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Research Article

A RETROSPECTIVE STUDY ON THE RISK FACTORS IN PATIENTS ADMITTED WITH SEVERE HYPOGLYCAEMIA IN TYPE -2 DIABETIC PATIENTS IN TERTIARY CARE HOSPITAL, SVIMS, TIRUPATI

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Abstract:

Background: Hypoglycemia is a pathological condition in which the plasma glucose concentration is less than 70 mg/dl. It is commonest in patients with diabetes mellitus (DM). Age, gender, body weight, Duration of diabetes, use of insulin, oral hypoglycemic drugs, body mass index, presence of diabetic micro and macro vascular complications, hospital admission, infection are the possible risk factors for increasing the risk of hypoglycemia.

Aim: To study the frequency of risk factors of Severe Hypoglycemia in type-2 diabetic patients attending in tertiary care hospital, SVIMS, Tirupati.

Methodology: This retrospective study was performed in the Department of Endocrinology and metabolism in SVIMS, Tirupati, over a period of 6 months. All the patients with type-2 DM aged 20 or above presented with hypoglycemia symptoms are included in the study. Pregnant and lactation women and type-1 DM patients are excluded from the study. Demographic details, laboratory parameters, treatment details were collected in the pre-designed annexure form (Patient data collection proforma).

Results: A total of 100 diabetic patients admitted with hypoglycemia were included in the study. Out of which 54% were males, 32% of the patients were under age group 60-70 years. 63% had diabetes for 10 years and 43% took insulin and 76% using OHAs. Hypertension was most common co-morbid condition 76% followed by CAD. Diabetic nephropathy was the most common complication when compared to diabetic retinopathy and neuropathy. The mean plasma glucose at admission was 40 ± 14 mg/dl. Mean HbA1c was 7.1 ± 1.82 and 48% had eGFR < 60 ml/min/1.73m². Most of them 48% had history of hypoglycemic episodes in preceding one month. Meal related factors such as missed, inadequate or delayed meals are the precipitating factors followed by alcohol use and drug over dose.

Conclusion: Hypoglycemia is a potential risk in the management of patients suffering from type-2 DM. Awareness, knowledge and better understanding of the risk factors for hypoglycemia in patients with type-2 DM and identification of the patients who are at risk for severe hypoglycemia can help the physician or care guide with providing optimal patient treatment and management.

Key words: Severe hypoglycemia, Type-2 diabetes mellitus, Risk factors, oral hypoglycemic drugs, plasma glucose concentration.

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INTRODUCTION:

Hypoglycemia may be common and high effect of diabetes mellitus (DM).^[1] Consistent with American diabetes association (ADA), it is defined because the plasma glucose concentration which is smaller amount than 70 mg/dl.^[2] It occurs because of the excessive insulin present with in the blood, which results in low plasma glucose levels and is categorized by either mild or severe based the severity of the episode and whether a patient requires external assistance or is self-sufficient.^[3] It is also caused by usage of glucose-lowering therapies.^[4] It is one of the acute complications diabetes mellitus patients usually face. Although it occurs more frequently in type-1 DM, hypoglycemia also has clinical significance in type-2 DM. It is linked together with increasing number of hospital admission, extended hospitalization, morbidity and mortality in diabetes patients.^[5] Reoccurring hypoglycemic episodes can cause poor quality of life, mood swings, anxiety and depression.^[6]

Diabetic patients who are treated with insulin and oral diabetic drugs are at greater risk of developing hypoglycemia than patients treated by maintaining a correct diet and regular exercise.^[7] Hypoglycemia is additionally in patients with type-2 diabetes is also being linked with increased symptoms of chest pain, ECG changes and should account for sudden mortality.^[3]

CLASSIFICATION OF HYPOGLYCEMIA:

Hypoglycemia further classified in to five distinct categories. Severe hypoglycemia (an event causing neurological changes on require assistance of another person), documented hypoglycemia (plasma glucose concentration at or less than 70 mg/dl with typical hypoglycemic symptoms), asymptomatic hypoglycemia, probable hypoglycemia and relative hypoglycemia (symptoms implicational of hypoglycemia with plasma glucose concentration greater than 70 mg/dl).^[8]

RISK FACTORS OF HYPOGLYCEMIA:

Hypoglycemia in patients with diabetes is multi factorial. The duration of diabetes and progressive insulin deficiency, Oral anti diabetic drugs (OADs), and tight glycemc control contributes to reducing diabetic micro vascular complications, also an increased risk of hypoglycemia.^[9] Dietary errors like missed, inadequate or delayed meals, excessive physical activity, wrong drug dosage and wrong time of drug administration are the precipitating factor of hypoglycemia.^[10] Patients with diabetes who have chronic renal disorder, liver diseases and pancreatic or non-islet cell tumors, autoimmune conditions,

organ failure, endocrine diseases (Hypothyroidism, Addison's disease dyspituitarism), inborn error of metabolism, toxins present in food, consumption of alcohol, infections and other conditions like sepsis and starvation have a higher frequency of hypoglycemia.^[11]

Hypoglycemia unawareness and former history of hypoglycemic episodes are risk factors for severe hypoglycemia. Unawareness of symptoms related to a 6 to 9 times increase chances of severe hypoglycemia in type-2 diabetic patients.^[12] Elderly patients are at increased risk of hypoglycemia because of deteriorating renal functions and impaired cognitive functioning. Female gender also identified as a risk factor for hypoglycemia. Prior history of hypoglycemia is one among the strongest predictor for severe hypoglycemic episodes.^[11] It is going to also accompany other diseases like adrenal insufficiency, hepatic parenchymal diseases or ethanol intoxication and post resection syndrome.^[13] Hypoglycemia can also occur in patients with cancer because chemotherapy causes loss of appetite.^[14] Insulinomas (insulin producing tumors of the pancreas) causes hypoglycemia by releasing high amount of insulin. Some tumors of the liver referred to as hepatoma or other tumors like fibro sarcomas and mesothelioma can cause hypoglycemia by releasing insulin like factors. Insulin autoimmune syndrome may be a sort of autoimmune disease. It is a condition during which body makes antibodies that attack insulin causes hypoglycemia and it are often caused by certain medications.^[15]

CLINICAL MANIFESTATIONS:

Clinical manifestations of hypoglycemia depends not only on the present plasma glucose levels but also include the duration of the diabetes control, age of the patient, diabetic complications, previous history of severe hypoglycemia and therefore the sorts of medications used for diabetes. It is going to ranges from mild lowering of glucose (60-70 mg/dl) with minimal or no symptoms to severe hypoglycemia with very low levels of glucose concentration.

Symptoms of hypoglycemia are classified as autonomic and Nueroglycopenic symptoms. Autonomic symptoms include sweating, palpitations, shakiness, dizziness, hunger, pallor, anxiety, irritability and headache because of increased secretion of Catecholamine'. Nueroglycopenic symptoms like confusion, drowsiness, speech difficulty, odd behavior, incoordination, seizures and unconsciousness because of deprivation glucose to the brain.

Moderate hypoglycemia is related to dizziness, anxiety, confusion, ataxia, blurred vision because of dysfunction of central system nervosum. Blood sugar levels which are lower than 45 mg/dl or 2.5mmol/L can produce interferences with in the central nervous system with loss of consciousness and generalized convulsions. Untreated severe hypoglycemia may result in brain degeneration with mood disorders and diminished cognitive function. Severe and moderate hypoglycemia has also been linked with the induction of ventricular arrhythmias (QT prolongation).^[16, 17]

MATERIALS AND METHODS:

This Retrospective study was conducted for six months (Dec-2020 to May-2021) in the department of Endocrinology and Metabolism in Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati. The protocol of the study was approved by the institutional review board of the hospital, IEC.NO-1155. Within the study, the sample size taken was 100 patients and every onethe available patient medical records. All the Patients with type-2 diabetes mellitus (DM) aged 20 or above, who admitted within the department with signs and symptoms of hypoglycemia were included within the sample. Pregnant, lactating women, patients with other critical illness and with non- diabetic hypoglycemia were excluded. Plasma glucose concentration <70 mg/dl was considered for the threshold for diagnosis of hypoglycemia. 100 patients who had biochemically confirmed hypoglycemia were finally selected for the study. Demographic details, laboratory parameters, treatment details were collected in the pre- designed annexure form.

Data includes age, gender, Duration of diabetes, previous history of hypoglycemia, comorbidities, complications, decreased food intake, alcohol use, present medications, laboratory tests and plasma glucose levels on admission. Laboratory tests abstracted were HbA1c, serum creatinine, TSH, Glomerular filtration rate (GFR), serum cortisol. Comorbidities include hypertension (HTN), coronary artery disease (CAD), sepsis, hypothyroidism, renal disease, liver disorders, and alcoholism. Complication like Diabetic Retinopathy, Neuropathy, and nephropathy. Medications included oral hypoglycemic agents (OHAs), insulin, anti-hypertensive drugs.

STATISTICAL ANALYSIS:

All data was entered and saved to excel software of Microsoft windows 7. Base line demographic, clinical and laboratory data was summarized in the form of mean \pm standard deviation for continuous variables, numbers and percentages for categorical variables. Graphic representation like bar graphs and

pie charts were used for visual interpretation to analyze the data. There were no ethical issues as present study was a retrospective study based on existing patient medical records.

RESULTS:

A total of 100 patients were included in the study based on the inclusion and exclusion criteria. Gender distribution of the study population out of 100 patients 54 (54%) patients were males and 46 (46%) patients were females. Male patients were found to be higher when compared to female patients. The age wise distribution in the study population, the mean age of the study population was 65.07 ± 13.1 . In this 2 patients were under age group of 20-30 years, 4 patients were under the age group of 30-40 years, 4 patients were under the age group of 40-50 years, 23 patients were under the age group of 50-60 years, 32 patients were under the age group of 60-70 years, 26 patients were under the age group of 70-80 years, 9 patients were under the age group of above 80 years. In our study the more than half (63%) of the patients have duration of diabetes 1-10 years, followed by 10-20 years (30%), and remaining patients were having different years of duration of diabetes.

Out of 100 patients 76% of the patients were having hypertension (HTN), followed by 20% of the patients were having CAD. In our study out of 100, majority of the patients having Nephropathy (39%), where as 10% of the patients with Retinopathy and 9% of the patients with Neuropathy. In this 49% of the patients had a history of hypoglycemia in the preceding one month. History of hypoglycemia, missing meals and alcohol use are the predisposing factors for severe hypoglycemia. Among 100 patients the mean HbA1c level was 7.7 ± 1.6 %. The mean plasma glucose level was 40 ± 14 mg/dl. The mean serum creatinine concentration was 1.47 ± 0.98 mg/dl, the mean TSH levels was 2.47 ± 1.8 and 48% had estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m². Out of 100 patients 49 patients had recurrent hypoglycemia. In this group higher percentage of patients were under the age group of 50-60 years. The recurrent hypoglycemic patients had a great percentage of patients (31%) with missing meals. The patients had a significant longer duration of diabetes (1-10 years). The initial plasma glucose level and glomerular filtration rate (GFR) were significantly lower in the recurrent hypoglycemic patients. When examining comorbidities, 82% of the patients had hypertension and lower percentage (22%) of patients had CAD.

The significant risk factors for recurrent hypoglycemia were missing meals, duration of

diabetes, admitting plasma glucose level, glomerular filtration rate (GFR), serum creatinine, hypertensive drugs, and the presence of CAD and diabetic complications includes nephropathy, retinopathy, and neuropathy.

In our study the following medication were given to the patients, out of 100 patients 76% of the patients were taking oral hypoglycemic agents(OHAs), 43% of the patients were taking insulin therapy and 30% of the patients were taking oral hypoglycemic agents with insulin. Sulfonyl urea's are the main risk factor for hypoglycemia in diabetic patients, under sulfonyl urea's 53% of the patients were on glimepiride (1mg,2mg,4mg), 9% of the patients were on glibenclamide (2.5mg,5mg), 8% of the patients were on gliclazide (60mg,80mg), 5% of the patients were on glipizide (5mg).

DISCUSSION:

In the present study we retrospectively evaluate the risk factors of severe hypoglycemia in type-2 diabetes mellitus patients attending in tertiary care hospital. In our study, males (54) were more in number compared to females (46%). In a study conducted by AK Paul et.al on 100 subjects, females were higher in number compared to males.

Majority of the patients fell under the age group of 60-70 years and the mean age of the patients was (65.07±13.1). In a study conducted by AK Paul et.al from Bangladesh, most (53%) of the patients were in the age group of 60-70 years, and more half (63%) of the patients had diabetes for 10 years or longer. In a study conducted by AK Paul et.al 60% of the study subjects had diabetes for 10 years or longer.

In our study 49% of the patients had a history of hypoglycemia in the preceding one month. In a study conducted by AK Paul et.al, more half (51%) of the subjects had a history of hypoglycemia. The mean HbA1c level of the patients was 7.1±1.82, in a study conducted by Kasia J. Lipska et.al, the mean HbA1c level was 7.7±1.6 %. The mean plasma glucose level was 40±14mg/dl. The mean serum creatinine concentration was 1.47±0.98 mg/dl and 48% had estimated glomerular filtration rate (eGFR) <60ml/min/1.73m². In another study conducted by AK Paul et.al, the mean serum creatinine concentration was 1.76±0.74 mg/dl and the majority 86% had estimated glomerular filtration rate was <60ml/min/1.73m².

We focused on the patients who are admitted due to severe hypoglycemia. As follows we estimates 49% of the patients were admitted with recurrent

hypoglycemia. In another study conducted by Yen-Yue Lin *et.al*, 31.8% of the patients were admitted that subsequently developed recurrent hypoglycemia. Patients with longer duration of diabetes may be associated with a defect in the counter regulatory response to hypoglycemia. Use of anti -hypertensive drugs such as Beta blockers, Diuretics, Calcium channels blockers are the identifiable risk factors for recurrent hypoglycemia. Diuretics in diabetic patients associated with glucose intolerance and insulin resistance.

Coronary artery disease is the additional risk factor for severe hypoglycemia; it is a marker for dyslipidemia which is associated with insulin resistance and metabolic abnormalities. Missing meals was a significant risk factor for recurrent hypoglycemia. Decreased carbohydrate in take can lead to a low energy reservoir, which increases the development of severe hypoglycemia.

In our study most of the patients (76%) taking OHAs, 43% only insulin and 30% of patients using insulin and OHAs combination therapy. In another study conducted by AK Paul et.al, most of the patients 88% were insulin treated, 68% only insulin and 20% insulin and oral hypoglycemic agents.

CONCLUSION:

The present study comprised of 100 diabetic patients with hypoglycemia in which males were higher in number when compared to females, most of the patients were in the age group of 60-70 years. Hypertension is the most common comorbidity associated with hypoglycemia in diabetic patients followed by CAD. Longer duration of diabetes, prior history of hypoglycemia, missed meals and alcohol use are the predisposing factors for severe hypoglycemia.

Diabetic nephropathy was the most prevalent complication followed by diabetic retinopathy and diabetic neuropathy, and also liver disease also one of the important risk factor for hypoglycemia. Most of the patients were on OHAs therapy alone, some were on OHAs and insulin combination therapy, and few were on insulin therapy alone. Insulin preparations and sulphonyl urea are known to induce hypoglycemia more commonly when compared to other class of anti-diabetic medications.

Hypoglycemia is a potential risk in the management of patients suffering from type-2 DM. awareness, knowledge and better understanding of the risk factors for hypoglycemia in patients with type-2 DM and identification of the patients who are at risk for

severe hypoglycemia can help the physician or care guide with providing optimal patient treatment and management.

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