics	0.98	(-7.78 – 7.62) ^
Non-diabetics	0.64	(-9.16 – 14.74) ^
Mean Albumin		
Diabetics	0.06	(-0.92 to 0.02) ^
Non-diabetics	**0.02**	(-1.69 – -0.11) ^
Mean Hba1c		
Diabetics	0.65	(-2.17 – 1.37) ^
Non-diabetics	0.81	(0.58 – 0.73) ^
Mean Haemoglobin		
Diabetics	0.11	(-2.91 – 0.28) ^
Non-diabetics	0.45	(-3.01 – 0.39) ^
Mean Creatinine		
Diabetics	**0.001**	(0.92 – 2.30) ^
Non-diabetics	**0.03**	(0.05 – 0.85)^

[@]No history of past TB among the non-diabetics; *No smokers among the non-diabetics

[#]No IHD in the non-diabetic group;[$]No COPD in the non-diabetic group;

[&]All patients in the non-diabetic group had anemia; ^ 95% CI of difference of means

There was a significant association between Creatinine levels, the presence of CKD and mortality in the entire study group and in the DM, NDM sub groups. Ischaemic heart disease and a lower mean weight were associated with mortality in the entire population. Anemia was associated with mortality in the entire study group and in the DM sub-group. Low albumin levels were associated with mortality in the entire study group and in the non-diabetic sub group. Hypertension was significantly associated with Mortality in the NDM sub group. However, in the entire study population, there was no association between hypertension, smoking, COPD and fatal outcomes.

Multivariate analysis

Delayed sputum conversion

Table 13. Multivariate analysis for factors affecting sputum conversion

Parameters	**p Value**	**Adjusted Odds ratio, (95% CI)**
Cavitatory lung lesions	0.05	6.7 (1.01 to 45.61)
COPD	0.006	60.1 (3.23 to 1116.47)
High bacillary load	0.001	22.5 (3.34 to 151.21)

Cavitatory lung lesions, COPD and a high bacillary load were significantly associated with delayed sputum conversion. Smoking was significantly associated with delayed sputum conversion on a univariate analysis.

Mortality

Table 14. Multivariate analysis for factors affecting sputum conversion

Parameters	**p Value**	**Adjusted Odds ratio, (95% CI)**
IHD	0.14	5.2 (0.56 to 47.97)
Albumin	**0.02**	3.5 (1.24 to 9.94)
High bacillary load	0.16	22.5 (3.34 to 151.21)
CKD	**0.03**	6.1 (1.11 to 33.5)
Anemia	0.26	3.5 (0.39 to 32.21)

On logistic regression, lower albumin levels and CKD were significantly associated with mortality. IHD, high bacillary load and anemia did not influence mortality.

Treatment outcomes

Table 15. Treatment outcomes

Treatment outcomes	Diabetics (N = 68)	Non-Diabetics (N = 56)
Cured	17 (25)	14 (25)
Treatment completed	22 (32)	14 (25)
Died	10 (15)	4 (7)
Not Evaluated	19 (28)	24 (43)

*Percentages in brackets

Out of the 27 diabetics had followed up at 6 months, 9 were unable to give sputum samples as they did not have expectoration. Hence their outcomes were, in accordance with the WHO case definitions taken as treatment completed. Similarly, in the NDM group 23 patients followed up at 6 months and 6 did not give sputum samples as they were unable to expectorate, and their outcomes were taken as treatment completed. Patients who were sputum negative at any point of time before the 5^{th} month and had not followed up at 6 months, were taken as treatment completed as per the WHO case definitions. There was no significant association between treatment completion or cure in both the groups and DM [p value - 0.47, RR– 1.14, 95 % CI – (0.83 – 1.6)]. 57 % in the DM group and 50 % in the NDM group were either cured or had completed treatment successfully.

DISCUSSION

In this prospective observational cohort study, we aimed to look at the effect of DM on the outcomes of sputum positive pulmonary TB. We wished to look at the cure rates, sputum conversion rates at 2 months and the determinants of treatment outcomes of patients with pulmonary TB and DM. We also planned to assess the effects of glycaemic control on the treatment outcomes of sputum positive pulmonary TB.

Demographics

In our study, 124 patients were included with 68 diabetics and 58 non-diabetics.

The baseline demographic characteristics were mostly similar in both the groups except for a higher mean age and a male predominance in the DM group.

Clinical characteristics

The DM group had a significantly higher percentage of hypertensives. Ethanol consumption and smoking was also significantly higher in the DM group. Symptoms at presentation were equal in both the groups. The anthropometric and laboratory parameters were significantly different among both the groups. The mean weight and BMI were significantly lesser in the NDM group as compared to the DM group. This suggests that degree of immunosuppression caused by DM was as severe as the under nutrition in the NDM group and was enough to lead to an increased risk of contracting TB. Factors causing this level of immunosuppression in patients with DM need to be studied. This co relates with a systematic review of literature which looked at 13 observational studies and showed a threefold risk of developing TB in diabetics (12). These studies were conducted in Asian countries - Taiwan, Korea, India; the United

Kingdom, Russia and the United states of America. The diabetics in our study did not have a higher number of patients with past TB as was described in a few studies from Egypt, China and the Republic of the Congo which demonstrated higher rates of relapse of TB in diabetics (83,84,87). Extrapulmonary TB was more prevalent in the non-diabetic group (9% in the DM group vs 19% in the NDM group) with a trend towards significance (p value – 0.08). This finding was demonstrated in a study conducted in Guinea and another study conducted in Mexico (60,69).

Investigations

Haemoglobin levels were significantly lower in the non-diabetics when compared with the diabetics. The mean albumin levels were lower than normal in both the groups (Normal albumin levels- 3.5- 5.5 in our institution) and the albumin levels were significantly lower in the non-diabetics. The mean HbA1c was 9.5 in the DM group and 5.3 in the NDM group. In the DM group, 9% were newly diagnosed to have DM. Nearly 70 % of the diabetics were on oral diabetic agents and 18 % were on insulin. The most common microvascular complication was diabetic neuropathy which was seen in around 30% of the patients. Ischaemic heart disease was the most common macrovascular complication which was seen in 7% of the patients.

The most common X-ray finding in both the groups was consolidation. The presence of Fibrocavitatory lesions was similar in both the groups and our study did not demonstrate an association between poor glycaemic control and the presence of cavitatory lesions, as was demonstrated in a study from Iran (91). 7% of diabetic patients with cavities were using insulin. However, there was no significant association between insulin use and the presence of cavitatory lesions (p value – 0.49) This finding was in contrast to the finding

in a study done in Turkey which showed increased frequency of cavitatory lesions in diabetic patients using insulin (62).

Sputum characteristics of patients

Sputum smears were negative in 15 % and 26 % in the DM and NDM group respectively. These patients had positive sputum Xpert PCR reports. High bacillary load (3+ sputum AFB) was seen in 30 % of the non-diabetics as compared with 13% in the diabetics, which was statistically significant. These results corroborate with studies done in Indonesia and Turkey which showed lower sputum mycobacterial load in diabetics and no co relation between sputum mycobacterial load and DM respectively(62,71). However, Among the 9 patients with a high bacillary load in the DM group, HbA1c levels were available for 8 of the patients and all of them had uncontrolled Dm (HbA1c > 7), which was demonstrated in a study conducted in Korea where uncontrolled diabetics had a higher bacillary load as compared with diabetics with optimum diabetic control(72). Among these patients, 4 had HbA1c levels > 9 but there was no significant association between patients with HbA1c > 9 and high bacillary load (p value – 0.71) as was demonstrated in a study from Taiwan (64).

Drug induced Liver injury

Though a study done in the United States of America (USA) had shown DM to be an independent risk factor for the development of DILI (95), this was not demonstrated in our study.

Delayed sputum conversion

11 patients were sputum positive at 2 months of which 6 (15%) were diabetics and 5 (18%) were non-diabetics. In agreement with other studies conducted in the USA and India (17,68,79) our study did not show any relationship between DM and delayed sputum conversion. In our study, Smoking was associated with delayed sputum conversion in the entire study group [RR - 7.5, 95% CI (2.26 to 25.42), p value- 0.0001] and in the DM and NDM subgroup. This finding was in keeping with other studies done in Japan, China, the Netherlands and Canada (89–93). COPD was also significantly associated with delayed sputum conversion in the entire study group [RR – 6.1, 95% CI (2.57 to 14.41), p value- 0.001] and in the DM sub-group, this could be inferred from the association between smoking and delayed sputum conversion. The presence of fibro-cavitatory lesions was significantly associated with delayed sputum conversion in the entire population [RR - 3.59, 95% CI (1.29 to 9.97) p value = 0.014] and in the DM sub group. This finding was in keeping with a study from China (98). Uncontrolled DM (HbA1c > 7) was not associated with delayed sputum conversion as was demonstrated in a few studies (36,82,92). High bacillary load was significantly associated with delayed sputum conversion in our study

[RR – 6.9, 95% CI (2.34 to 20.23), p value = 0.001]. This was demonstrated in the NDM group as 100 % of the delayed convertors in the NDM group had a high bacillary load. This was in agreement with a few other studies. These studies also demonstrated delayed sputum conversion in males. However, this was not shown in our study (104,105). Though there was significant association between hypoalbuminemia and delayed sputum conversion, we demonstrated a trend towards delayed sputum conversion in this study [RR – 3.15, 95% CI (0.736 to 13.484), p value - 0.09].

A relationship between delayed sputum conversion and hypoalbuminemia could be demonstrated in larger studies.

There was no statistically significant relationship between having a past history of TB, Ethanol consumption, being underweight, anemia and delayed conversion of sputum smears which could be demonstrated in our study.

Effect of Treatment of TB on glycaemic control

There was a significant impact of TB treatment on glycaemic control as demonstrated by a significant reduction in the mean HbA1c before and after treatment of TB in diabetics [Mean difference – 1.76, 00195% CI of difference – (1.01 – 2.52) p value – 0.001]. To the best of our knowledge, there are very few studies looking at the effect TB treatment has on glycaemic control. A study from China looked at fasting blood glucose levels in patients with newly diagnosed DM during initiation of ATT and reported that their blood sugar levels were uncontrolled during and after treatment. We could not find any studies which look at the glycaemic control after initiation of ATT in patients who are known diabetics. Our finding of a decline in HbA1c after ATT treatment has not been reported and further studies are needed to look at glycaemic control in known diabetics after ATT initiation.

Mortality

The mortality rates were 15 % and 7% in the DM and NDM groups respectively. All the patients with fatal outcomes had a significant co existing chronic disease or a severe infection or a severe metabolic complication like Diabetic Ketoacidosis and Hyperglycaemic Hyperosmolar state. A significant association between DM and mortality rates could not be demonstrated in our study, which has been demonstrated in other studies performed in Tanzania, The USA, India and Taiwan (17,67,69,73,74).

There was a significant association between the presence of CKD and IHD contributing to mortality in the entire study population and in the DM, NDM sub groups. Anemia was also significantly associated with mortality in the entire study group [RR – 6.6, 95% CI (0.90 – 49.18), p value - 0.02]

Patients with fatal outcomes had a lower albumin level [F-0.425, p value – 0.01, mean difference -0.53, 95 % CI of difference (-0.945 to – 0.106)] and higher creatinine levels [F-71.9, p value – 0.001, mean difference 1.29, 95 % CI of difference (0.84 to 1.74)].

Treatment outcomes

There was no treatment failure recorded in our study. However, there was a significant loss to follow up. Of the initial 68 diabetics and 56 non – diabetics, only 27 and 23 patients were followed up at 6 months respectively. At 2 months 41 diabetics and 30 non-diabetics had followed up. The treatment outcomes were comparable in the DM and NDM groups. 57 % in the DM group and 50 % in the NDM group were either cured or had completed treatment successfully. Varying effects of DM on TB outcomes have been described with some studies conducted in Korea, Saudi Arabia and The USA showing no negative effects of DM on TB treatment outcomes or mortality (68,72,79) while a few other studies including studies conducted in India, Taiwan, China and Spain which have shown increased risk of treatment failure and mortality (78,123–125).

Multivariate analysis

Delayed sputum conversion

Cavitatory lung lesions [p value - 0.05; RR - 6.7, 95% CI - (1.01 to 45.61)],

COPD [p value - 0.006; RR - 60.1, 95% CI - (3.23 to 1116.47)] and a high bacillary load [p value - 0.001; RR - 22.5, 95% CI - (3.34 to 151.21)] were significantly associated with delayed sputum conversion. Smoking was significantly associated with delayed

sputum conversion on a univariate analysis. However, Smoking and COPD had almost similar relative risks and a 95% CI, hence due to the co linearity of the variables, one of them had to be excluded from the multivariate analysis. The relationship between COPD and delayed sputum conversion could in effect be secondary to the effect smoking has delayed sputum conversion and as a risk factor for developing COPD. This could explain the extreme value seen in the upper bound of the 95% class interval.

Mortality

On logistic regression, lower albumin levels [p value - 0.02; RR - 3.5, 95% CI - (1.24 to 9.94)] and CKD [p value - 0.03; RR - 6.1, 95% CI - (1.11 to 33.5)] were associated with mortality.

CONCLUSION

1. In this study, we demonstrated that Diabetes was not associated with poor outcomes or failure of treatment in patients with pulmonary TB.
2. There was also no association between DM and delayed sputum conversion.
3. We could not demonstrate any association between poor glycaemic control and delayed sputum conversion or mortality.

LIMITATIONS

1. There was a significant loss to follow up in this study.
2. We were unable to achieve the target sample size.

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ANNEXURES

Annexure 1: IRB Approval

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

June 08, 2017

Dr. John Titus George,
PG Registrar,
Department of Medicine,
Christian Medical College,
Vellore - 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Outcomes of Sputum Positive Pulmonary tuberculosis in patients with Diabetes Mellitus– a prospective observational cohort study.
Dr. John Titus George, Dept. of Medicine Unit-III, Dr. Sowmya Sathyendra, Employment Number: 28181, Associate Professor Dr . Alice Joan Mathuram, Associate Professor, 28529, Dr. Vignesh Kumar , Assistant Professor 33782, Dr. Angel Miraclin, Assistant Professor, 29115, Dr. O.C. Abraham, Professor, 05638, Dr. Ramya. I. Professor, 31571, Department of Medicine, Dr. Joy Sarojini Michael, Professor, 50199, Department of Microbiology Dr. Jasmin Helan , 20080, Dr. Asha Elizabeth Mathew, 29880, Department of Community Health, Dr. Visali, Statistician, Department of Biostatistics.

Ref: IRB Min No: 10518 [OBSERVE] dated 01.02.2017

Dear Dr. John Titus George,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Outcomes of Sputum Positive Pulmonary tuberculosis in patients with Diabetes Mellitus– a prospective observational cohort study" on February 01st 2017.

The Committee reviewed the following documents:

1. IRB Application format
2. Consent form and Information Sheet
3. Proforma
4. Cv's Of Drs. Angel, Alice Mathuram, Asha, O C Abraham, Jasmin, Sowmya, Ramya, John Titus, Joy Sarojini and Vignesh.
5. No. of documents 1 – 4.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on February 01st 2017 in the Jacob Chandy Hall, Paul Brand Building, Christian Medical College, Vellore 632002.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Dr. Rajesh Kannangai	MD, PhD.	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, Vellore	External, Scientist &Epidemiologist
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
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Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
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Chairperson, Ethics Committee.

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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Santhanam Sridhar	MBBS, DCH, DNB	Professor, Neonatology, CMC, Vellore	Internal, Clinician
Dr. Vivek Mathew	MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC, Vellore	Internal, Clinician
Dr Sneha Varkki	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal, Clinician
Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Outcomes of Sputum Positive Pulmonary tuberculosis in patients with Diabetes Mellitus– a prospective observational cohort study." on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 1,00,000/- INR (Rupees One Lakh Only) will be granted for 2 years. 50,000/- INR (Rupees Fifty Thousand only) will be granted for 12 months as an Ist Installment. The rest of the 50,000/- INR (Rupees Fifty Thousand only) each will be released at the end of the first year as 2 nd Installment.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min No: 10518 [OBSERVE] dated 01.02.2017

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Annexure 2 : Consent Form

CONSENT FORM

STUDY OF OUTCOMES OF SPUTUM POSITIVE PULMONARY TUBERCULOSIS IN DIABETIC PATIENTS – A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Subject ID: _____

Subject's Name: _____

Date of Birth (if available):

Age (in completed years): _____

(i) I confirm that I have read and understood the information sheet dated January 1st 2017 for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative

Date: ____/____/_____

Witness : _____

Signatory's Name: _____ Signature:

Annexure 3: Patient Information Sheet

PATIENT INFORMATION FORM:

STUDY OF OUTCOMES OF SPUTUM POSITIVE PULMONARY TUBERCULOSIS IN DIABETIC PATIENTS – A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Date: Jan 1st 2017

Tuberculosis affects a large proportion of our population and despite continuing efforts to control the illness, it still remains a public health problem in our country. India is also the diabetic capital of the world with the maximum number of diabetics in the world. Diabetes increases the risk of contracting tuberculosis and has been shown to affect treatment outcomes. This study is aimed at finding out the relationship between diabetes and treatment outcomes of pulmonary tuberculosis. This study will also look at how the outcome differs in these patients with diabetes and uncontrolled diabetes. Any publications arising from the study will not have any patient identifiable data. You can opt out of the study if you wish to do so at any time.

By enrolling yourself into this study you subject yourself to no risk at all. You will be followed up 2 months of commencement of therapy and if your sputum is positive for AFB, you will be asked to follow up with monthly sputum AFB samples until negative and at 6 and 12 months after commencement of therapy. At the end of 2 months if your sputum is negative for AFB, you will be asked to follow up at at 6 and 12 months after commencement of therapy. There are no risks associated with this study as you will be receiving treatment as per the existing guidelines for tuberculosis and diabetes. Blood samples will also collected at your initial visit which will be used for HbA1c testing (A marker of blood glucose levels) and stored for further testing later on. Your sputum samples will also be stored for futher testing. You will also be followed up via telephonic conversation for monitoring and for reminders about up coming follow up dates. Your treatment will not be altered in any form as a consequence of your participation in this study. You will also be required to answer some questions regarding your health status at each visit to the hospital and give sputum samples. All information provided by you will be kept confidential and your identity will not be revealed to a third party under any circumstances. By participating in this study, you will go a long way in helping the health care community better understand the mechanisms of the illness so that diagnosis can be made early and correct treatment be instituted in time to prevent the many complications of the disease.

Annexure 4: Data Extraction Form

STUDY OF OUTCOMES OF SPUTUM POSITIVE PULMONARY TUBERCULOSIS IN DIABETIC PATIENTS – A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Proforma

1. Serial No : | | | |
2. Name :_____
3. Hospital No: | | | | | | | |
4. Age : _____
5. Date of Birth: __ /__/___
6. Address :

   _____

   _____

   _____

   _____
7. Phone Number : _____
8. No. of members in family: _____
9. Area of residence: _____
10. Number of people staying at home :_____
11. Number of rooms: _____

12. Eductaion

1.	**Profession or Honours**	**7**
2.	**Graduate or post graduate**	**6**
3.	**Intermediate or post high school diploma**	**5**
4.	**High school certificate**	**4**
5.	**Middle school certificate**	**3**
6.	**Primary school certificate**	**2**
7.	**Illiterate**	**1**

13. Occupation

1.	**Profession**	**10**
2.	**Semi-Profession**	**6**
3.	**Clerical, Shop-owner, Farmer**	**5**
4.	**Skilled worker**	**4**
5.	**Semi-skilled worker**	**3**
6.	**Unskilled worker**	**2**
7.	**Unemployed**	**1**

14. Income

Latest revision (in Rs./month)				
1.	20266		and above	12
2.	10133	-	20265	10
3.	7600	-	10132	6
4.	5066	-	7599	4
5.	3040	-	5065	3
6.	1023	-	3039	2
7.	1022		and below	1

15. SES

SCORING	
Total score	Socioeconomic Class
26-29	Upper
16-25	Upper middle
11-15	Lower middle
5-10	Upper lower
< 5	Lower

* Kuppuswamy B. Manual of Socioeconomic Status (Urban) 1st ed. Delhi: Manasayan; 1981. pp. 66–72

*Sharma R. Kuppuswamy's socioeconomic status scale - revision for 2011 and formula for real-time updating. Indian J Pediatr 2012;79(7):961-2.

16. Date of Diagnosis of Tuberculosis: __/__/___

17. Symptoms : Fever / Cough / expectoration / hemoptysis / chest pain / others

18. Have You Been Diagnosed to have Tuberculosis in the past?

19. Have You Been Treated for Tuberculosis in the past?

20. If yes.:

    a. For how long was treatment taken

    b. Treatment outcome : Cured / Failure / completed

21. Diabetes : Y /N

22. If yes :

    I. Duration:

    II. Treatment: OHAs / Insulin

    III. Complications: Neuropathy / nephropathy / retinopathy CVA / IHD / PVD

23. Co morbid illness: CKD / CLD / IHD / COPD / Hypothyroidism /others

24. Smoking : Y / N

25. If Yes:

    a. Pack years

Assessment At Enrollment:

1. Height : _____cm.
2. Weight :_____kg.
3. BMI: _____
4. Sputum AFB – Quantitate - _____
5. Hba1c | | | |

6. AFB Culture _____

Assessment at 2 months

1. Weight : _____kg
2. ATT Adverse effects : Vomiting / hepatitis / Neuropathy / others
3. Have you been complicant with ATT drugs ? Y / N
4. Have you been complicant with with diabetic medications : Y / N
5. How many days have you missed atleast one drug in the last 2 months?
   _____
6. Sputum AFB : _____

Assessment at 5 months

1. Weight : _____kg
2. Hba1c : | | | |
3. ATT Adverse effects : Vomiting / hepatitis / Neuropathy / others
4. Sputum AFB : _____
5. Have you been complicant with ATT drugs ? Y / N

6. Have you been complicant with with diabetic medications : Y / N

7. How many days have you missed atleast one drug in the last 2 months?

Assessment at 6 months

1. Weight : _____kg
2. ATT Adverse effects : Vomiting / hepatitis / Neuropathy / others
3. Sputum AFB : _____
4. Have you been complicant with ATT drugs ? Y / N
5. Have you been complicant with with diabetic medications : Y / N
6. How many days have you missed atleast one drug in the last 2 months?

Annexure 5: Data Entry Form

serialnumb	cavities	Age	Sex	residence	peoplestay	rooms	education	occupatior
1	2.00	45	1	2	5	3	4	5
2	2.00	45	1	1	5	3	3	3
3	2.00	72	1	1	8	3	4	5
4	1.00	19	2	2	5	3	6	4
5	2.00	29	1	2	2	1	4	2
6	2.00	18	2	2	14	6	6	4
7	2.00	21	1	1	4	3	6	10
8	1.00	49	2	1	5	2	5	5
9	1.00	36	1	1	4	3	3	3
10	2.00	42	1	1	4	3	4	3
11	2.00	26	1	1	3	3	6	4
13	2.00	26	1	2	4	2	4	4
14	2.00	54	1	1	3	3	5	10
15	2.00	34	1	2	4	2	4	3
16	2.00	46	1	1	6	3	3	4
17	1.00	67	1	1	7	3	2	3
18	2.00	38	1	2	5	3	3	4
19	2.00	60	2	1	15	6	6	6
20	2.00	69	1	2	10	6	4	3
21	2.00	30	1	2	5	2	4	3
22	2.00	19	2	1	5	2	6	3
23	2.00	18	1	1	5	2	4	3
24	1.00	31	1	2	12	6	2	3
25	2.00	22	2	1	4	2	4	4
26	2.00	38	2	1	4	3	4	3
27	2.00	37	1	2	10	2	5	5
28	2.00	40	2	2	5	2	3	3
29	2.00	56	1	1	5	1	6	6
30	2.00	29	2	2	6	4	7	10
31	2.00	58	1	2	5	2	6	10
32	2.00	55	2	1	10	5	5	5
33	1.00	67	1	2	6	3	7	10
34	2.00	57	1	2	4	3	4	3
35	1.00	33	2	2	6	2	5	5
36	2.00	28	2	2	4	2	4	5
37	2.00	56	1	2	8	3	3	2
38	2.00	24	1	2	5	2	6	5
39	1.00	63	1	1	4	2	6	5
40	2.00	28	1	1	4	2	4	3
41	2.00	19	2	1	5	3	6	6
42	2.00	78	1	1	5	2	7	10
43	2.00	71	1	2	6	4	6	5
44	2.00	42	1	2	2	2	4	5
45	2.00	45	1	2	4	2	4	5
46	1.00	46	2	2	5	3	3	4
47	1.00	18	2	2	5	2	2	2
48	1.00	33	2	1	2	2	4	3
49	1.00	46	1	2	4	2	4	6
50	1.00	64	1	1	6	4	5	5

51	1.00	44	1	2	6	3	3	3
52	1.00	28	1	2	5	3	5	5
53	2.00	27	2	1	10	5	4	3
54	2.00	58	1	2	6	3	4	3
55	2.00	44	2	2	8	3	3	3
56	2.00	21	2	1	4	3	6	6
57	1.00	62	2	2	5	3	5	5
58	2.00	40	1	2	5	3	2	1
59	2.00	73	1	1	4	2	6	10
60	2.00	64	1	2	5	4	6	10
61	2.00	67	1	2	11	3	4	2
62	2.00	53	1	2	3	2	4	4
63	1.00	74	1	1	5	3	7	10
64	1.00	48	2	2	4	2	4	5
65	2.00	29	1	2	4	2	6	6
66	1.00	56	1	2	4	2	5	5
67	2.00	65	1	2	8	4	3	4
68	2.00	45	1	2	5	3	4	4
69	1.00	66	2	2	4	2	6	6
70	2.00	55	2	1	5	3	4	5
71	2.00	36	2	2	5	3	4	5
72	2.00	57	1	1	5	2	6	10
73	2.00	57	2	1	4	2	5	5
74	2.00	70	1	2	5	3	4	5
75	1.00	44	1	1	4	3	5	5
76	2.00	60	1	1	7	4	3	4
77	2.00	59	1	2	4	2	4	5
78	2.00	35	1	2	4	2	4	4
79	2.00	35	2	1	12	3	6	10
80	1.00	65	2	2	5	2	4	4
81	2.00	65	1	2	5	2	4	4
82	2.00	24	2	2	4	4	4	4
83	2.00	28	1	1	4	2	3	3
84	2.00	18	2	2	6	1	2	3
85	1.00	63	1	1	4	2	6	6
86	1.00	63	1	1	4	2	5	5
87	2.00	55	1	1	4	3	5	5
88	1.00	58	2	2	4	2	4	5
89	2.00	68	1	2	5	2	5	5
90	2.00	63	1	1	4	2	4	3
91	2.00	42	2	2	6	3	5	5
92	2.00	32	1	1	4	2	5	5
93	2.00	40	1	2	4	2	5	4
94	2.00	70	2	2	7	2	4	5
95	2.00	45	1	2	4	2	4	4
96	2.00	50	1	2	4	2	5	5
97	2.00	39	2	2	3	2	5	6
98	1.00	65	2	2	4	2	4	4
99	2.00	67	1	2	5	3	3	3
100	2.00	55	1	2	5	2	5	5

101	1.00	67	1	2	4	1	4	4
102	2.00	44	2	1	4	2	5	5
103	2.00	22	2	2	4	2	6	6
104	2.00	66	1	1	4	3	6	6
105	2.00	45	1	1	4	2	4	4
106	2.00	54	1	2	6	3	5	5
107	2.00	20	1	1	4	3	6	6
108	2.00	71	1	2	5	3	4	4
109	2.00	26	1	1	3	2	6	6
110	2.00	26	1	1	3	2	5	5
111	1.00	74	1	2	3	2	4	4
112	2.00	36	1	2	5	3	4	5
113	2.00	54	1	2	4	3	3	4
114	2.00	50	1	2	5	2	4	3
115	2.00	21	2	2	6	1	1	2
116	2.00	22	1	2	4	1	2	2
117	2.00	39	1	2	7	3	5	4
118	2.00	18	2	1	4	3	7	10
119	2.00	56	1	1	5	2	4	5
120	2.00	40	1	2	5	1	1	2
121	2.00	29	1	2	5	2	3	3
122	1.00	40	1	2	6	4	4	5
123	2.00	54	1	1	5	3	5	6
124	2.00	38	1	1	4	3	3	3
125	2.00	22	1	1	4	3	7	10

income	Kuppusam	diagnosisdate	fever	cough	expectorat	hemoptysi	chestpain	breathlesn
6	3	10-Feb-17	1	1	1	2	2	1
6	3	13-Feb-17	1	1	1	2	2	2
6	3	28-Feb-17	1	1	1	2	2	1
10	4	06-Mar-17	1	1	1	2	2	1
2	2	22-Feb-17	2	1	1	2	2	2
10	4	08-Mar-17	1	1	1	2	2	1
12	1	01-Mar-17	1	1	1	2	2	2
6	2	21-Feb-17	1	1	1	1	2	1
4	4	08-Mar-17	1	1	1	1	2	2
4	3	15-Mar-17	1	1	2	2	2	2
10	2	11-Mar-17	1	1	1	2	2	1
6	3	20-Mar-17	1	1	1	2	2	2
12	1	20-Mar-17	1	1	1	1	1	1
10	2	22-Mar-17	1	1	1	2	2	2
6	3	26-Mar-17	1	1	1	2	2	2
4	4	25-Mar-17	1	1	1	2	2	1
4	3	28-Mar-17	1	1	1	2	2	1
10	2	24-Mar-17	1	1	1	2	2	1
10	2	05-Apr-17	1	1	1	2	2	1
4	3	03-Apr-17	1	1	1	2	2	2
6	3	19-Apr-17	1	1	2	2	2	2
6	3	25-Apr-17	1	1	1	2	2	2
2	4	31-Mar-17	1	1	1	1	1	1
6	3	12-Apr-17	1	1	1	2	2	2
6	3	14-Apr-17	1	1	1	2	2	2
10	2	08-May-17	2	1	1	2	2	2
4	4	09-May-17	1	1	1	2	2	1
6	2	03-May-17	1	1	1	1	2	1
12	1	13-May-17	1	1	1	2	2	2
12	1	16-May-17	1	1	1	1	2	2
10	2	20-May-17	2	1	1	2	2	2
4	2	23-May-17	1	1	1	2	2	2
4	3	24-May-17	1	1	1	2	2	2
6	2	24-May-17	2	1	1	2	2	1
6	3	31-May-17	1	1	1	2	2	2
2	4	05-Jun-17	1	1	1	2	2	2
5	2	05-Jun-17	1	1	1	1	1	1
6	2	09-Jun-17	1	1	1	2	2	1
6	3	12-Jun-17	1	1	1	2	2	1
10	2	14-Jun-17	1	1	1	2	2	2
12	1	28-Jun-17	1	1	1	2	2	1
10	2	03-Jul-17	2	1	1	2	2	1
6	3	20-Jul-17	1	1	1	2	2	2
6	3	22-Jul-17	1	1	1	2	2	1
4	3	26-Jul-17	1	1	1	2	2	2
2	4	31-Jul-17	1	1	1	2	2	2
10	2	01-Aug-17	1	1	1	2	2	2
4	3	04-Aug-17	1	1	1	2	2	2
6	2	02-Aug-17	1	1	1	2	2	1

4	4	04-Aug-17	1	1	1	2	2	2
6	2	09-Aug-17	1	1	1	2	2	1
10	2	04-Aug-17	1	1	1	2	2	1
6	3	11-Aug-17	1	1	1	2	2	2
4	4	09-Aug-17	1	1	1	2	2	2
10	2	12-Aug-17	1	1	1	2	2	2
10	2	25-Aug-17	1	1	1	2	2	2
1	4	28-Aug-17	1	1	2	2	2	2
12	1	29-Aug-17	2	1	2	2	2	2
12	1	31-Aug-17	2	1	1	2	2	2
3	4	04-Sep-17	1	2	1	2	2	2
4	3	06-Sep-17	2	1	1	2	2	2
12	1	08-Sep-17	2	1	1	2	2	2
4	3	08-Sep-17	2	1	1	2	2	2
10	2	09-Sep-17	1	1	1	2	2	1
6	2	12-Sep-17	2	1	1	2	2	2
4	3	12-Sep-17	1	1	1	2	2	2
6	3	13-Sep-17	2	1	1	2	2	2
10	2	15-Sep-17	2	1	1	2	2	1
6	3	24-Sep-17	1	1	2	2	2	2
4	3	18-Sep-17	1	1	1	2	2	1
12	1	29-Sep-17	1	1	1	2	2	1
12	2	30-Sep-17	1	1	1	1	2	1
6	3	08-Oct-17	2	1	1	2	2	1
6	2	10-Oct-17	1	1	1	2	2	2
6	3	10-Oct-17	1	1	1	2	2	2
6	3	12-Oct-17	2	1	1	2	2	1
4	3	20-Oct-17	1	1	1	2	2	1
10	1	21-Oct-17	1	1	1	2	2	2
4	3	24-Oct-17	1	1	1	2	2	2
6	3	12-Sep-17	1	1	2	2	2	2
4	3	18-Nov-17	1	1	1	2	2	2
4	2	18-Nov-17	2	1	1	2	2	2
3	2	09-Oct-17	2	1	1	1	2	2
10	2	29-Sep-17	1	1	1	2	2	2
6	2	29-Sep-17	1	1	1	2	2	2
6	2	26-May-17	2	1	1	2	2	1
6	2	28-Mar-17	1	1	1	2	1	1
6	2	17-Dec-17	1	1	2	2	2	2
4	3	02-Nov-17	1	1	1	2	2	2
6	2	07-Jul-17	2	1	1	2	2	1
6	2	30-Dec-17	1	1	1	2	2	2
6	2	28-Dec-17	2	1	1	2	2	1
6	3	20-Oct-17	1	1	2	2	2	2
6	3	12-Dec-17	1	1	2	2	2	2
6	2	10-Nov-17	2	1	1	2	2	1
10	2	07-Nov-17	2	1	1	2	2	1
3	3	08-Dec-17	1	1	1	2	2	1
3	4	19-Oct-17	1	1	1	2	2	2
6	2	13-Oct-17	2	1	1	2	2	1

6	2	16-Oct-17	1	1	2	2	2	1
6	2	18-Dec-17	1	1	2	2	2	2
10	2	02-Dec-17	1	1	2	2	2	2
10	2	07-Nov-17	1	1	1	2	2	1
4	3	29-Sep-17	1	1	1	2	2	2
6	2	22-Sep-17	1	1	1	2	2	1
10	2	14-Nov-17	1	1	1	1	2	1
4	3	10-Nov-17	1	1	2	2	2	1
10	2	30-Dec-17	1	1	1	2	2	2
10	2	05-Oct-17	1	1	2	2	2	2
4	3	23-Dec-17	1	1	1	2	2	1
6	3	01-Nov-17	1	1	1	2	2	1
4	3	30-Dec-17	1	1	1	2	2	1
4	3	11-Dec-17	1	1	1	2	2	1
2	4	22-Dec-17	1	1	1	2	2	2
1	1	29-Dec-17	2	1	1	2	2	2
4	3	26-Dec-17	1	1	1	2	2	2
12	1	11-Nov-17	1	1	1	2	2	2
6	3	01-Nov-17	2	1	1	2	2	2
1	2	16-Nov-17	1	1	1	2	2	1
4	4	12-Apr-17	1	1	1	2	2	1
6	3	04-Oct-17	1	1	1	2	2	2
6	2	06-Oct-17	1	1	1	2	2	2
6	3	06-Oct-17	1	1	1	2	1	1
12	1	27-Oct-17	1	1	1	2	2	2

LOA	LOW	Othersymptoms	priortb	priortreatn	durationof	howmanyy	outcomes
1	1		2				
1	1		2				
1	1		2				
1	1		2				
2	2		2				
1	1		2				
2	2		2				
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1	1		2				
1	1		2				
1	1		2				
1	1	headaceh, seziures	2				
1	1		2				
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1	1		2				
1	2		2				
1	1		2				
1	1		2				
1	2		1	1	1	4	4
1	1		2				
1	1		2				
1	1		1	1	1	3	4
1	1		2				
1	2		2				
1	2		2				
1	1	altered sensorium	2				
1	1		2				
1	1		2				
1	1		2				
1	1		1	1	2	6	1
1	1		2				
1	2		2				
1	1		2				
1	1		2				

1	1		1	1	1	3	4
1	1		2				
1	1		2				
1	1		2				
2	2		2				
1	1		2				
1	1	swelling low back	2				
1	2		2				
1	1		2				
1	2		2				
1	2	paraplegia	2				
1	2		2				
1	2		2				
1	2		2				
1	1		2				
1	1	altered sensorium	1	1	10	6	1
1	2		2				
2	2		2				
1	1		2				
1	2		2				
1	1		2				
1	1		2				
1	1		2				
1	1		2				
1	1		2				
1	1		2				
1	1		2				
2	1		2				
1	1		1	1	1	6	1
1	2		2				
1	2		2				
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2	1		2				
1	1		2				
2	2		2				
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1	1		2				
1	1		2				
2	2		2				
1	1		2				
1	1		2				
1	1	altered sensorium	2				
1	1		1	1	4	6	1
1	1		1	1	10	6	1
1	1		2				
1	2		2				
2	2		2				
1	1	altered sensorium, weakne	2				
1	1	altered sensorium	2				
1	1		2				
1	2		1	1	2	6	1
1	1		2				
1	2		2				
1	1		2				
1	1		2				
1	1		2				
1	1		2				
1	1		2				
2	2		2				
1	1		2				
1	1		2				

DM	DurationDI	Treatment	Neuropath	Nephropat	Retinopath	CVA	IHD	PVD
1	3	1	2	1	2	2	2	2
1	10	1	2	1	1	2	1	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	1	1	2	2	2	2	2	2
1	8	3	1	2	2	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	4	1	2	2	2	2	2	2
2						2	2	2
1	15	2	1	1	1	2	2	2
2						2	2	2
1	10	1	1	1	2	2	2	2
1	4	1	2	2	2	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	2	1	2	1	2	2	2	2
2						2	2	2
1	6	2	1	2	1	2	2	2
2						2	2	2
2						2	2	2
1	1	1	2	2	2	2	2	2
1	3	2	2	2	2	2	2	2
1	0	1	2	2	2	2	2	2
2						2	2	2
1	10	1	1	2	2	1	1	1
1	15	1	1	1	1	2	2	2
2						2	2	2
2						2	2	2
1	0	1	2	2	2	2	2	2
1	3	2	2	2	2	2	2	2
1	1	1	2	2	2	2	2	2
1	0	4	2	2	2	2	2	2
2						2	2	2
1	35	2	1	1	1	1	1	2
1	10	1	2	2	2	2	2	2
1	5	1	2	2	2	2	2	2
1	3	1	2	2	2	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	2	1	2	2	2	2	2	2
1	25	2	1	1	1	2	2	1

1	3	1	2	2	2	2	2	2
2						2	2	2
2						2	2	2
1	1	1	2	2	2	2	1	2
1	2	3	2	2	2	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	15	1	1	1	1	1	2	2
2						2	2	2
2						2	2	2
1	5	1	1	2	2	2	2	2
2						2	2	2
1	8	1	1	2	2	2	2	2
2						2	2	2
2						2	2	2
1	1	1	2	2	2	2	2	2
1	1	1	2	2	2	2	2	2
1	2	3	2	2	2	2	2	2
1	0	1	2	2	2	2	2	2
1	7	3	1	1	2	2	2	2
1	6	1	2	1	2	2	2	2
1	6	1	2	1	2	2	2	2
1	3	2	2	2	2	2	2	2
2						2	2	2
1	1	1	2	2	2	2	2	2
1	10	1	1	1	1	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	10	2	1	1	1	2	2	2
1	10	2	1	1	2	2	1	2
2						2	2	2
2						2	2	2
1	5	1	2	2	2	2	2	2
1	10	1	1	2	1	2	2	2
1	2	1	2	2	2	2	2	2
1	4	1	2	2	2	2	2	2
1	4	1	2	2	2	2	2	2
1	5	1	2	2	2	2	2	2
1	2	1	2	2	2	2	2	2
1	0	4	2	2	2	2	2	2
1	3	1	2	2	2	2	2	2
1	10	1	1	1	2	2	2	2
2						2	2	2
1	5	1	2	2	2	2	2	2

1	10	1	1	2	2	2	2	2
1	3	1	2	2	2	2	2	2
2						2	2	2
1	10	2	1	1	1	2	2	2
2						2	2	2
1	3	1	2	2	2	2	2	2
2						2	2	2
1	10	1	1	1	1	2	2	2
1	3	2	2	2	2	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	5	1	2	2	2	2	2	2
2						2	2	2
2						2	2	2
2						2	2	2
1	6	2	2	2	2	2	2	2
2						2	2	2
1	5	1	2	2	2	2	2	2
1	6	1	2	2	2	2	2	2
1	0	1	2	2	2	2	2	2
1	1	1	2	2	2	2	2	2
1	3	1	2	2	2	2	2	2
1	1	1	2	2	2	2	2	2
2						2	2	2

Extrapulm	Typeofextr	CKD	ckdcreat	CLD	COPD	Hypothyro	HTN
2		2	0.7	2	2	2	2
2		2	0.9	2	2	2	2
2		2	1.2	2	1	2	1
2		2	0.5	2	2	2	2
2		2	0.8	2	2	2	2
1	1	2	0.7	2	2	2	2
2		2	1.1	2	2	2	2
2		2	1.0	2	2	1	2
2		2	1.2	2	2	2	2
2		2	1.0	2	2	2	1
2		2	0.8	2	2	2	2
2		2	0.7	2	2	2	2
2		2	1.2	2	1	2	2
2		2	0.8	2	2	2	2
1	1	2	0.9	2	2	2	2
2		2	1.3	2	2	2	1
2		2	0.9	2	2	2	2
2		2	1.1	2	2	2	2
1	1	2	0.7	2	2	2	2
2		2	0.8	2	2	2	2
2		2	0.9	2	2	2	2
2		2	0.8	2	2	2	2
2		2	0.8	2	2	2	1
1	1	2	0.7	2	2	2	2
2		2	1.0	2	2	2	2
2		1	2.6	2	2	2	1
2		2	0.7	2	2	2	2
2		2	0.8	2	2	2	1
2		2	0.5	2	2	2	2
2		2	0.8	2	2	2	2
2		2	1.2	2	2	1	2
2		2	1.3	2	2	2	1
2		2	1.1	2	2	2	1
2		2	0.7	2	2	2	2
2		2	0.8	2	2	2	2
2		2	1.2	2	1	2	2
2		2	0.9	2	2	2	2
2		2	1.2	2	2	2	1
2		2	0.8	2	2	2	2
1	2	2	1.0	2	2	2	2
1	1	2	1.3	2	2	2	1
2		2	0.9	2	2	2	1
2		2	0.8	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.8	2	2	2	2
2		2	0.8	2	2	2	2
2		2	0.8	2	2	2	2
2		2	0.9	2	2	2	2
2		2	0.9	2	2	2	1

2		1	2.8	2	2	2	2
2		2	0.9	2	2	2	2
1	3	2	0.5	2	2	2	2
2		2	0.6	2	2	2	2
2		2	#NULL!	2	2	2	1
2		2	0.5	2	2	2	2
1	2	2	0.5	1	2	2	1
1	1	2	0.8	2	2	2	2
2		2	0.8	2	2	1	1
2		1	2.0	2	2	2	1
2		1	1.4	2	2	2	2
2		2	0.5	2	2	2	2
2		2	0.6	2	1	2	1
2		2	0.8	2	2	1	2
1	2	2	0.7	2	2	2	2
1	1	2	0.8	2	2	2	2
2		2	0.8	2	2	2	1
2		2	0.5	2	2	2	2
2		2	0.9	2	2	2	2
2		2	1.3	2	2	2	2
2		2	0.4	2	2	2	2
2		2	0.7	2	2	2	2
2		2	1.2	2	2	2	2
2		1	5.4	2	2	2	1
2		2	0.4	2	2	2	1
2		2	1.0	2	2	2	1
2		2	1.1	2	2	2	2
2		2	0.5	2	2	2	2
1	4	2	1.6	2	2	2	2
2		2	0.7	2	2	2	1
2		2	0.5	2	2	2	1
2		2	0.3	2	2	2	2
2		2	0.9	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.6	1	2	1	1
2		2	1.3	1	2	2	1
2		2	0.9	2	2	2	2
2		2	0.6	2	2	2	2
2		1	1.7	1	2	2	1
2		1	2.0	2	2	2	1
2		2	0.8	2	2	2	2
2		2	0.9	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.6	2	2	2	1
2		2	0.8	2	2	2	2
2		2	0.5	2	2	2	2
2		2	1.3	2	2	2	1
2		2	0.6	2	2	2	2
2		2	0.5	2	2	2	2

2		2	0.6	2	2	1	1
2		2	0.6	2	2	2	2
2		2	0.2	2	2	2	2
2		1	8.6	2	2	2	1
2		2	0.4	1	2	2	2
1	1	2	1.0	2	2	2	2
2		2	0.7	2	2	2	2
2		1	1.5	2	2	2	1
2		2	0.6	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.5	2	2	2	2
1	1	2	1.0	2	2	2	2
1	1	2	0.9	2	1	2	2
2		2	0.8	2	2	2	2
2		2	0.2	2	2	2	2
2		2	0.2	2	2	2	2
1	1	2	0.7	2	2	2	2
1	2	2	0.6	2	2	2	2
2		2	1.0	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.7	2	2	2	2
2		2	0.7	2	2	1	2
2		2	0.8	2	1	2	2
2		2	0.5	2	2	2	2
2		2	0.9	2	2	2	2

Comorbiditiesothers	Smoking	Packyears	ethanol	duration
	1	10	2	
	2		2	
	1	15	2	
	2		2	
	1	8	1	5.0
Disseminated TB - TBM, Pulm TB	2		2	
	2		2	
	2		2	
	1	2	2	
	2		1	2.0
	1	2	2	
	1	10	2	
	1	15	2	
	2		2	
Tuberculous meningitis	2		2	
	2		2	
	1	6	2	
	2		2	
Disseminated TB - LN, pulmonary, psoas abcess	2		2	
	2		2	
	2		2	
	2		2	
	2		2	
Tb mwningitis, pulmonary TB	2		2	
	2		2	
Post renal transplant on steroids and tacrolimus	2		2	
	2		2	
	2		2	
hemolytic anemia on rituximab, cyclosporine	2		2	
	2		2	
	2		2	
	1	40	1	10.0
	1	15	2	
	2		2	
	2		1	5.0
	1	20	2	
	2		2	
	1	10	2	
	2		2	
	2		2	
PUlm TB , TB meningitis	2		2	
cholangiocarcinoma	1	15	2	
	1	10	2	
	2		2	
	2		2	
	2		2	
SLE	2		2	
	2		2	
	2		2	

Mucromycosis	1	10	2	
	2		2	
	2		2	
	1	15	2	
	2		2	
	2		2	
	2		2	
	2		2	
	2		2	
	1	5	2	
disseminated malignancy	2		2	
	1	5	1	10.0
	1	35	1	15.0
	2		2	
	2		2	
	2		2	
CAD, AKI	2		2	
	2		1	7.0
	2		2	
Rheumatoid arthritis	2		2	
	2		2	
	1	15	1	20.0
aplastic anemia, HCV, GN sepsis	2		2	
CKD	1	15	1	20.0
	1	10	1	10.0
	2		2	
	2		2	
	1	10	1	7.0
SLE	2		2	
	1	20	2	
	2		2	
	2		2	
	1	5	1	5.0
	2		2	
	2		1	25.0
	1	10	1	20.0
	1	5	2	
	2		2	
	2		1	20.0
	2		2	
	2		2	
	1	6	2	
	1	5	1	5.0
	2		2	
	2		1	4.0
	1	6	1	8.0
	2		2	
	2		2	
	1	10	1	5.0
	1	5	2	

	1	15	1	10.0
	2		2	
	2		2	
non hodgkins lymphoma, CKD	1	5	1	10.0
	2		2	
	2		2	
	2		2	
	2		1	10.0
chronic pancreatitis	2		2	
seziure disorder	2		2	
	2		2	
	2		2	
	1	20	1	20.0
	2		2	
	2		2	
seziure disorder	2		2	
	1	10	1	10.0
	2		2	
	2		2	
	1	5	1	10.0
	2		2	
	2		2	
	1	20	2	
	1	10	1	7.0
	1	1	2	

Frequency	ATTinitiation	Regimen	DILI	Changeinre	Ht	Wt	BMI	Underweig
	10-Feb-17	1	2		174	65	21.50	2.00
	13-Feb-17	1	2		175	69	22.50	2.00
	28-Feb-17	1	2		159	48	19.20	2.00
	06-Mar-17	1	2		160	54	21.10	2.00
2	22-Feb-17	2	1		162	40	15.20	1.00
	08-Mar-17	1	2		160	42	16.14	1.00
	16-Mar-17	1	2		179	50	17.30	1.00
	10-Mar-17	1	2		141	41	21.10	2.00
	10-Mar-17	1	2		165	43	15.80	1.00
1	15-Mar-17	1	2		174	54	17.80	1.00
	17-Mar-17	1	2		188	70	19.80	2.00
	20-Mar-17	1	2		172	55	18.60	2.00
	20-Mar-17	1	2		164	55	20.40	2.00
	24-Mar-17	1	2		171	60	20.50	2.00
	26-Mar-17	1	2		165	54	19.80	2.00
	25-Mar-17	1	2		165	56	20.50	2.00
	30-Mar-17	1	1	3	162	52	19.10	2.00
	28-Mar-17	1	2		155	65	27.00	2.00
	07-Apr-17	1	2		159	42	16.00	1.00
	06-Apr-17	1	2		165	48	17.60	1.00
	16-Apr-17	1	2		162	35	13.00	1.00
	26-Apr-17	1	2		161	52	20.00	2.00
	31-Mar-17	1	2		170	53	18.30	1.00
	12-Apr-17	1	2		160	42	16.40	1.00
	15-Apr-17	2	1		155	65	27.00	2.00
	09-May-17	1	1	1	165	52	19.10	2.00
	09-May-17	1	2		155	40	16.60	1.00
	05-May-17	1	2		165	58	21.30	2.00
	13-May-17	1	2		155	34	14.50	1.00
	16-May-17	1	2		164	55	20.40	2.00
	20-May-17	1	1	1	143	33	16.10	1.00
2	23-May-17	1	1	1	164	56	20.00	2.00
	24-May-17	1	2		164	55	20.00	2.00
	24-May-17	1	2		156	38	15.60	1.00
1	31-May-17	1	2		155	50	20.80	2.00
	02-Jun-17	1	2		170	70	24.20	2.00
	05-Jun-17	1	1	1	160	33	12.90	1.00
	10-Jun-17	1	2		164	72	26.70	2.00
	14-Jun-17	1	1	3	170	56	19.40	2.00
	14-Jun-17	1	2		161	55	21.40	2.00
	29-Jun-17	1	2		170	65	22.40	2.00
	03-Jul-17	1	2		162	59	22.50	2.00
	20-Jul-17	1	2		170	38	13.00	1.00
	22-Jul-17	1	2		164	56	20.80	2.00
	26-Jul-17	1	2		145	22	10.50	1.00
	31-Jul-17	1	2		160	40	15.60	1.00
	01-Aug-17	1	2		150	60	26.70	2.00
	04-Aug-17	1	2		170	57	19.70	2.00
	02-Aug-17	1	2		170	60	20.80	2.00

	04-Aug-17	1	2		162	38	14.50	1.00
	09-Aug-17	1	2		168	72	25.00	2.00
	04-Aug-17	1	2		158	35	14.00	1.00
	11-Aug-17	1	2		157	40	18.50	2.00
	08-Aug-17	2	1		154	34	14.30	1.00
	11-Aug-17	1	2		150	31	13.80	1.00
	25-Aug-17	1	2		155	47	19.80	2.00
	28-Aug-17	1	2		170	36	12.40	1.00
	29-Aug-17	1	2		165	54	19.80	2.00
	31-Aug-17	1	2		166	35	12.70	1.00
	04-Sep-17	1	2		165	60	22.00	2.00
2	07-Sep-17	1	2		167	41	14.70	1.00
2	08-Sep-17	1	2		165	68	25.00	2.00
	08-Sep-17	1	2		150	37	16.80	1.00
	09-Sep-17	1	2		175	40	13.10	1.00
	12-Sep-17	1	2		165	41	15.10	1.00
	12-Sep-17	1	2		162	48	17.00	1.00
1	13-Sep-17	1	2		175	65	21.00	2.00
	15-Sep-17	1	2		160	40	15.60	1.00
	24-Sep-17	1	2		162	41	15.60	1.00
	18-Sep-17	1	2		155	65	27.10	2.00
2	29-Sep-17	1	2		162	42	16.00	1.00
	29-Sep-17	1	2		170	65	22.50	2.00
1	08-Oct-17	1	2		174	48	15.70	1.00
1	10-Oct-17	1	2		165	43	16.00	1.00
	10-Oct-17	1	2		176	73	23.50	2.00
	12-Oct-17	1	2		164	54	20.10	2.00
1	20-Oct-17	1	2		168	65	23.00	2.00
	21-Oct-17	1	2		152	40	17.30	1.00
	24-Oct-17	1	2		160	54	23.40	2.00
	12-Sep-17	1	2		150	58	25.80	2.00
	18-Nov-17	1	2		158	50	20.00	2.00
1	18-Nov-17	1	2		178	78	24.00	2.00
	09-Oct-17	1	1	1	154	40	16.90	1.00
1	29-Sep-17	1	2		166	78	28.30	2.00
1	29-Sep-17	2	1		168	76	28.00	2.00
	26-May-17	1	2		166	64	23.10	2.00
	28-Mar-17	1	2		154	50	21.10	2.00
2	17-Dec-17	1	2		161	60	23.10	2.00
	02-Nov-17	1	2		160	40	15.60	1.00
	09-Jul-17	1	2		160	54	21.00	2.00
	30-Dec-17	1	2		168	60	21.20	2.00
1	28-Dec-17	1	2		168	54	19.10	2.00
	20-Oct-17	1	2		151	65	28.50	2.00
3	12-Dec-17	1	2		170	46	15.90	1.00
2	10-Nov-17	1	2		165	57	20.70	2.00
	07-Nov-17	1	2		160	60	23.40	2.00
	08-Dec-17	1	2		148	42	19.20	2.00
2	19-Oct-17	1	2		151	51	22.40	2.00
	13-Oct-17	1	2		167	65	23.30	2.00

1	16-Oct-17	1	2		151	49	21.50	2.00
	18-Dec-17	1	2		167	55	19.70	2.00
	02-Dec-17	1	2		156	35	14.40	1.00
1	07-Nov-17	1	2		168	54	19.10	2.00
	29-Sep-17	1	2		173	51	17.00	1.00
	22-Sep-17	1	1	1	156	36	15.60	1.00
	14-Nov-17	1	2		161	45	17.40	1.00
3	14-Nov-17	1	2		167	60	21.50	2.00
	30-Dec-17	1	2		161	51	19.70	2.00
	30-Oct-17	1	1	2	164	45	16.70	1.00
	23-Nov-17	1	2		157	34	13.80	1.00
	01-Nov-17	1	2		155	38	15.80	1.00
2	30-Dec-17	1	2		168	41	14.70	1.00
	11-Dec-17	1	2		159	58	23.20	2.00
	22-Dec-17	1	2		151	25	11.00	1.00
	29-Dec-17	1	2		165	40	14.70	1.00
2	29-Dec-17	1	2		159	62	24.50	2.00
	03-Nov-17	1	1		155	40	16.60	1.00
	01-Nov-17	1	2		176	70	22.50	2.00
1	16-Nov-17	1	2		156	44	18.00	1.00
	12-Apr-17	1	2		179	70	22.00	2.00
	04-Oct-17	1	2		160	40	15.60	1.00
	05-Oct-17	1	2		150	50	22.20	2.00
1	06-Oct-17	1	2		179	50	15.80	1.00
	27-Oct-17	1	2		180	70	27.60	2.00

SputumAFB	HbA1c	Ac	Pc	Hb	Creat	SGOT	SGPT	Chestxray
4	14.0			13.1	0.7	31	28	1
2	11.4			12.1	0.9	18	12	1
0		105	171	13.0	1.2	24	18	2
2	5.2			10.9	0.5	18	9	5
3	5.3			10.0	0.8	260	288	2
0	5.8			8.6	0.7	12	16	4
1	4.8			14.0	1.1	22	14	9
0	5.7			10.2	1.0	18	16	5
2	10.9			13.6	1.2	26	16	5
1	11.4			11.8	1.0	24	22	2
4	4.7			13.6	0.8	34	32	1
4	5.2			13.6	0.7	22	26	1
3	5.9			15.4	1.2	34	30	2
1	11.2			14.0	0.8	16	8	2
1	5.4			9.8	0.9	34	26	4
1	11.7			12.8	1.3	26	28	5
0	6.1			14.2	0.9	1390	241	1
3	11.4			9.6	1.1	24	24	2
4	6.8			11.4	0.7	20	16	1
3	4.8			13.6	0.8	24	26	2
3	5.8			10.2	0.9	14	16	2
3				18.0	0.8	12	16	2
1	7.5			13.8	0.8	18	22	5
0				10.0	0.7	24	28	1
1	12.0			10.1	1.0	16	18	4
4	5.2			10.2	2.6	28	30	1
3	6.2			11.4	0.7	12	18	4
1	9.0			13.8	0.8	26	22	2
1	6.8			9.4	0.5	20	16	4
0	5.7			14.8	0.8	18	14	1
3	5.5			12.6	1.2	26	32	9
4	10.9			13.0	1.3	28	32	5
2	13.4			14.2	1.1	26	20	2
3	5.4			11.6	0.7	17	24	5
0	5.3			7.0	0.8	15	23	2
1	10.9			12.8	1.2	25	30	2
1	14.0			14.0	0.9	33	22	2
1	8.6			13.4	1.2	35	31	5
0	6.4			15.0	0.8	21	17	9
1				12.1	1.0	14	13	2
1	9.8			10.6	1.3	36	33	9
2	9.7			11.4	0.9	32	40	2
0	8.3			14.6	0.8	15	17	4
2		157	243	16.2	0.7	25	21	2
2	5.0			9.0	0.8	25	7	5
3		88	112	8.9	0.8	18	6	5
1	5.0			13.2	0.8	13	17	5
3		130	290	9.6	0.9	27	18	5
1	7.5			10.3	0.9	29	19	5

0	9.5			12.0	2.8	14	9	5
1	5.2			12.9	0.9	20	24	5
2	5.7			10.3	0.5	14	9	1
0	9.4			6.8	0.6	54	39	1
1	11.3			11.0		89	42	1
4	5.8			9.5	0.5	21	22	4
1	5.8			11.7	0.5	23	13	6
2	4.9			13.2	0.8	17	13	1
0	6.2			9.8	0.8	29	36	1
0	6.4			9.8	2.0	24	19	2
0	5.7			7.7	1.4	28	14	7
1	4.9			10.2	0.5	19	10	4
2	6.0			9.1	0.6	17	14	5
2	6.1			10.7	0.8	27	28	6
0	4.7			11.0	0.7	40	22	1
3	7.3			14.0	0.8	14	11	6
3	5.8			9.6	0.8	19	11	8
2	10.2			15.0	0.5	18	12	2
3		78	68	11.8	0.9			5
3	4.6			6.2	1.3	32	20	2
1	8.9			9.5	0.4	32	32	4
3	8.9			9.1	0.7	62	35	4
1	12.0			8.9	1.2	89	64	2
0	6.9			11.0	5.4	67	24	9
3	7.9			9.4	0.4	26	10	5
1	12.2			10.3	1.0	19	9	2
1	9.3			10.8	1.1	25	13	1
2	12.1			13.4	0.5	63	20	2
0	5.7			5.7	1.6	70	25	1
2	6.5			10.3	0.7	20	4	5
1	14.5			12.2	0.5	35	34	1
1		86	162	9.1	0.3	16	17	9
2	4.8			12.0	0.9	29	33	2
2	5.0			7.6	0.7	340	104	2
1	9.4			9.5	0.6	83	46	5
1	5.6			11.3	1.3	120	74	5
3	5.4				0.9			2
3		88	134	12.1	0.6	20	9	5
4	6.8			11.1	1.7	112	87	2
4	14.0			7.2	2.0	11	23	2
3	12.0			13.0	0.8	20	9	4
2	12.9			15.1	0.9			1
2	14.3			13.6	0.7	16	9	9
2	6.5			13.4	0.7	27	20	2
2	8.2			6.6	0.6	23	19	2
4	6.6			14.9	0.8			9
0	9.7			13.9	0.5	11	18	2
1	9.6			13.4	1.3	24	29	5
2				11.0	0.6			2
2	8.3			14.1	0.5	16	11	2

1	8.2			12.7	0.6	33	40	5
2	9.6			9.2	0.6	24	26	2
2	5.0			8.4	0.2	30	14	2
1	6.4			6.0	8.6	15	29	4
3	5.4			9.3	0.4	74	27	1
0	6.6			12.2	1.0	67	53	4
3		90	146	14.8	0.7	44	26	4
0	6.0			12.3	1.5	20	20	1
1	14.0			12.3	0.6	10	3	2
0	5.6			11.4	0.7	27	28	1
2	6.2			8.1	0.5	26	12	5
0		93	96	9.0	1.0	36	21	1
0	7.5			8.8	0.9	33	13	2
0	6.3			7.2	0.8	35	30	1
3	4.3			7.0	0.2	23	15	2
4				11.2	0.2	26	18	2
1	14.0			14.2	0.7	39	46	2
0	4.4			9.7	0.6	149	124	1
3	12.6			11.2	1.0	24	29	2
3	7.5			7.8	0.7	75	46	4
3	9.7			14.3	0.7	26	19	2
2	9.0			12.7	0.7	13	11	5
2	6.9			14.3	0.8			2
2	7.5			9.2	0.5	13	18	8
1	5.2			15.4	0.9	21	29	1

Albumin	AFBculture	Sensitivity	GeneXpert	Rifresistan	assesment	Reasonnot	Death	Wt2m
3.70	1	1	1	2	1			69
3.80	1	1	1	2	1			65
4.10	1	1	1	2	1			49
3.60	1	1	1	2	1			55
2.90			1	2	1			39
2.80	1	1	1	2	1			45
3.60	1	1	1	2	1			62
4.10	1	1	1	2	1			48
3.00	1	1	1	2	1			45
4.60	1	1	1	2	1			54
3.70	1	1	1	2	2	1	2	
4.00			1	1	2	1	2	
3.50	1	1	1	2	1			60
4.50			1	2	1			60
1.90	1	1	1	2	2	4	1	
2.90	1	1	1	2	2	2		
2.80	2		1	2	1			57
3.40	1	1	1	2	1			64
3.10	1	1	1	2	1			45
3.60	1	1	1	2	2	3	2	
3.50	1	1	1	2	1			36
1.10	1	1	1	2	2	2		
2.70	1	1	1	2	1			55
1.10	1	1	1	2	2	4	1	
2.20	1	1	1	2	1			62
2.70	1	1	1	2	2	4	1	
2.30			1	2	2	3	2	
3.20	1	1	1	2	1			62
2.00	1	1	1	2	2	1	2	
1.70	1	1	1	2	1			59
2.60	1	1	1	2	2	2		
2.90	1	1	1	2	2	2		
4.20	1	1	1	2	1			57
2.70	1	1	1	2	1			40
1.60	2		1	2	2	3	2	
2.00	1	1	1	2	2	4	1	
3.30	1	1	1	2	1			33
4.10	1	1	1	2	2	3	2	
3.60	1	1	1	2	1			59
3.50			1	2	1			58
3.60	1	1	1	2	2	4	1	
2.70	1	1	1	2	2	2	1	
2.90	2		1	2	2	2		
3.90			1	2	1			60
3.50	2		2		2	1	2	
3.30			1	2	1			46
3.10	1	1	1	2	2	1	2	
3.90	1	1	1	2	2	2		
3.70	1	1	1	2	2	2		

2.60	2		1	2	2	4	1	
4.00	1	1	1	2	2	2		
2.00	1	1	1	2	1			36
2.10	1	1	1	2	2	2		
3.70	1	1	1	2	2	2		
3.20	2		2		1			34
2.60	2		1	2	2	2		
3.60					1			36
3.90	1	1	1	2	2	1	2	
2.70	1	1	1	2	2	2		
2.80	2		1	2	2	2		
3.20	1	1	1	2	1			46
3.10	1	1	1	2	1			68
4.30	2		1	2	1			44
3.10	2		1	2	2	2		
4.20	1	1	1	2	1			46
2.90	1	1	1	2	2	4	1	
3.80	1	1	1	2	1			70
3.70			1	2	2	1	2	
2.50	1	1	1	2	1			42
3.40	1	1	1	2	1			67
2.40	1	1	1	2	2	2		
2.30	2		1	2	2	2	1	
3.60	1	1	1	2	2	2		
3.00	2		1	2	2	2		
3.50	1	1	1	2	1			74
4.40	1	1	1	2	1			58
3.10	1	1	1	2	1			70
3.20	2		1	2	1			45
2.50	1	1	1	2	2	2		
3.40			1	2	1			60
2.40	1	1	1	2	1			54
3.80	1	1	1	2	2	2		
3.20			1	2	1			46
2.60	1	1	1	2	2	2		
2.60	1	1	1	2	2	4	1	
2.80	1	1	1	2	1			67
3.00			1	2	1			53
2.40	1	1	1	2	1			64
4.00			1	2	1			61
3.20	1	1			1			57
4.00					2	2		
3.00	1	1	1	2	2	2		
3.90	1	1			2	2		
2.80	1	1	1	2	1			50
3.20	1	1	1	2	1			60
	1	1	1	2	1			65
4.10	1	1	1	2	1			49
3.00			1	2	2	2		
3.10	1	1			1			72

3.10	1	1	1	2	1			50
3.20	1	1	1	2	2	1	2	
1.40	1	1	1	2	1			39
2.90	1	1	1	2	2	4	1	
2.10	1	1	1	2	1			53
2.80	1	1	1	2	1			38
2.80	1	1	1	2	2	2		
4.30	1	1	1	2	1			64
3.60	1	1	1	2	1			55
3.90	2		1	2	1			48
	1	1	1	2	2	2		
2.60	1	1	1	2	1			42
3.30	2		1	2	2	4	1	
2.90	2		1	2	2	2		
2.00	1	1	1	2	2	2		
3.00	1	1	1	2	2	1	2	
4.10	2		1	2	1			66
1.70	2		1	2	1			44
3.20	1	1	1	2	1			76
2.70					1			48
3.60			1	2	2	2		
4.10	1	1	1	2	1			45
4.60	1	1	1	2	1			51
2.10	1	1	1	2	1			52
4.50	1	1	1	2	2	2		

Vomiting2	Hepatitis2	Neuropath	Complianc	Complianc	sputumpos	AFB2m	AC2m	PC2m
2	2	2	1	1	2.00	0	140	229
2	2	2	1	1	2.00	0	78	152
2	2	2	1		2.00	0	112	230
2	2	2	1		2.00	0		
2	1	2	1		1.00	4		
2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1	1	1.00	4	159	315
1	2	2	1	1	2.00	0	231	367
2	2	2	1		1.00	4		
2	2	2	1	1	2.00	0	208	331
2	2	2	1		2.00	0		
1	2	2	1	2	1.00	1	437	601
2	2	2	1	1	2.00	0	95	249
2	2	2	1		2.00	0		
2	2	2	1	1	2.00	0	146	186
2	2	2	1	1	2.00	0	166	205
2	2	2	1	1	2.00	0	115	157
2	2	2	1	1	2.00	0	133	236
2	2	2	1	1	2.00	0	182	246
2	2	2	1		1.00	1		
2	2	2	1	2	2.00	0	454	537
2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1	1	2.00	0	128	226
2	2	2	1		2.00	0		

2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1	1	1.00	4	118	150
2	2	2	1		2.00	0		
2	2	2	1	1	2.00	0	191	231
2	2	2	1	1	2.00	0	125	250
2	2	2	1		2.00	0	#NULL!	#NULL!
2	2	2	1	1	2.00	0	168	305
2	2	2	1	1	2.00	0	72	114
2	2	2	1	1	2.00	0	144	174
2	2	2	1	1	2.00	0	150	284
2	2	2	1		2.00	0		
2	2	2	1	2	2.00	0	381	462
2	2	2	1		2.00	0		
2	2	2	1		2.00	0		
2	2	2	1		1.00	4		
2	2	2	1		1.00	4		
2	2	2	1	1	2.00	0	157	355
2	2	2	1	2	2.00	0	208	427
2	2	2	1	1	2.00	0	170	240
2	2	2	1	1	2.00	0	103	187
2	2	2	1		2.00	0	104	148
2	2	2	1	2	2.00	0	129	249
2	2	2	1	1	2.00	0	139	222
2	2	2	1	2	2.00	0	119	151

2	2	2	1	1	1.00	1	113	153
2	2	2	1	1	2.00	0		
2	2	2	1		2.00	0		
1	1	2	1	1	2.00	0	100	136
2	2	2	1	1	2.00	0	134	266
2	2	2	1	1	2.00	0	170	240
1	1	2	1		2.00	0		
2	2	2	1		2.00	0	104	157
2	2	2	1	2	2.00	0	254	311
2	2	2	1		2.00	0		
2	2	2	1	1	2.00	0	82	196
2	2	2	1	2	1.00	4	157	249
2	2	2	1	1	2.00	0	109	176
2	2	2	1	1	1.00	4	111	244
2	2	2	1	1	2.00	0	132	199

assesment	Wt3m	Vomiting3r	Hepatitis3r	Neuropath	OtherATT3	Complianc	Complianc	AFB3m
2								
2								
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1	64	2	2	2		1	1	2
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1	40	2	2	2		1		1
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1	67	2	2	2		1		4
1	54	2	2	2		1		4
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1	49	2	2	2		1	1	0
2								
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1	52	2	2	2		1	1	0
2								
2								

AC3m	PC3m	Hba1c3m	assesment	Wt4m	vomiting4r	hepatitis4r	neuropath	AFB4m
			2					
			2					
			2					
			2					
			1	39	2	2	2	2
			2					
			2					
			2					
			2					
			2					
			2					
			2					
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			2					
			2					
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272	241		2					
			2					
			2					
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			2					
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			2					
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			2					
			2					
			1	38	1	2	2	0
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			1	52	2	2	2	2
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120	180		2					
			2					
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		7.0	2					
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COmpliand	Complianc	Ac4m	PC4m	Hba1c4m	assesment	Wt5m	Vomiting5	Hepatitis5
					2			
					2			
					2			
					2			
1					2			
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					2			
					2			
					1	46	2	2
					2			
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					1	65	2	2
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1	1	120	170		2			
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Neuropath	AFB5m	Complianc	Complianc	Misseddru	AC5m	PC5m	Assesment	Followup
							1	
							1	
							1	
							1	
							1	
							1	
							1	
							1	
2	0	1	1	0	104	146	1	
							2	2
							2	1
							2	1
							2	2
							1	
							2	2
							1	
2	0	1	1	0	229	149	1	
							1	
							2	3
							1	
							2	2
							1	
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							2	3
							1	
							2	1
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Wt6m	Vomiting6	Hepatitis6	neuropath	AFB6m	AFBculture	cure	treatment	Hba1c6m
75	2	2	2	0	2	1	1.00	12.0
65	2	2	2	0	2	1	1.00	6.1
50	2	2	2	0	2	1	1.00	
56	2	2	2	0	2	1	1.00	5.4
41	2	2	2	0	2	1	2.00	5.6
50	2	2	2	0		1	1.00	
64	2	2	2	0	2	1	1.00	5.2
47	2	2	2	0	2	1	1.00	5.5
48	2	2	2	0		1	1.00	6.1
						1	2.00	
						2	6.00	
						2	6.00	
						2	6.00	
62	2	2	2	5	3	1	2.00	9.2
						2	4.00	
						2	6.00	
58	2	2	2	0	3	1	1.00	6.2
66	2	2	2	0	2	1	1.00	9.7
45	2	2	2			1	2.00	6.1
						2	6.00	
38	2	2	2			1	2.00	5.7
						2	6.00	
56	2	2	2			1	2.00	7.3
						2	4.00	
58	2	2	2	0	2	1	1.00	12.7
						2	4.00	
						2	6.00	
63	2	2	2	0	2	1	1.00	6.2
						2	6.00	
62	2	2	2	0	2	1	1.00	6.0
						1	2.00	
						2	6.00	
60	2	2	2	5	3	1	2.00	8.7
						2	6.00	
						2	6.00	
						2	4.00	
						2	4.00	
						2	6.00	
62	2	2	2	0	2	1	1.00	5.7
58	2	2	2	5	3	1	2.00	5.7
						2	4.00	
						2	4.00	
						2	6.00	
62	2	2	2	5	3	2	6.00	
						2	6.00	
48	2	2	2	0	3	1	1.00	
						2	6.00	
						2	6.00	
						2	6.00	

						2	4.00	
						2	6.00	
40	2	2	2	5	3	1	2.00	5.6
						2	6.00	
						2	6.00	
38	2	2	2	5	3	1	2.00	5.5
						2	6.00	
40	2	2	2	0	3	1	1.00	4.9
						2	6.00	
						2	6.00	
						2	6.00	
48	2	2	2	0	2	1	1.00	4.6
66	2	2	2	0	2	1	1.00	5.9
45	2	2	2	0	2	1	1.00	6.1
						2	6.00	
47	2	2	2	5	3	1	1.00	8.1
						2	4.00	
72	2	2	2	0	2	1	1.00	7.3
						2	6.00	
44	2	2	2	0	2	1	1.00	
						1	2.00	
						2	6.00	
						2	4.00	
						2	4.00	
						2	6.00	
76	2	2	2	0	2	1	1.00	7.5
60	2	2	2	5	3	1	2.00	8.4
72	2	2	2	0	2	1	1.00	
47	2	2	2	5	3	1	2.00	
						2	6.00	
61	2	2	2	5	3	1	2.00	10.1
56	2	2	2	0	2	1	1.00	5.0
						2	6.00	
48	2	2	2	5	3	1	2.00	5.2
						2	6.00	
						2	4.00	
68	2	2	2	0	2	1	2.00	5.4
55	2	2	2	0	2	1	2.00	5.6
						1	2.00	
						1	2.00	
						1	2.00	
						2	6.00	
						2	6.00	
						2	6.00	
58	2	2	2	5	3	1	2.00	7.6
						1	2.00	
68	2	2	2	0	2	1	1.00	8.5
						1	2.00	
						2	6.00	
						1	2.00	

						2	6.00	
						2	6.00	
						1	2.00	
						2	4.00	
56	2	2	2	0	2	1	1.00	5.4
41	2	2	2	0	2	1	1.00	5.1
						1	1.00	
65	2	2	2	5	3	1	2.00	6.2
						1	2.00	
50	2	2	2	0	2	1	1.00	5.4
						1	2.00	
						1	1.00	
						2	4.00	
						2	6.00	
						2	6.00	
						1	1.00	
						1	2.00	
						1	2.00	
76	2	2	2	0	2	1	1.00	10.7
50	2	2	2	0	2	1	1.00	7.0
						2	6.00	
45	2	2	2	0	2	1	1.00	6.5
						1	2.00	
						1	2.00	
						2	6.00	

AC6m	PC6m	ATT6mcom	DMdrugs6	deathfinal
263	349	1	1	2
		1	1	2
112	98	1	1	2
		1		2
		2	2	2
		1	1	2
		1		2
		1		2
		1	1	2
				2
				2
				2
				2
		1	2	2
				1
				2
		1		2
		1	1	2
		1	1	2
				2
		1		2
				2
		1	1	2
				1
		1	1	2
				1
				2
		1	1	2
				2
		1	1	2
				2
				2
		1	1	2
				2
				2
				1
				1
				2
		1		2
		1		2
				1
				1
				2
132	104	1	1	2
				2
76	114	1		2
				2
				2
				2

				1
				2
		1	1	2
				2
				2
		1		2
				2
		1		2
				2
				2
				2
		1		2
		1	1	2
		1		2
				2
		1	2	2
				1
		1	1	2
				2
		1		2
				2
				2
				1
				1
				2
		1	1	2
		1	1	2
272	517	1	2	2
105	94	1		2
				2
		1	1	2
		1		2
				2
		1	1	2
				2
				1
		1		2
		1		2
				2
				2
				2
				2
				2
				2
106	209	1	1	2
				2
		1	2	2
				2
				2
				2

				2
				2
				2
				1
		1		2
		1	1	2
				2
		1	1	2
				2
		1		2
				2
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				1
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				2
				2
				2
		1	1	2
		1	1	2
				2
		1	1	2
				2
				2
				2