FASTING SERUM GROWTH HORMONE LEVELS IN NEWLY DIAGNOSED PATIENTS OF PULMONARY TUBERCULOSIS WITH AND WITHOUT COEXISTENT DIABETES MELLITUS TYPE2

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ABSTRACT
The aim of this cross-sectional comparative study was to determine and compare the serum growth hormone (GH) and fasting blood glucose (FBG) levels in the newly diagnosed patients of pulmonary tuberculosis (TB) with and without diabetes mellitus type2 (DM type 2). Eighty four male subjects were included in this study and divided into three groups. Group 1, healthy controls (n=28), group 2 were patients of pulmonary tuberculosis without DM (n=28) and group three were pulmonary TB patients with newly diagnosed DM type 2 (n=28). Serum GH and fasting blood glucose levels were determined before starting anti-TB treatment in the TB patients and treatment of hyperglycemia in diabetic patients. Statistically significant difference was observed between serum GH and FBG levels of the three study groups. There was a significant difference between serum GH and FBG levels of TB patients with and without diabetes mellitus before starting anti-TB treatment. It is concluded that the hyperglycemic effects of GH on glyemic control should be taken into consideration when treating TB diabetic patients.

Keywords: Pulmonary tuberculosis, Growth hormone, Fasting blood glucose.

INTRODUCTION
World Health Organization (WHO) estimated that 1.5 million people died from TB around the world in 20131. Pakistan is one of the five countries that carry almost half the world’s TB burden2.

Diabetes mellitus is a chronic disease that occurs either due to insufficient insulin production from pancreas or when the body cannot effectively use the insulin it produces. There are two types of this disease, Type 1 due to complete loss of insulin production by pancreatic beta cells 3 and Type 2 results from the body’s ineffective use of insulin. 3

Ninety percent diabetics around the world have type 2 DM4. Prevalence of DM in Pakistan’s urban areas is 6% in males and 3.5% in females 5.

DM is found in 10-30% tuberculous patients 6,7 and studies do suggest that these two diseases are linked with each other and coexist in many patients8.

The endocrine disturbances in tuberculosis involve raised growth hormone level 9 and up to 5-18 times higher levels were observed in such patients due to release of cytokines during an immune response to the disease that activates the hypothalamus-pituitary-adrenal axis 10.

Growth hormone is secreted from anterior pituitary gland in form of pulses throughout day and night11. The basal level in humans is < 0.1microgram/L 12. It has important effects on growth and metabolism of proteins, fats and carbohydrates13.

Previously it was reported that ATT drugs such as Rifampicin are potent hepatic enzyme inducers and lead to hyperglycemia in diabetic patients. These may stimulate clinical features of DM in previously non-diabetic patients by enhancing intestinal glucose absorption14.

The aim of this study was to determine and compare the levels of fasting serum GH and FBG in newly diagnosed male pulmonary TB patients with and without DM type 2 before starting anti-TB treatment since these levels were yet not reported in the Pakistani population.

METHODOLOGY
This was across sectional comparative study. Subjects were selected from Lahore General Hospital and Gulab Devi Chest Hospital, Lahore for nine consecutive months. Sample size was calculated using power of the study 90% and α level of 5%. The study population consisted of 84 male subjects between 30-55 years of age and with a normal body mass index. These were divided equally into 3 groups. Inclusion criteria for group: 1 was no history of TB and DM (n=28), for Group: 2 newly diagnosed patients of pulmonary TB with no history of DM, Group 3 newly
diagnosed patients of pulmonary TB and DM type 2 or known diabetic not getting treatment for past 1 month. Diagnosis was based on WHO criteria: Fasting blood glucose ≥7.0mmol/L (126mg/dl) or random blood glucose ≥11.1mmol/L\textsuperscript{15}. Subjects with history of current GH or current steroid intake, hypertension, major surgical intervention in past 3 months, endocrine disorders leading to raised GH levels and extrapulmonary TB were excluded. The Sampling technique was non-probability convenience sampling. Permission was taken from the hospitals for sample collection from the patients. Data was collected after obtaining fully informed, understood and voluntary consent of the subjects. Confidentiality of the data was ensured. Body mass index (BMI) of the patients was calculated using the following formula:

\[ \text{BMI} = \frac{\text{Weight in kilograms}}{\text{Height in meter}^2} \]

Fasting Blood Glucose was measured in all the patients using a hand held glucometer (Accu-Check) based on glucose oxidase method. The patients were then instructed to come next morning at 8:00 a.m after an overnight fast of 12 hours for blood sample collection. The patients were also instructed not to do strenuous exercise and not to take a high protein diet 12 hours before coming for sampling. All samples were drawn in sitting position after a rest of at least 10-15 minutes. Five milliliter (ml) of venous blood was collected in yellow topped vaccutainers. The blood was centrifuged at 3000 revolutions per minute for 20 minutes to separate the serum for subsequent hormone analysis. The serum was divided into aliquots and stored at -80°C.

Quantitative determination of Glucose in serum was done by a glucose oxidase kit of Pointe Scientific, Inc. USA using photoelectric colorimeter, AE-11, Tokyo Erma Optical works, LTD. Japan. Quantitative determination of fasting serum GH was done by using enzyme linked immunosorbent assay (ELISA) test kit of Bio Check, Inc. USA and ELISA analyzer Rayto RT 2100 C, USA.

**STATISTICAL ANALYSIS**

Statistical analysis was conducted using statistical package of social sciences (IBM SPSS 20). Fasting serum GH, FBG level and sociodemographic variables (age and socioeconomic status) were tested for significance using tests of normality (Kolmogorov-Smirnov test). The quantitative variables of the cases were presented as median and interquartile ratio (IQR). Since the data was not normally distributed Kruskal Wallis test was used for comparison of medians of the three study groups. Mann Whitney U test was applied for pair wise comparison of the variables. A P-value ≤ 0.05 was considered statistically significant.

**RESULTS**

A statistically significant difference (p=0.001) was found between the median BMI of the three study groups by applying Pearson Chi-Square test. A highly statistically significant difference was found between the fasting GH levels (p= 0.001) and the fasting blood glucose levels of the three study groups (p= 0.000) by applying Kruskal Wallis test(Table:1). A highly statistically significant difference was found between median fasting GH levels of group 1 and 2 (p= 0.001, Table:2) and group 1 and 3 (p= 0.018, Table:3) by applying Mann Whitney U test.

**Table 1:** Comparison of serum GH and FBG between the study groups using Kruskal-Wallis test

<table>
<thead>
<tr>
<th>Biochemical parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH (ng/ml)</td>
<td>0.241(0.1-2.183)</td>
<td>1.039(0.986-1.106)</td>
<td>0.001*</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>68(63.25-76.50)</td>
<td>75(69.25-81.75)</td>
<td>0.035*</td>
</tr>
</tbody>
</table>

**Table 2:** Comparison of serum GH and FBG between group 1 and 2 using Mann-Whitney U test

- GH (ng/ml): 0.241 (Group 1) vs 1.039 (Group 2), p=0.001*
- FBG (mg/dl): 68 (Group 1) vs 75 (Group 2), p=0.035*

*P ≤0.05 considered statistically significant
A highly statistically significant difference was found between FBG levels of group 1 and 3 (p= 0.000, Table: 3), group 2 and 3 (p= 0.000, Table: 4) and group 1 and 2, (p= 0.035, Table 2).

**Table 3:** Comparison of serum GH and FBG between group 1 and 3

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>Group 1 (n=28) Median(IQR)</th>
<th>Group 3 (n=28) Median (IQR)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH (ng/ml)</td>
<td>0.241(0.1 22-2.183)</td>
<td>1.131(0.38 4-2.99)</td>
<td>0.018*</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>68(63.25-76.50)</td>
<td>154(104.25-214.75)</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

**Table 4:** Comparison of serum GH and FBG between group 2 and 3

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>Group 2 (n=28) Median(IQR)</th>
<th>Group 3 (n=28) Median (IQR)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH (ng/ml)</td>
<td>1.039(0.98 6-1.106)</td>
<td>1.131(0.3 84-2.99)</td>
<td>0.974</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>75(69.25-81.75)</td>
<td>154(104.25-214.75)</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

**DISCUSSION AND CONCLUSION**

In the present study, serum GH levels were significantly different (p= 0.001) between the three study groups. The median serum GH level was highest in TB diabetic group and lowest in the healthy control group. These results are consistent with the findings of a previous study that reported that the altered immune-endocrine environment of M.TB infection, favors a significantly higher serum GH level in pulmonary TB cases as compared to healthy controls. In pulmonary TB raised serum GH levels will be beneficial to contain M.TB infection in lungs since it primes macrophages for increased reactive oxygen species (ROS) production and also activates human monocytes for enhanced hydrogen peroxide release. In addition, administration of GH to hypopituitary animals restores many macrophage functions relevant to infection and inflammation. The ability to release TNF-α and superoxide (O2-) was increased in triggered macrophages taken from hypopituitary animals treated with GH. GH mediates majority of its effects through production of IGF-1. Serum IGF-1 level was not determined in the present study since there are certain limitations to measurement of IGF-1 in TB and DM. It has been reported that the concentration of IGF-1 is affected by under-nutrition, chronic illness and diabetes mellitus. In the present study it was found that there is a statistically significant difference (p=0.035) between fasting blood glucose levels of healthy control and TB groups. GH itself is known to be a hyperglycemic hormone. Studies conducted in GH deficient adults showed that GH replacement therapy induces glucose intolerance. A statistically significant difference was found between fasting blood glucose levels of TB non-diabetic patients and healthy controls. GH levels are raised in TB and TB diabetic patients as compared to healthy controls. Since GH is a hyperglycemic hormone, its effects should be considered before treating TB patients.

**REFERENCES**