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## Original Research Article

## Estimation of glycemic control in patients with type 2 diabetes mellites with various forms of tuberculosis with dots

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## ABSTRACT

**Background:** Since ancient times people are aware of the association between tuberculosis and diabetes mellitus. Patients with tuberculosis and diabetes experience worse clinical manifestations, increased risk of treatment failure, recurrence, and death. The present study was conducted to evaluate glycosylated hemoglobin (HbA1c) and blood glucose levels, in patients with Type - 2 diabetes mellitus with various forms of tuberculosis who are on RNTCP DOTS and antidiabetic regimens.

**Materials and Methods:** The study subjects included Type-2 diabetes mellitus with tuberculosis who are registered under RNTCP DOTS, in Dept of Pulmonology, PESIMSR, Kuppam, Chittoor district. Study groups comprises. 20 cases of type 2 DM WITH TB who are on oral hypo glyceemic agents (OHA), 20 cases of Type 2DM WITH TB who are on oral hypoglycemic agents (OHA) with insulin, 20 cases of Type 2 DM WITH TB who are on insulin. HbA<sub>1c</sub> is measured by fully automatic Bio-Rad D10 - HbA<sub>1c</sub> Analyzer. Blood glucose levels are estimated by auto analyser VITROS 250 in PESIMSR, Kuppam.

**Results:** The mean HbA<sub>1c</sub> levels showed good control in those patients kept on insulin alone compared to OHA and OHA with insulin groups (P <0.001). The mean HbA<sub>1c</sub> levels were high in OHA alone group compared to other groups (P<0.001).

**Conclusion:** The study revealed that increased levels of Glycosylated haemoglobin (HbA<sub>1c</sub>) are observed in those patients kept on OHA alone with DOTS as compared with other two groups. There is strong interaction between anti tubercular drugs and OHA which in turn leads to poor glycemic control. Poor glycemic state in diabetic patients is having strong impact on TB treatment outcome.

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### 1. Introduction

Diabetes mellitus is a chronic metabolic disorder virtually affecting every organ system in the human body.<sup>1</sup> HbA<sub>1c</sub> is regarded as the gold standard for assessing glycemic control in diabetic patients.<sup>2</sup> Individuals with DM have three times the risk of developing TB and there are now more individuals with TB-DM co-morbidity than TB-HIV co-infection.<sup>3</sup> Tuberculosis has been a major cause of suffering and death since times of immemorial.<sup>4</sup> India has the largest number of TB cases estimated globally to

be 2 million per annum and accounts for more than 60 million people with type 2 diabetes.<sup>5</sup> After Introduction of Revised national tuberculosis control programme RNTCP there is significant improvements in case detection and control of TB disease, but tuberculosis is complicating diabetes.<sup>6</sup> Another important challenge is the growing body of evidence suggesting diabetes as a risk factor for new as well as reactivated old TB cases.<sup>7</sup> As a protocol those patients with tuberculosis having diabetes should kept on insulin to achieve glycemic control and good TB treatment outcome. But practically majority of these patients are kept on oral hypoglycemic agents (OHA) alone. This adversely affects tuberculosis treatment outcome. There is strong

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interaction between OHA's and anti tuberculosis drugs leading to worsening of glycemic control.<sup>8</sup> Poor glycemic control results in higher levels of HbA<sub>1c</sub>. On careful observation those patients kept on insulin alone with DOTS recovered fast from TB infection by showing early sputum conversion and achieved glycemic control.<sup>9</sup> These patients showed lower level of HbA<sub>1c</sub> as compared with other two groups. This study aims at influence of glycemic control on treatment outcomes in patients with type 2 diabetes mellitus with various forms of tuberculoses.

## 2. Materials and Methods

The present study comprises patients with tuberculosis and known diabetic state registered under revised national tuberculosis control programme (RNTCP) in Dept of Pulmonology, PESIMSR, Kuppam, Chittoor district, Andhra Pradesh. Adult aged 30yrs to 80 yrs of both genders were included. Total 60 samples were tested among those 20 were OHA alone patients (Group I), 20 were OHA plus Insulin (Group II) and 20 were insulin alone (Group III) samples were analyzed at clinical Biochemistry lab PESIMSR, Kuppam. The patients with end stage complications of DM such as proliferative retinopathy and nephropathy and with history suggestive of bleeding diathesis or fits with creatinine levels  $\geq 2$  mg/dl were excluded from study. 5ml of blood was collected from the patients from the cubital vein under aseptic precautionary measures with 5ml syringe out of this 2ml was collected in EDTA tube for estimation of HbA<sub>1c</sub>. Remaining 3ml was collected in clot activator tube for blood glucose estimation. Measurement of HbA<sub>1c</sub> done by fully automatic Bio-Rad D10 - HbA<sub>1c</sub> Analyzer. Blood glucose levels were estimated by auto analyser VITROS 250.

## 3. Statistical Analysis and Results

Statistical data calculated by using SPSS software, analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patient (Table 1). Post hoc test has been employed to find the pair wise significance (Table 2). A P value  $< 0.05$  was considered as significant.

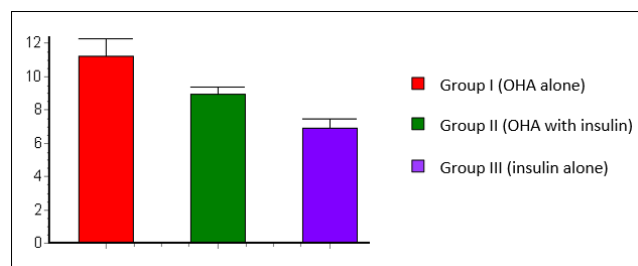


Fig. 1: HbA<sub>1c</sub> mean and SD values in three groups

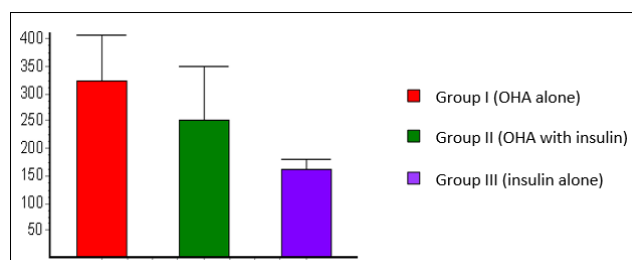


Fig. 2: RBS mean and SD values in three groups

The Tables 1 and 2 and Figures 1 and 2 shows that there was significant increased HbA<sub>1c</sub> and blood glucose levels in group I patients compared with other two groups. The mean levels of HbA<sub>1c</sub> and blood glucose in group III were  $6.91 \pm 0.57$  and  $161.2 \pm 18.71$  and group II the mean levels of HbA<sub>1c</sub> and blood glucose were  $8.92 \pm 0.471$  and  $215 \pm 97.05$ . In group I the mean levels of HbA<sub>1c</sub> and blood glucose were  $11.21 \pm 1.08$  and  $321.85 \pm 85.53$ . The level was significantly increased ( $p < 0.001$ ) in the group I as compared with group II and group III people.

## 4. Discussion

Glycemic status should be strictly watched while diabetic patients kept on DOTS. HbA<sub>1c</sub> is considered to be a contributory factor to tissue hypoxia by increasing the affinity of hemoglobin-oxygen, while low tissue oxygen concentration is detrimental and causes oxidative stress.<sup>10</sup> It has come to light that oxidative stress plays a crucial role in the activation and anti-TB action of isoniazid.<sup>11,12</sup> Rifampicin increases the hepatic metabolism of all sulphonylurea derivatives, the most widely used class of oral diabetes drugs worldwide. This effect on sulphonylurea derivatives has great inter-individual variation, which makes dose adjustments difficult and increases a patient's risk of hyperglycaemia or hypoglycaemia. Inter-individual variation in the induction of the metabolism of diabetes drugs makes dose adjustment difficult when rifampicin treatment is interrupted or stopped; the same is true for most other oral antidiabetes drugs.<sup>13,14</sup> Then the oral hypoglycemic agents are rapidly eliminated. Isoniazid antagonizes the action of sulphonylureas and worsens glycemic control.<sup>15</sup> In some situations, isoniazid decreases the metabolism of oral antiglycemic agents and increases their plasma levels, such as cytochrome P2C9 (CYP2C9) involved in the metabolism of sulphonylureas.<sup>16</sup> That's what oral hypoglycemic patients difficult to achieve glycemic control. Most recently, some investigators have suggested that for TB-DM patients, higher blood glucose levels contribute to the occurrence of drug resistance by delaying sputum conversion.<sup>17,18</sup> Glycosylated haemoglobin was very high in the patients who kept on OHA alone. Those patients kept on insulin

**Table 1:** Comparison of study variables in three groups by one-way ANOVA

Study variables	Group I	Group II	Group III	p value
HbA <sub>1c</sub>	11.21 ± 1.08	8.92 ± 0.38	6.91 ± 0.57	<0.001**
Random blood glucose	321.85 ± 85.53	251.4 ± 97.05	161 ± 18.71	<0.001**

Results are presented in mean ± SD

\*\* Strongly significant (p value: p ≤ 0.01)

**Table 2:** Pair wise comparison in three groups by multiple comparison post-hoc test

Study variables	Group I vs Group II	Group I vs Group III	Group II vs Group III
HbA <sub>1c</sub>	<0.001**	<0.001**	<0.001**
RBS	<0.01*	<0.001**	<0.001**

Results are presented in mean ± SD

\* Moderately significant (p value: 0.01 < p ≤ 0.05)

\*\* Strongly significant (p value: p ≤ 0.01)

and insulin with OHA was achieving glycaemic control. The study showed improvement in insulin alone and along with OHA's with DOTs showed improvement in glycogen control and lowered HbA<sub>1c</sub> levels as compared to OHA group patients.

## 5. Conclusion

The association between DM and TB is well documented and there is substantial evidence to support this fact. There is adverse interaction between anti-TB drugs and oral hypoglycaemic agents. Particularly rifampicin is a potent inducer of hepatic enzyme cytochrome P450. cytochrome P450 rapidly metabolizes the oral hypoglycaemic agents particularly sulphonylureas and brings the diabetic patients to uncontrolled glycaemic status. Isoniazid decreases the metabolism of oral antiglycaemic agents and increases their plasma levels, such as cytochrome P2C9 (CYP2C9) involved in the metabolism of sulphonylureas. Those patients kept on OHA alone there is more failure rates as compared with other two groups. TB patients kept on insulin and insulin with OHA showed better response and early sputum conversion, lowered blood glucose levels and HbA<sub>1c</sub> as compared with OHA people. Limitations of present study: small sample size.

## 6. Conflict of Interest

None declared.

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