Hemoglobin Level Increases During The First Detected Phase of Overt Diabetes Mellitus

ABSTRACT
Diabetes Mellitus is a metabolic disease where due to hyperglycemia multiple complications are manifested in the course of time. Persistent hyperglycemia causes irreversible glycosylation of the hemoglobin called HbA1c. Glucose is converted to L-deoxyfructose. Glycosylation increases with the increase of hyperglycemia and also with the duration of suffering. This causes relative hypoxia in the tissues. Erythropoietin (EPO), a glycoprotein produced in the kidney is the major humoral regulator of Rbc production. Hypoxia induces increased synthesis of EPO. Therefore, hemoglobin level also increases. In the present study it is found that hemoglobin level of all the newly detected diabetic patients were high as compared to normal individuals. For male diabetic patients it was 15 (+0.87) gm/dl and for female it was 14 (+0.83) gm/dl as compared to the control 13.14 (+1.34) gm/dl and 12.15 (+ 0.87)gm/dl respectively. After receiving hypoglycemic drugs HbA1c level falls and tissue hypoxia reduces. Hemoglobin level also comes down to normal level.

Introduction
Diabetes Mellitus (DM) is a global health problem of human being. As of 2014, an estimated 387 million people suffer from DM in the world. The figure is expected to increase to 592 million by 2035. This metabolic disorder is characterized by persistent hyperglycemia along with other typical symptoms. If hyperglycemia is not kept under control, in course of time different complications may occur. Acute common complications are diabetic ketoacidosis and non-ketotic hyperosmolar coma. The common chronic complications are nephropathy, neuropathy, retinopathy, cardiovascular diseases, stroke, foot ulcer etc. Diabetics is mainly due to either less production of Insulin by the β cell of Islets of Langerhans of Pancreas (type-1) or reduced number of Insulin receptors in the cells (type-2). Diabetes is mainly due to either less production of Insulin by the β cell of Islets of Langerhans of Pancreas (type-1) or reduced number of Insulin receptors in the cells (type-2).3. Diabetes is characterized by persistent hyperglycemia along with the hemoglobin synthesis7.

Materials and Method-
Total 150 number of diabetic patients (80 male, 70 female) with equal number of normal individuals were included in this study. All the diabetic patients were diagnosed for the first time following WHO guideline. Fasting and post-prandial plasma glucose level were estimated by glucose oxidase-peroxidase method (GOD POD). HbA1c level of all the patients and control were assayed by immunoturbidimetry method using semi autoanalyzer. Hemoglobin level of all the patients and control were estimated by cromath method along with the complete blood count. After receiving hypoglycemic drugs for six months all the above parameters were assayed again and compared with the previous results.

Result
Total 150 patients (Male-80, Female-70) and equal number of control were tested for fasting and postprandial blood sugar, HbA1c,Hb and complete blood count. It is observed that at the time of first detection of DM, most of the patients had very high postprandial blood glucose level. But the fasting glucose levels were not so high for most of the patients. The mean fasting sugar was 161.88 (+22.21) mg/dl and postprandial sugar was 363.75 (+48.38) mg/dl. The mean HbA1c was 11.25 (+1.13) %. This reveals the fact that Insulin fails to cope with the postprandial hyperglycemia. The HbA1c values were correspondingly high. It was very interesting to find that hemoglobin level of all the diabetic patients were high as compared to normal individuals (table-1). For male diabetic patients it was 15 (+0.87) gm/dl and for female it was 14 (+0.83) gm/dl as compared to the control 13.14 (+1.34) gm/dl and 12.15 (+ 0.87)gm/dl respectively. The complete blood count showed no significant difference between both the groups.

After six months of treatment with hypoglycemic drugs blood sugar was under control. Again all the parameters were repeated. It was found that Hb % came down to normal as the control.
Table 1. Comparative values of Hb.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Control</th>
<th>Blood Sugar Mean (±SD)</th>
<th>HbA1c Mean (±SD)</th>
<th>Hb% of Patient Mean (±SD)</th>
<th>Hb% of Control Mean (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>150</td>
<td>161.88 (±22.21)</td>
<td>36.75 (±48.38)</td>
<td>11.25 (±1.13)</td>
<td>15 (±0.87)</td>
</tr>
<tr>
<td>(M-80, F-70)</td>
<td>(M-80, F-70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>150</td>
<td>150</td>
<td>Fasting</td>
<td>Post-prandial</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 (±0.87)</td>
<td>14 (±0.83)</td>
<td>13.14 (±1.34)</td>
<td>12.15 (±0.87)</td>
</tr>
</tbody>
</table>

Discussion
In many cases patients do not know about their glycemic status. They come to the clinic with the complaints of weakness and loss of weight. On investigation it is found that they are suffering from DM. But by this time blood sugar increases to very high and so also HbA1c. Very few patients are well aware and health conscious. During the investigation process we have noticed the fact that these patients had unusually high hemoglobin level as compared to normal individuals (table-1). For male diabetic patients it was 15 (+0.87) gm/dl and for female it was 14 (+0.83) gm/dl as compared to the control 13.14 (+1.34) gm/dl and 12.15 (+0.87) gm/dl respectively. The complete blood count showed no significant difference between both the groups.

Persistent hyperglycemia leads to non-enzymatic glycosylation of the N-terminal Valine of the β chain of hemoglobin and the reaction is irreversible. Therefore it remains for the lifetime of the Rbc. Increased HbA1c shifts the oxyhemoglobin dissociation curve to the left reducing the hemoglobin’s ability to release the oxygen at the tissue bed. This causes relative hypoxia in the tissues.

EPO, a glycoprotein produced in the kidney is the major humoral regulator of Rbc production. Hypoxia induces increased synthesis of EPO. EPO gene contains sequences that are oxygen sensitive and are involved in the regulation of EPO gene expression. There is an oxygen sensitive enhancer in the EPO gene called Hypoxia inducible factor-1 (HIF-1). This DNA binding protein is tightly regulated by oxygen tension and is considered to be the physiological regulator of EPO transcription. Probably this is the reason why in early phase of diabetes when blood sugar level is very high with elevated HbA1c, hemoglobin level increases. After receiving hypoglycemic drugs blood sugar comes under control and glycosylation also reduces. Rbcs are now little free to transfer oxygen to the tissues and hemoglobin level also comes to normal.

Conclusion
Persistent hyperglycemia causes nephropathy and other complications. EPO which is synthesized from kidney, is the major regulator of production of Hb. In case of nephropathy EPO synthesis reduces and leads to anemia. But in early phase of overt diabetes, due to very high HbA1c, hemoglobin dissociation curve shifts to the left which create an environment of hypoxia in the tissue bed. Hypoxia induces transcription of more EPO, leading thereby the increased hemoglobin synthesis. Further study may reveal additional causes of increased Hb in the early phase of diabetes. Eventually Hb level reduces to normal after receiving hypoglycemic drugs.

Reference