

Original Research Article

Clinical profile of hypoglycemia in diabetic patients : A prospective study in a tertiary care hospital

Abstract

Background: The term hypoglycemia refers to a clinical condition resulting from an abnormally low plasma glucose level (≤ 40 mg/dl). Clinically, it is characterized by varying degree of neurological dysfunction and is responsive to the administration of glucose. Hypoglycemia is commonly caused by drugs used to treat diabetes mellitus.

Objective: To study the clinical profile, precipitating factors and outcome in the patients of hypoglycemia.

Material and Methods: This hospital based 2 years prospective study was conducted in the Department of Medicine, Kasturba Medical College and hospital, Manipal, Karnataka. Clinical profile of 100 diabetic patients on OHA's or Insulin treatment with the diagnosis of hypoglycemia were analysed.

Results:

Out of 100 patients, 30 (30%) patients were of type 1 diabetes mellitus and 70 (70%) patients of type 2 diabetes mellitus. The male:female ratio was 1:1.7. The most common precipitating factor was found to be delaying or skipping meals (80%),

24 followed by decreased carbohydrate intake (70%), increase in insulin or OHAs
25 dosage (54%), decrease in insulin requirement (10%). The most common autonomic
26 symptom was sweating (90%) followed by palpitation (80%). Neuroglycopenic
27 symptoms were observed at much lower blood glucose level. Majority of
28 hypoglycemic patients (68%) had blood glucose in the range 31-40 mg/dl. 64
29 patients (64%) were on only insulin therapy and 16 (16%) patients were on OHAs.
30 20 (20%) patients were on combination (insulin+OHAs) therapy. Maximum incidence
31 of hypoglycemia was reported among patients who were on combination of short
32 acting plus intermediate acting (i.e Premix – 30/70) Insulin. However, within the set
33 of patients developing hypoglycaemia due to OHA's, the frequency was much higher
34 (62.5%) with a combination therapy of OHA's as compared to monotherapy (37.5%).
35 Present study did not show any mortality due to hypoglycemia.

36 **Conclusion:**

37 Hypoglycemia is the most common acute metabolic complication of diabetes mellitus
38 on treatment. Elderly diabetics, patients with chronic kidney disease and patients on
39 long acting insulin/sulfonylureas (used either alone or in combination) are more
40 prone to develop hypoglycemia. Diabetic patients should be familiar with
41 hypoglycemia symptom profile so that they can perceive the early onset of
42 hypoglycemia and an appropriate action can be taken immediately.

43 **Key words:** Hypoglycemia, Blood sugar, OHAs (oral hypoglycemic agents)

44 **INTRODUCTION**

45 Hypoglycemia is the most common endocrine emergency faced by physicians. It is
46 defined arbitrarily as a blood glucose of less than 50mg/dl with neuroglycopenic

47 symptoms or less than 40 mg/dl in the absence of symptoms.^[1] Hypoglycemia
48 impedes safe achievement of optimal glycemia. Severe hypoglycemia – that require
49 the assistance of another person – is a clinical red flag. ^[1]

50 Hypoglycemia remains the most common and serious iatrogenic cause of morbidity
51 in diabetic patients.^[2] Large trials such as Veterans affairs diabetes trial and Action to
52 control cardiovascular risk in diabetes trial have shown that there was a higher
53 mortality in the group that had been treated intensively to achieve glycemic control
54 .^{[3],[4]} Hence, the American Diabetes Association (ADA) guidelines emphasized on
55 individualizing targets and reducing risk of hypoglycemia in patients with long
56 duration of diabetes and co-morbidities.^[5] Targeted HbA1c levels in patients with
57 Type 1 Diabetes and Type 2 Diabetes should be tailored to the individual, balancing
58 the micro vascular complication with risk of hypoglycaemia. ^[6-9] The American
59 Diabetes Association's most recent guidelines still recommended HbA1C goal for
60 most adults to be less than 7 %, but also recognizes that less stringent goals (such
61 as <8%) may be appropriate for patients with a history of severe hypoglycemia,
62 limited life expectancy, advanced complications and comorbid conditions. ^[10]

63 MATERIAL AND METHODS

64 The study was conducted on patients admitted in in Department of Medicine
65 Kasturba Medical College and hospital, Manipal, Karnataka during a span of 2 years
66 (2016-2107). A total of 100 diabetic Patients (diabetes diagnosed as per American
67 diabetes Association criteria) with Hypoglycemia (as per inclusion criteria) were
68 selected for the study. The detailed history, clinical examinations and relevant
69 laboratory investigations done for all the patients were evaluated and analyzed in

70 detail. (Using Accu-Chek Nano Glucose meter, Roche Diagnostics, USA, Beckman
71 Coulter Auto analyzer, USA and COBAS 6000, Auto Analyzer, Roche Diagnostics, USA).

72 **INCLUSION CRITERIA**

73 Plasma glucose ≤ 40 mg/dl

74

75 **RESULTS**

76 Out of 100 patients of diabetes (under treatment) included in study, 30 (30%)
77 patients were suffering from type 1 diabetes mellitus and 70 (70%) patients from
78 type 2 diabetes mellitus. The male:female ratio was 1:1.7. The maximum number of
79 patients (44%) were in age group of 41 to 60 years. Majority of hypoglycemic
80 patients (n=68, 68%) had blood glucose in the range 31-40 mg/dl and 26 (26%) had
81 blood glucose between 21-30 mg/dl. Only 6 (6%) patients had blood glucose <20
82 mg/dl.

83 The most common symptom was sweating (90%) followed by palpitation
84 (80%), incoordination (80%) and altered sensorium (64%). 6% of patients had
85 tremors. Hunger and speech difficulty were reported in 50% of patients. Visual
86 disturbance and headache were present in 40% of patients. 10% of patients had
87 nausea. Two patients of hypoglycemia presented with hemiplegia but it recovered
88 completely on treatment. (Figure 2)

89 The most common precipitating factor was found to be delaying or skipping
90 meals (80%), followed by decreased carbohydrate intake (70%). In 54% patients,
91 precipitating factor for hypoglycemia was increase in insulin or dose of oral
92 hypoglycemic agent. In 10% of patients, hypoglycemia was due to decrease in
93 insulin requirement due to clearance of infection, reduced renal clearance of Insulin

94 (progression to chronic kidney disease). Most of the patients had more than one
95 precipitating factor. (Figure 1)

96 Out of 100 patients, 64 (64%) were on only insulin therapy and 16 (16%)
97 patients were on oral hypoglycemic agents. 20 (20%) patients were on combination
98 (insulin+OHA) therapy. Out of 64 patients who were on insulin therapy alone, 36
99 (56.25%) were on mixture of short acting+intermediate acting insulin (i.e Premix
100 Insulin 30/70) and 18 (28.12%) patients were on short acting (regular insulin).

101 Out of 16 patients who were on oral hypoglycemic agents alone, 6 (37.5%)
102 patients were on Sulfonylureas (Glibenclamide) and other 10 (62.5%) patients were
103 on various combination of oral hypoglycemic agents. None of the patients was on
104 biguanidemonotherapy. All hypoglycemia patients recovered fully following treatment
105 without any neurological sequelae.

106

107 **DISCUSSION**

108

109 Iatrogenic hypoglycemia is the limiting factor in the glycemic management of
110 diabetes mellitus. ^[5] It causes recurrent symptomatic and sometimes (at least
111 temporarily) disabling episodes in most patients with type 1 diabetes as well as in
112 those with advanced type 2 diabetes, and is sometimes fatal.^[11] Drug induced
113 hypoglycemia occurs more frequently in older patients with underlying hepatic or
114 renal dysfunction.^[12]

115 Present study showed that 70% hypoglycemic patients had Type 2 diabetes as
116 compared to 30% patients with type 1 diabetes. In conformity with our observations,
117 Heller ^[13] has reported that risks of hypoglycemia are less in type 2 diabetes mellitus
118 patients, but are higher during insulin treatment. Hepburn et al. ^[14] in their study

found that when matched for duration of insulin therapy (mean duration 12 years) and HbA_{1c}, the frequency of severe hypoglycemia is similar in type 1 and type 2 diabetes mellitus patients. Higher incidence of hypoglycemia in type 2 diabetic patients in the present study may be due to the fact that some of these patients were admitted for surgical intervention and were temporarily put on insulin therapy as a part of pre-operative management of diabetes. The mean age of patients in this study was 57.68 years. Although, any age group is prone to hypoglycemia on treatment, however elderly patients on long acting preparations are more susceptible to hypoglycemic episodes. Independent risk factors for severe hypoglycemia include recent hospitalization, advanced age and polypharmacy.

Delaying or skipping meals was observed as the most important precipitating factor for hypoglycemia (80% of patients). Decreased carbohydrate intake as a causative factor was found in 70% of patients. These patients were eating less as compared to their regular diet during sick days or had anorexia due to their primary illness. Increase in insulin or OHA dosage to achieve good glycemic control was the precipitating cause for hypoglycemia in 54% of patients. Decrease in insulin requirement was found in 10% of patients. This decrease was due to clearance of the primary infection like treatment of diabetic foot or delayed insulin clearance due to progression to Chronic kidney disease.

Symptom profile provoked by hypoglycemia is idiosyncratic and varies in character, pattern and intensity between individuals.^[14] Symptoms of hypoglycemia vary depending on the age of the individual but the symptoms appear to be similar whether induced by sulfonylureas, insulin analogues, animal or human insulin.^[15] Although, no single symptom is present consistently during hypoglycemia in all patients with diabetes, some symptoms are more common than other.^[16] In the

present study sweating was the most common autonomic symptom (90%) followed by palpitation and inco-ordination (80%), altered sensorium (64%), tremors (60%), hunger and speech difficulty (50%), visual disturbances and headache (40%). Consistent to our results, McAulay et al ^[17] have reported similar prevalence of symptoms in their study with sweating in 80% of patients, palpitation (55%), incoordination (75%), altered sensorium (40%). Hunger and slurred speech were present in 60% and 40% of patients respectively. Visual disturbance in 20% and headache in 30% of patients. There is no single symptom that is exclusive to hypoglycemia alone. However, hypoglycemia unawareness is a major clinical problem in the management of Diabetic patients on Insulin therapy. The risk of severe episode of hypoglycemia increases 6-7 folds in these patients.^[18] Moreover, in a study by Pennebaker et al^[19] has found that no single symptom correlate significantly with a specific blood glucose concentration in humans. Hence, it is important that diabetic patient on treatment should be familiar with their own symptom profile, so that they can perceive the early onset of hypoglycemia and know what appropriate action has to be taken.

Our study showed insulin therapy was the most common cause of hypoglycemia accounting for 64% of diabetic patients. Carroll et al ^[2] also found that insulin treatment of diabetes is the most common cause of severe hypoglycemia in adults. United Kingdom Prospective Diabetes Study (UKPDS) ^[20] reported severe hypoglycaemia in 11.2% of patients treated with insulin. In the present study, the majority of hypoglycaemia cases were receiving combination of OHA's rather than monotherapy. And the most common monotherapeutic offending agent was sulfonylurea. United Kingdom Prospective Diabetes Study (UKPDS) ^[20] has reported severe hypoglycemia due to sulfonylureas in 3.3% of patients and 2.4% of

those treated with biguanides. Jennings et al.^[22] have found, that hypoglycemia in patients receiving sulfonylurea treatment vary widely but were reported to be as high as 20% over a 6 month treatment period. Shorret al.^[23] described a crude rate of serious hypoglycemia (hospitalization, emergency department admission or death) of 1.23 per 100 person-years in users of sulfonylureas aged 65 years or older.

All hypoglycemic patients recovered fully following treatment without any neurological sequelae and no mortality was seen in this study. Usually, death from cerebral edema caused by hypoglycemia is extremely rare.^[16] However, hypoglycemia had been implicated in “dead-in-bed” syndrome and in chronic cognitive impairment.^[24] Klatt et al.^[25] found 0.2% of death due to hypoglycemic coma. Macleod et al.^[26] found “dead-in-bed” syndrome may account for 6% of deaths in diabetic patients under the age of 40. Sartor^[27] reported the greatest incidence of mortality in childhood onset insulin dependent diabetes between 15-19 years of age. In our study, 100% recovery rate may be attributed to the fact that all patients had hypoglycemia in the hospital, so early detection and effective treatment was given.

CONCLUSION

Delaying or skipping meals was found to be the most common precipitating factor for hypoglycemia. Insulin treatment alone was the most common causative factor for hypoglycemia. Among sulfonylureas, glibenclamide was the most common offending agent causing hypoglycemia in elderly. Elimination of hypoglycemia from the lives of people with diabetes will likely be accomplished by new treatment methods that provide plasma glucose-regulated insulin secretion with newer treatment modalities such as automated insulin pumps and artificial/ bionic pancreas.^[21]

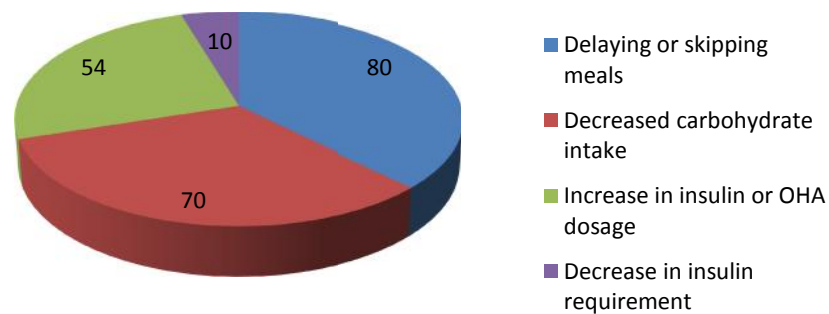


Figure 1. Precipitating factors for hypoglycemia

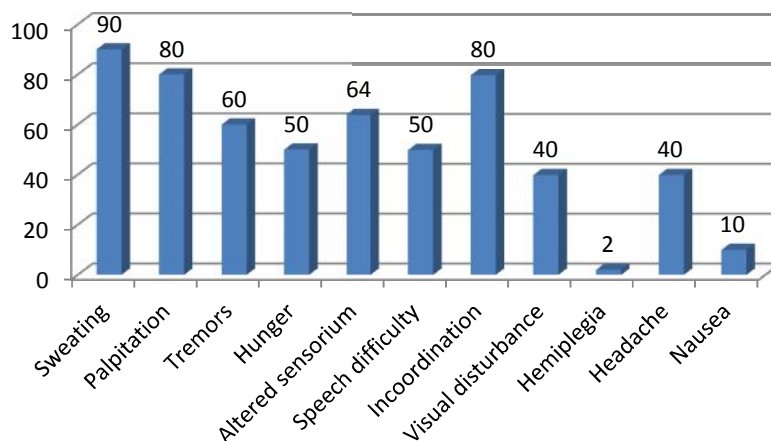


Figure 2. Symptomatology in patients with hypoglycemia (Percentage)

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