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Hyperosmolar Hyperglycemic Syndrome in Type 2 Diabetes Mellitus –A Case Control Study in North Coastal Andhra Pradesh

Biological Science

KEYWORDS : Diabetes mellitus, Osmolarity, Hyperosmolarity, Hyperglycemia

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ABSTRACT

INTRODUCTION*:In the present study we try to investigate the association and severity of hyperosmolar hyperglycemic syndrome in patients of type 2 Diabetes mellitus.* ***METHOD*** *:A total of fifty(50) patients of type 2 diabetes mellitus were included in the study. Twenty five(25) healthy controls were also included in the study for comparison.* ***RESULTS:*** *Serum osmolarity values are increased in cases with 342.53 ± 37.0 mosm/l (mean± SD) when compared to controls with 284.62 ± 6.1 mosm/l (mean ± SD) with a statistically significant 'p' value of < 0.0001 along with a significant increase of blood urea and serum electrolytes like sodium. The mean blood glucose values are also increased in cases with 217.48±28.02 mg/dl (mean ± SD) when compared to controls with 96.06 ± 11.3 mg/dl (mean ± SD) with a statistically significant 'p' value of < 0.001.So hyperosmolar hyperglycemic state is seen in patients of type 2 diabetes with increased blood glucose values.* ***CONCLUSION****: Hyperosmolar hyperglycemic syndrome is a life threatening complication in patients of type 2 diabetes mellitus with increased blood glucose values.*

INTRODUCTION :Diabetes mellitus is a syndrome of disordered metabolism of carbohydrates, fats and proteins, usually due to a combination of hereditary and environmental causes resulting in abnormally high blood glucose levels (hyperglycemia).It is a clinical syndrome characterized by an increase in blood glucose[1].Diabetes mellitus(DM) is mainly of 2 types. Type 1 DM is a T-cell mediated auto immune disease involving destruction of insulin secreting β cells in pancreatic islets, leading to insulin deficiency. In individuals of Type 1 DM HLA DR_3/DR_4[2] association is seen. Along with that environmental factors like viruses (mumps,coxsackie etc),specific drugs or chemicals also play a very important role in causation of type 1DM.Type 2 DM is a condition where relative insulin resistance is the feature. In type 2 DM genetic predisposition is more common. It is more commonly seen in monozygotic twins (100%).Variations in TCF7L2[3] is seen in type 2 DM. Environmental factors like diet and body weight also plays a key role in causation of type2 DM.

Normally the blood glucose levels are maintained in the range of 70-110mg/dl. DM can be diagnosed when the fasting blood glucose level is more 126mg/dl and post prandial blood glucose level (2hrs after an oral glucose) is more than 200mg/dl for at least two times(American Diabetic Association –ADA). Blood glucose along with other solutes like electrolytes (Na-Sodium) and urea maintains the plasma osmolarity. Whenever there is an increase in the solute level as in DM where the blood glucose level is increased, it causes osmotic diuresis which causes increased concentration of blood (hyperosmolarity) due to increased water loss.

Osmolarity is a measure of number of the dissolved particles (molecules or ions) in a solution. So osmolarity can be defined as the number of osmoles of solute per litre of solution (osmol/l).The normal serum osmolarity is 280-296 mosm/l[1].Sodium,blood urea nitrogen and blood glucose levels are major factors in determining the serum osmolarity.

Hyperosmolar hyperglycemic syndrome(HHS) is a relatively common, life threatening endocrine emergency, most frequently affects older patients with type 2 diabetes[4].The hallmark of hyperosmolar hyperglycemic syndrome is profound dehydration with marked hyperglycemia. The initiating event is glucosuric diuresis. Due to increased blood glucose levels as well as decreased concentrating capacity of kidneys glucose is excreted in the urine (glucosuria).Glucosuria itself impairs the concentrating capacity of kidneys causing increased water loss. Normally kidneys act as safety valves to eliminate glucose above a certain threshold and prevent further accumulation. But decreased intravascular volume or underlying renal disease decreases GFR, causing the glucose level to increase. The loss of more water than sodium leads to hyperosmolarity[5].Insulin is present but is not adequate to reduce blood glucose levels, particularly in the presence of significant insulin resistance[6].Precipitating factors for HHS includes infections, medications, undiagnosed diabetes, co-existing diseases etc out of which infections play the major role. In addition to one or more precipitating factors, patients present with weakness, visual disturbances and later develop neurological symptoms like lethargy, confusion, hemiperesis. Physical findings reveal profound dehydration, low grade fever, abdominal distension etc. Coma occurs when osmolarity exceeds 350 mosm/kg[7].Laboratory findings include: Blood glucose >600mg/dl[1],Serum osmolarity >320 mosmol/kg[1].Treatment includes:Vigorous intravenous rehydration, electrolyte replacement, administration of I.V.Insulin, diagnosis and management of co-existing problems.

In the present study we want to estimate the blood glucose, blood urea and sodium levels and calculate serum osmolarity in patients of type 2 DM.

MATERIALS AND METHODS: Present study was conducted on fifty (50) patients of type 2 diabetes in age group of 40 – 70 years. Along with that twenty five (25) healthy controls of same age group are also included for comparison.

Inclusion criteria: Patients of type 2 diabetes with symptoms of hyperosmolarity without ketoacidosis.

Exclusion criteria: Patients of type 1 diabetes and those with hyperosmolarity due to other conditions.

Methods:

1.Estimation of blood glucose by Glucose oxidase – peroxidase (GOD-POD) method by Mindray 300 autoanalyzer.

Principle: Glucose present in the sample in the presence of glucose oxidase is converted to gluconic acid and hydrogen peroxide. Hydrogen peroxide reacts with 4-aminoantipyrine and phenol in the presence of the enzyme peroxidase to form quinoneimine, which is pink in colour.

2.Estimation of Urea by GLDH-urease method by Mindray 300 autoanalyzer.

Principle:

Urea + H_2O $\xrightarrow{\text{urease}}$ $2NH_3 + CO_2$

NH_3 + α KG + NADH $\xrightarrow{\text{GLDH}}$ Glutamate + NAD

(NH_3 = Ammonia ,α KG = Alpha keto glutarate ,NAD = Nicotinamide adenine dinucleotide , GLDH = Glutamate dehydrogenase.)

3.Serum Sodium (Na^+) is estimated by electrolyte analyzer.

Serum osmolarity is calculated by using sodium, glucose and urea values by the following formula :

Osmolarity = 1.86 (Na in mEq/l) + $\frac{\text{Glucose (mg/dl)}}{18}$ + $\frac{\text{Urea(mg/dl)}}{2.8}$ + 9.

RESULTS & OBSERVATIONS :

In the present study the mean blood glucose value in cases is 217.48 ±28.02 mg/dl (mean ± SD) and that in controls is 96.06 ± 11.30 mg/dl (mean ± SD) with a statistically significant 'p'value of < 0.01.

Serum osmolarity in cases is 342.53 ± 37.0 mosm/l (mean± SD) and that in controls is 284.62 ± 6.1mosm/l (mean± SD) with a statistically significant 'p' value of < 0.001.Serum urea value in cases is 67.94 ± 10.29 mg/dl(mean ± SD) when compared to controls with a mean value of 30.9 ± 11.3 mg/dl(mean ± SD).

Serum Sodium (Na^+) value in cases is 175.04± 23.52 mEq/l (mean± SD) and that in controls is 136.0± 6.1meq/l (mean ± SD) with a statistically significant 'p' value of <0.001.

DISCUSSION: Osmolarity or osmotic concentration is the measure of solute concentration and is defined as the number of osmoles(osm) of solute per litre of solution. Normal plasma osmolarity is 280 – 296 mosm/l. Osmotic concentration of plasma is mainly due to the presence of solutes like electrolytes and also due to other solutes like glucose and urea to a lesser extent. Whenever the water content of blood is decreased as in dehydration or when the solute is increased as in diabetes mellitus where the blood glucose levels are increased the osmolarity of plasma is increased causing hyperosmolarity. Hyperosmolar hyperglycemic state (HHS) is a serious metabolic derangement that occurs in patients with Diabetes mellitus sand is a life threatening condition.HHS most commonly occurs in older patients of type 2 Diabetes mellitus and in those with some concomitant illness that leads to reduced fluid intake. Infection is the most common preceding cause. HHS causes 10 -20% mortality.HHS is characterized by hyperglycemia, hyperosmolarity and dehydration along with some neurological deficits[8]. In patients with a preexisting lack of or resistance to insulin ,a physiological stress such as an acute illness can cause further net reduction in circulating insulin. The basic underlying mechanism of HHS is a relative or absolute reduction in effective circulating insulin with a concomitant elevation of counter regulatory hormones[9,10]. Decreased renal clearance and decreased peripheral utilization of glucose leads to hyperglycemia. Hyperglycemia and hyperosmolarity results in an osmotic diuresis and an osmotic shift of fluid to the intravascular space resulting in further intracellular dehydration. Diuresis causes loss of electrolytes like sodium and potassium along with water. Normally all the glucose filtered by the kidney is reabsorbed. But when the blood glucose level exceeds the renal threshold of 180mg/dl, proximal tubular transport of glucose from the tubular lumen into the renal intestitium becomes saturated and further glucose reabsorption is no longer possible. The glucose that remains in the renal tubules continues to travel into the distal nephron and eventually lost in the urine carrying water and electrolytes with it, resulting in osmotic diuresis. Along with that if the water intake is also decreased as in old people or with some disease, it further aggravates the hyperosmolarity.

Conclusion: Hyperosmolar hyperglycemic syndrome is a very important life threatening complication of type 2 diabetes mellitus with increased blood glucose levels. The condition can be prevented by proper maintenance of blood glucose values in the normal range.

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