EVALUATION OF CHANGES IN LEVELS OF GLYCA TED HEMOGLOBIN, TOTAL PROTEIN AND ALBUMIN IN PATIENTS DIAGNOSED WITH TYPE 2 DIABETES MELLITUS
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Abstract
Insulin resistance in Type 2 diabetes mellitus metabolism of carbohydrates, lipids and proteins gives an estimate of the average blood glucose the previous three months in diabetes. Protein and HbA1c have been shown to be involved complications of diabetes mellitus. Hence based on above findings the present study was planned for Evaluation of Changes in Levels of Glycated Hemoglobin, Total Protein and Albumin in Patients Diagnosed with Type 2 Diabetes Mellitus.

The present study was planned in Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India. In the present study 50 cases were evaluated. The 25 cases were enrolled on the Group A as normal cases in Control group. The remaining 25 cases were enrolled in the Group B as Diabetic Patients as study group patients. Glycated Haemoglobin level was determined using immunoturbidimetric method as described by Wolf et al., (1984). Serum albumin level was estimated Bromo Cresol green Method as described by Doumas et al., (1971). Estimation of serum total protein level was done using Biuret Method according to Weichselbaum, (1946).

The data generated from the present study concludes that significantly higher mean levels of HbA1c in the diabetic patients compared with the control subjects. However, the mean serum of levels of Albumin and total protein did not differ significantly when compared between the diabetic patients and controls. This finding implies that there was a poor glycemic control in the diabetic subjects studied. Therefore, there is need for better management of diabetic patients through medication and use of diet and exercise.

Keywords: Albumin, HbA1c, total proteins, Type 2 Diabetes mellitus, etc.

Introduction
Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time. Symptoms often include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, and damage to the eyes.

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is a combination of excessive body weight and insufficient exercise.[1]

The classic symptoms of untreated diabetes are unintended weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger).[23] Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes. Other symptoms of diabetes include weight loss and tiredness. [2]

Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurred vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Long-term vision loss can also be caused by diabetic retinopathy. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermatoes. [3]

People (usually with type 1 diabetes) may also experience episodes of diabetic ketoacidosis (DKA), a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. A rare but equally severe possibility is hyperosmolar hyperglycemic state.
(HHS), which is more common in type 2 diabetes and is mainly the result of dehydration. [4]

Treatment-related low blood sugar (hypoglycemia) is common in people with type 1 and also type 2 diabetes depending on the medication being used. Most cases are mild and are not considered medical emergencies. Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such as confusion, changes in behaviour such as aggressiveness, seizures, unconsciousness, and (rarely) permanent brain damage or death in severe cases. Rapid breathing, sweating, and cold, pale skin are characteristic of low blood sugar but not definitive. Mild to moderate cases are self-treated by eating or drinking something high in sugar. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon. [5]

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20) but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in people with diabetes are due to coronary artery disease. [6] Other macrovascular diseases include stroke, and peripheral artery disease.

The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems. It is recommended that people with diabetes visit an eye doctor once a year. [34] Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation. [33] Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. [7] The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle atrophy and weakness.

There is a link between cognitive deficit and diabetes. Compared to those without diabetes, those with the disease have a 1.2 to 1.5-fold greater rate of decline in cognitive function. [35] Having diabetes, especially when on insulin, increases the risk of falls in older people. [36]

Type 2 diabetes is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type of diabetes mellitus. Many people with type 2 diabetes have evidence of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) before meeting the criteria for type 2 diabetes. The progression of prediabetes to overt type 2 diabetes can be slowed or reversed by lifestyle changes or medications that improve insulin sensitivity or reduce the liver’s glucose production. [8]

Type 2 diabetes is primarily due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio. [9]

Dietary factors also influence the risk of developing type 2 diabetes. Consumption of sugar-sweetened drinks in excess is associated with an increased risk. The type of fats in the diet is also important, with saturated fat and trans fats increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating lots of white rice also may increase the risk of diabetes, whereas substitution of brown rice or other whole grains for white rice may lower the risk of diabetes. A lack of physical activity is believed to cause 7% of cases. [10]

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1. Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus. [11]

The body obtains glucose from three main sources: the intestinal absorption of food; the breakdown of glycogen (glycogenolysis), the storage form of glucose found in the liver; and gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body. Insulin plays a critical role in regulating glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen. [12]

Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas,
response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body’s cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin. [13]

If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin resistance), or if the insulin itself is defective, then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency.[14]

When glucose concentration in the blood remains high over time, the kidneys reach a threshold of reabsorption, and the body excretes glucose in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume is replaced osmotically from water in body cells and other body compartments, causing dehydration and increased thirst (polydipsia). In addition, intracellular glucose. [15]

Insulin resistance in Type 2 diabetes mellitus metabolism of carbohydrates, lipids and proteins gives an estimate of the average blood glucose the previous three months in diabetes. Protein and HbA1c have been shown to be involved complications of diabetes mellitus. Hence based on above findings the present study was planned for Evaluation of Changes in Levels of Glycated Hemoglobin, Total Protein and Albumin in Patients Diagnosed with Type 2 Diabetes Mellitus.

Methodology:
The present study was planned in Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India. In the present study 50 cases were evaluated. The 25 cases were enrolled on the Group A as normal cases in Control group. The remaining 25 cases were enrolled in the Group B as Diabetic Patients as study group patients. Glycated Haemoglobin level was determined using immunoturbidimetric method as described by Wolf et al., (1984). [16] Serum albumin level was estimated Bromo Cresol green Method as described by Doumas et al., (1971). [17] Estimation of serum total protein level was done using Biuret Method according to Weichselbaum, (1946). [18]

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: freshly diagnosed years duration) of diabetes mellitus.

Exclusion Criteria: All patients who were Obese, under nourished, anemic, hypertensive, had chronic inflammatory liver disease, epilepsy, renal disorders, known chronic diabetics, smokers and psychiatric patients.

Results & Discussion:
Diabetes mellitus is considered to be one of the most challenging health problems of the 21st century. Type 2 Diabetes Mellitus (T2DM) constitutes 90 to 95% of diabetes mellitus in the adults and is characterized by a combination of insulin resistance and insulin secretory defect. T2DM is characterized by an asymptomatic phase between the actual onset of hyperglycemia and clinical diagnosis. This phase has been estimated to last at least 4–7 years, and consequently 30–50% of T2DM patients remain undiagnosed.

Protein glycation is involved in the long-term complications of diabetes. [19-20] Plasma proteins are the primary targets of glycation following elevated levels of glucose in diabetes. [21] Amongst plasma proteins, albumin is one of the heavily glycated proteins because of its abundance, comparatively longer half-life and a higher number of free lysine and arginine residues. [22] Glycation accelerates albumin degradation via increasing catabolic rate and decreasing protein half-life, [23] thus decreasing the albumin levels in diabetes. It has been mechanistically shown that albumin competes with other proteins for glycation [24] and low albumin level was associated with increased plasma protein glycation in diabetes. [25] This study was corroborated in a recent finding where low albumin levels were associated with increased fibrinogen glycation. [26] It has also been suggested that low plasma albumin predicts the glycated hemoglobin (HbA1c) in type 2 diabetes, [27] thus, strongly implicating albumin in regulation of plasma protein glycation and HbA1c.

Glycated hemoglobin is an important marker of glycemic control as it estimates average blood glucose of the previous 3 months. Recent guidelines by the American Diabetes Association also recommended HbA1c as a diagnostic tool for diabetes, in addition to its well-known use to define control. [28] Studies showed that its level correlates with average plasma glucose and the progression of diabetes complication. [29]
Table 1: Demographic Details

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Cases</td>
<td>Diabetic Cases</td>
<td></td>
</tr>
<tr>
<td>Age: 20 – 30</td>
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<td>1</td>
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<tr>
<td>years</td>
<td>3</td>
<td>4</td>
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<tr>
<td>31 – 40</td>
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</tr>
<tr>
<td>years</td>
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<td>6</td>
</tr>
<tr>
<td>41 – 50</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>years</td>
<td>51 – 60</td>
<td></td>
</tr>
<tr>
<td>years</td>
<td>61 &amp; above</td>
<td></td>
</tr>
<tr>
<td>Sex: Males</td>
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<td>17</td>
</tr>
<tr>
<td>Females</td>
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<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
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</tr>
</tbody>
</table>

Table 2: Levels of HbA1c, Protein & Albumin

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Cases</td>
<td>Diabetic Cases</td>
<td></td>
</tr>
<tr>
<td>HbA1c %</td>
<td>6.12 ± 0.75</td>
<td>9.64 ± 1.65</td>
</tr>
<tr>
<td>Protein(g/L)</td>
<td>76.52 ± 4.23</td>
<td>71.58 ± 3.21</td>
</tr>
<tr>
<td>Albumin(g/L)</td>
<td>39.15 ± 2.95</td>
<td>39.43 ± 2.79</td>
</tr>
</tbody>
</table>

During diabetes, persistent hyperglycemia leads to nonenzymatic glycation of various proteins such as hemoglobin, proteins of erythrocyte membrane, insulin, human serum albumin (HSA), high and low density lipoproteins, IgG, IgM, collagen and histones. [30-31] Proteins are glycated, when glucose is chemically bound to amino groups of proteins without the help of enzyme, which causes many structural and conformational changes in protein, and proceeds to various micro-macro complications in diabetic patients. [32] A strong link between Amadori albumin and diabetes specific complications have been demonstrated by studies in humans, [33] animals [34] and cell culture. [35]

Human serum albumin is mainly synthesized in the liver, and is the most abundant protein in human circulation. HSA has many physiological and pharmacological functions such as maintenance of colloid osmotic pressure, transport of fatty acids, hormones, drugs and metabolites. HSA also has anti-thrombotic, anti-inflammatory, antioxidant activity and regulates microvascular permeability. [36-37] Some physiological variables such as body mass index or age and pathological conditions such as thyroid dysfunction, Nephrotic syndrome and cirrhosis of the liver alter album metabolism and can affect GA levels. [36]

Earlier studies strongly suggest the involvement of biochemical disturbance that is caused due to the nonenzymatic glycation of serum proteins such as albumin in the development of diabetic nephropathy. It is revealed that hyperglycemia in streptozotocin or alloxan induced diabetic rats or in human patients with pancreatic insufficiency could cause thickening of the glomerular basement membrane, which may lead diabetic nephropathy. [38]

People with diabetes live healthily (diet and exercise) and maintain HbA1c levels below 7.0%. Diabetes-related complications are directly proportional to HbA1c levels increasing. HbA1c levels also increase the risk of such complications. Excessive use of vitamin C, B and E, as well as an increase in cholesterol, liver and kidney diseases can also lead to abnormally high levels of HbA1c. [39-40] Dyslipidemia, which is an imbalance of lipids and fats circulating in the blood, is another [41-42] debilitating disease associated with diabetes. However, maintaining a healthy glucose level is of fundamental importance for type 2 diabetics to be useful, in preventing vascular complications of micro and macropathologies. [43] HbA1c is also regularly used to evaluate gestational diabetes in pregnant women. [44] Other researchers used serum fructosamine and blood sugar to detect gestational diabetes in pregnant women. [45-46] Both Tests will allow Health professionals determine whether pregnant women with related risk factors before pregnancy have developed diabetes that may not have been diagnosed.

Conclusion:

The data generated from the present study concludes that significantly higher mean levels of HbA1c in the diabetic patients compared with the control subjects. However, the mean serum of levels of Albumin and total protein did not differ significantly when compared between the diabetic patients and controls. This finding implies that there was a poor glycemic control in the diabetic subjects studied. Therefore, there is need for better management of diabetic patients through medication and use of diet and exercise.

References:

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