



## HYPERGLYCEMIA IN TUBERCULOSIS. IS IT STRESS INDUCED OR TRUE DIABETES MELLITUS.

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**ABSTRACT** The worldwide increase in the prevalence of diabetes has been most notable in TB-endemic countries and has led to the re-emerging importance of the association between these two diseases. Today, type 2 diabetes is one of the most prevalent co morbidities and risk factors in TB patients, along with under nutrition and HIV/AIDS. However, it is striking how little we know about the underlying biology of the association between TB and diabetes. Diabetes increases tuberculosis risk, while tuberculosis, as an infectious disease leads to hyperglycemia. The metabolic alterations characteristics of diabetes (e.g., chronic hyperglycemia, metabolic inflammation [meta-inflammation], oxidative stress) are likely to contribute to the immune dysfunction to mycobacterium. The discovery of these mechanisms is providing the knowledge base to design host-directed therapies for TB patients with diabetes, and perhaps those without diabetes as well.

### METHODOLOGY:

A total of 112 patients, newly diagnosed as having pulmonary tuberculosis, in the department of pulmonary medicine, Alluri Sitaramaraju academy of Medical sciences, Eluru during Nov'2018 and October'2019 were taken into consideration. 88 patients met with inclusion criteria were included in the study. The RBS levels and HbA1c levels were taken before initiating the anti-tubercular therapy (ATT). Patients with HbA1c < 7% and with RBS > 140mg/dl were followed up with sugar levels and diet advice. HbA1c and RBS were repeated at the end of 2 months of intensive phase to see if the high RBS persisted.

### RESULTS:

- 112 patients were diagnosed with TB during this period. Of these 24 were already under treatment of Diabetes Mellitus and were hence excluded from the study
- Of the remaining 88 patients, 60 patients had RBS > 140mg/dl and HbA1c < 7% and were included and followed up for regular blood sugar levels monthly and HbA1c after 2 months
- During follow up 44 patients had blood sugar levels below 140mg/dl, after 2 months of ATT and HbA1c continued to be < 7
- 16 patients had high blood sugar levels above 140mg/dl and 3 among them had elevated HbA1c levels as well. All these patients had to be started on OHA

### CONCLUSION:

1. 68% of patients with no previous history of diabetes mellitus were found to have high blood sugar levels at the start of the study
2. 73% of the patients with high blood sugar levels came back to normal levels within 2 months of treatment
3. Only 4 patients (26%) had persistent high blood sugar levels who required treatment with OHA (oral hypoglycaemic agents)

**KEYWORDS :** Diabetes Mellitus, Tuberculosis, Random Blood Sugar, Hba1c Levels,

### INTRODUCTION:

Diabetes Mellitus and Tuberculosis are leading global health problems. Diabetes increases tuberculosis risk, while tuberculosis, as an infectious disease leads to hyperglycemia. Among patients with TB disease, the development of stress hyperglycemia may influence the clinical manifestation and treatment response of some patients and can complicate diabetes diagnosis. Research is needed to elucidate the relationship between TB disease and stress hyperglycemia and determine the extent to which stress hyperglycemia impacts TB treatment response. Currently, there is insufficient data to support clinical recommendations for glucose control among patients with TB disease, representing a major barrier for efforts to improve treatment outcomes for patients with TB and diabetes. Tuberculosis infection can stimulate free fatty acid synthesis and secretion, which mediates insulin resistance by elevating proinflammatory cytokines, specifically tumor necrosis factor- $\alpha$ . Some studies suggest that tuberculosis can cause diabetes, even in those not previously known to have diabetes. However, it is unclear whether diabetes mellitus persists in these patients or whether diabetes is more prevalent with tuberculosis than with other infectious diseases.

### AIMS AND OBJECTIVES:

To determine if the high blood sugar levels in tuberculosis patients is actually stress related or does it require treatment.

### METHODS:

1. The patients who were diagnosed to have tuberculosis between Nov'2018 and Oct'2019 Were included in the study
2. The RBS levels and HbA1c levels were taken before initiating ATT
3. Patients with HbA1c < 7% and with RBS > 140 mg/dl were followed up with blood sugar levels and diet advice

4. HbA1c and RBS were repeated at the end of 2 months of intensive phase of ATT to see if the high RBS persisted

### INCLUSION CRITERIA:

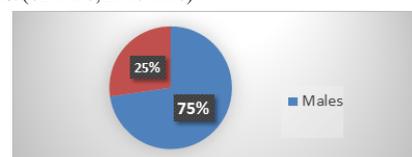
1. Newly diagnosed cases (microbiologically confirmed) of pulmonary tuberculosis
2. Patients having Random blood sugar values more than 140 mg/dL, HbA1c level less than 7%
3. Patients who are not previously diagnosed of having Diabetes Mellitus

### EXCLUSION CRITERIA:

1. Patients who are having HbA1c levels more than 7%
2. Patients who are already diagnosed of having Diabetes Mellitus and on treatment

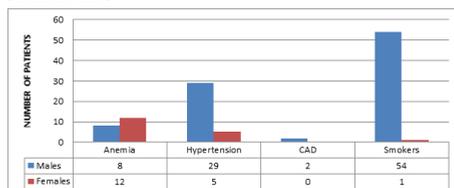
### STUDY SAMPLE:

88 Patients. (62 male, 22 female)

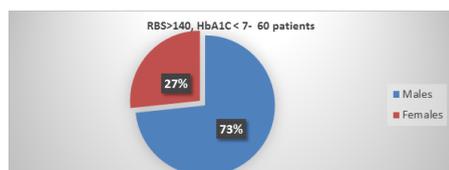
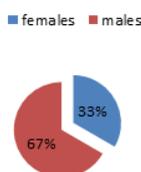


### AGE GROUPS:



**CO-MOBIDITIES:****RESULTS:**

- 112 patients were diagnosed with TB during this period. Of these 24 were already under treatment of Diabetes Mellitus and were hence excluded from the study
- Of the remaining 88 patients, 60 patients had RBS >140mg/dl and HbA1C <7% and were included and followed up for regular blood sugar levels monthly and HbA1c after 2 months
- During follow up 44 patients had blood sugar levels above 140mg/dl after 2 months and HbA1c continued to be <7
- 16 patients had persistent elevation of blood sugar levels above 140mg/dl and 3 among them had elevated HbA1c levels as well. All these patients had to be started on OHA

**RBS > 140- 16 patients****DISCUSSION:**

Hyperglycemia was transient in the large majority of patients with tuberculosis with newly diagnosed pre-DM and DM at the time of tuberculosis diagnosis. This transient hyperglycemia is well known in patients with sepsis. The normalization of glycemic status during tuberculosis treatment has already been described in small study samples (n = 20–50), using oral glucose tolerance tests. A larger study conducted in Iran also reported that, in one third of patients with a high HbA1c level at tuberculosis diagnosis, the HbA1c level returned to normal after 3 months of tuberculosis treatment. The cause of this transient hyperglycemic status is likely multifactorial and might reflect inflammation induced by tuberculosis, the hyperglycemic effect of tuberculosis treatment, and patient predisposition. Stress hyperglycemia results from a complex interplay between disturbed cytokine and hormone production, leading to excessive hepatic glucose production and insulin resistance.

This high frequency of transient hyperglycemia in untreated patients with tuberculosis raises the question of reverse causality between tuberculosis and DM and highlights the necessity to repeat DM screening later in the course of tuberculosis treatment. Furthermore, studies are needed to assess whether patients with tuberculosis with transient hyperglycemia are at increased risk of developing DM later. Hyperglycemia testing and control at tuberculosis diagnosis may have clinical utility in improving tuberculosis treatment outcome. A recent review showed that DM at tuberculosis diagnosis increases the risk of failure and death during tuberculosis treatment, and a large study conducted in Mwanza, Tanzania, showed an increased risk of death among patients with tuberculosis and DM, particularly among HIV-negative patients. Short-term glycemic control with insulin has been linked to better outcome in septic patients, but only when using nonintensive glycemic targets. This evidence indirectly suggests that short-term management of glycemia might also improve tuberculosis outcome. A recent study pointed to metformin as a potentially useful adjunct antituberculosis therapy. In mice, it enhances *Mycobacterium tuberculosis*-specific host immunity and reduces inflammation. In

patients with tuberculosis-DM, metformin, but not other DM drugs, improved tuberculosis outcome. The effect of controlling transient hyperglycemia, particularly with metformin, during tuberculosis treatment was not yet studied in a randomized trial.

**CONCLUSION:**

1. 68% of patients with no previous history of diabetes mellitus were found to have high blood sugar levels at the start of the study
2. 73% of the patients with high blood sugar levels came back to normal levels within 2 months of treatment
3. Only 16 patients (26%) had persistent high blood sugar levels who required treatment with OHA

In conclusion, our study showed that mild hyperglycaemia is very common in patients with tuberculosis but that, in most of them, the glucose status is normalized with tuberculosis treatment. First, a new diagnosis of DM in a patient with tuberculosis must be confirmed after tuberculosis treatment. Larger studies using point-of-care DM tests that are insensitive to infection-induced hyperglycaemia need to assess the role of DM as a risk factor for active tuberculosis in settings with a low DM prevalence and high tuberculosis burden, such as Sub-Saharan Africa. Second, FCG testing at enrolment best captures patients with tuberculosis at risk of treatment failure and death. This may give the opportunity to manage hyperglycaemia, but the effect of such interventions on tuberculosis outcome requires confirmation through randomized controlled trials including both HIV-infected and HIV-negative patients.

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