Original Article

Profile of Patients with Hypoglycemia Presenting to the Emergency Medicine Department of a Tertiary Care Hospital

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Background : Hypoglycemia is a common treatable endocrinological emergency. This study is aimed at profiling patients with Hypoglycemia presenting to the Emergency Department.

Materials and Methods : This is a prospective study aimed to know the clinical profile of patients more than 18years of age presenting with Capillary Glucose Random Blood Sugar value less than 70mg/dl from the period of September, 2018-May, 2020. Results: 123 participants were included in the study among which 69.1% of them were known Diabetes Mellitus with mean duration of 6.9 years. Using the American Diabetes Association (ADA)/ European Association for Study of Diabetes (ESAD) definitions 71.5% presented with severe Hypoglycemia. Neuroglycopenic symptoms were the most common presenting symptom among the diabetics however, autonomic symptoms were the most predominant symptom among non-diabetic population. Drug induced Hypoglycemia was the most common cause among diabetic population accounting for 43.5% and among non-diabetic group 28.9% it was probably due to food intake secondary to fasting. Modified Clarke's score of more than 4 indicated impaired awareness of Hypoglycemia.

Conclusion : Education about the prevention of hypoglycemia needs to be initiated from the Emergency Room. Spontaneous Hypoglycemia indicates impaired glucose tolerance. Development of risk stratification score helps in accurate disposition of patients from Emergency Room.

Diabetes Mellitus is the most common Metabolic Disorder which presents to the Emergency Department with life threatening emergencies and are important contributors to morbidity and mortality. Hypoglycemia is the most common diabetic emergency and is associated with adverse outcomes[1]. According to the Endocrine Society Guidelines Hypoglycemia is defined as a documented alert value of less than 70mg/dl; while the American Diabetes Association (ADA) stresses that a documented value of 54mg/dl whether symptoms are present or not, denotes clinically important Hypoglycemia[2].

The International Hypoglycemia Study Group proposed the levels of Hypoglycemia, which included level 1 is glucose alert value of 70 mg/dL or less, level 2 is glucose level of 54 mg/dL is sufficiently low to indicate serious, clinically important Hypoglycemia and level 3 being severe Hypoglycemia, as defined by the ADA denotes severe cognitive impairment requiring external assistance for recovery[3]. Hypoglycaemic coma occurs when Blood Sugar is less than 50mg/dl[4].

Spontaneous Hypoglycemia a condition referred as the occurrence of hypoglycemia without diabetes, is

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a puzzling clinical issue. Reactive Hypoglycaemia a entity of spontaneous Hypoglycemia[5] is defined as postprandial Hypoglycemia seen in non-diabetic individual[6]. But in our Indian background, Sepsis was more commonly associated with Spontaneous Hypoglycemia, however an episode of Spontaneous Hypoglycemia is indicator of Pre-diabetes state[7].

The body activates defence mechanisms against a hypoglycemic episode by hormonal counter regulation and increased behavioural response, this interplay mechanisms are compromised in advanced Diabetes Mellitus resulting in defective adreno-medullary response and defective neural and sympathetic responses which leads to unawareness of hypoglycemic symptoms. These are components of Hypoglycemia Associated Autonomic Failure (HAAF)[8]. Scoring systems namely Gold and Clarke's score are used to assess the impaired awareness of Hypoglycemia in recurrent episodes of Hypoglycemia, it is evident that high scores individuals have more

neuroglycopenic symptoms than autonomic symptoms[9].

MATERIALS AND METHODS

This is a prospective observational study using a semi -structured questionnaire done in Emergency Room of a Tertiary Care Teaching Institute in Bangalore. All patients above the age of except pregnant women, presenting with Hypoglycemia that is Random Capillary Blood Sugar value less than 70mg/dl to the Emergency department from September, 2018-May, 2020 were included.

Data and Statistical Analysis :

The results were averaged (mean ± Standard Deviation) for each parameter for continuous data the percentage for categorical data using student T test, Chi square test and multivariate logistic regression was calculated. In all the above test a "p" value of less than 0.05 was accepted as indicating statistical significance.

OBSERVATIONS

Among 123 patients included in the study,85 were already diagnosed Diabetes Mellitus among these patients 95.3% had Type 2 Diabetes Mellitus. The mean duration of Diabetes Mellitus was 6.9 years. According to the ADA/ European Association for Study of Diabetes (ESAD) definition 71.5% presented with severe Hypoglycemia (Fig 1).

The maximum number of Hypoglycemic episodes occurred among 60-69 years of age in diabetic population at 27.6% as compared to 23.7% episodes occurred among 30-39 years in non-diabetic population. The mean age of occurrence of hypoglycemic episode was 58.2±17 years.52.8% of hypoglycaemic episodes occurred in females. In 31.8% among diabetic population hypoglycemic episodes occurred in early morning hours. Among non-diabetic population 39.5% had presented with hypoglycemic episode in timeline of 12pm-6pm (Table 1).

Among the diabetic group 43.5% presented with altered sensorium,34.1% presented with both dizziness and loss of consciousness, 24.7% presented with fever, 22.4% presented with sweating and among non-diabetic population 39.5% presented with sweating, 36.8% with dizziness and 34.2% presented with altered sensorium.

Among 123 participants on comparing the onset of symptoms with different ranges of Glucose Random Blood Sugar (GRBS) values 54.1% presented with altered sensorium within
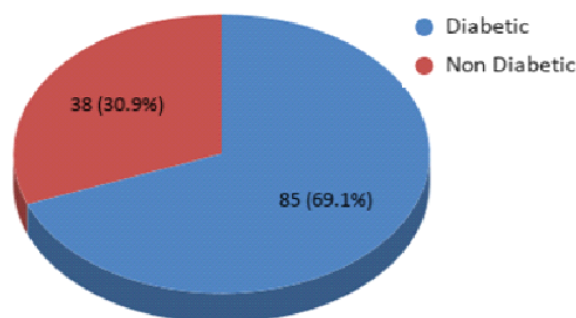

Fig 1 — Distribution of Diabetic Status among Hypoglycemia

GRBS range of 20-30mg/dl. Autonomic symptoms were the presenting symptom in patients with GRBS more than 30 mg/dl.

Most common cause for a hypoglycemic episode among the diabetic was drug induced Hypoglycaemia out of which 32.5% occurred in Oral Hypoglycemic Agents (OHA) users and 20.3% occurred in both oral hypoglycemic and insulin users. It was evident that sulphonylureas and insulin mixtard were the common offending agents. Among the non-diabetic group 28.9% hypoglycemic episodes were due to inadequate food intake, followed by Liver Cell Failure at 18.4%. Sepsis accounted for 15.8% cases of hypoglycemia, among the focus of Sepsis, Urosepsis ranked first followed by Pneumonia which included the COVID 19 infection also (Table 2).

Among the 85, who had already existing Diabetes Mellitus, 33% had a hypoglycemic episode in the past 12 months and all had Modified Clarke's score of more than 4. The association between onset of Hypoglycemia and Modified Clarke's scoring was significant.

Among 123 patients 60% were admitted ,44.7% were discharged against medical advice. Among non-diabetic population 28.9% went discharge against medical advice. Died in Emergency Room was 2.6% among non-diabetics.

Table 1 — Demographic Characteristics								
Parameter		Diabetic (N=85)		Non-diabetic (N=35)		Total (N=123)		P value
		N	%	N	%	N	%	
AGE	20-29 years	4	4.7%	6	15.8%	10	8.1%	<0.001
	30-39 years	0	0.0%	9	23.7%	9	7.3%	
	40-49 years	6	7.1	8	21.1	14	11.4	
	50-59 years	16	18.8	4	10.5	20	16.3	
	60-69 years	28	32.9	6	15.8	34	27.6	
	70-79 years	21	24.7	4	10.5	25	20.3	
	80-89 years	10	11.8	1	2.6	11	8.9	
Gender	Male	43	50.6	15	39.5	58	47.2	0.254
	Female	42	49.4	23	60.5	65	52.8	

Table 2 — *Percentage of Causes of Hypoglycemia*							
Causes	Diabetic (N=85)		Non-diabetic (N=38)		Total (N=123)		P value
	N	%	N	%	N	%	
Inadequate Food Intake	14	16.5%	11	28.9%	25	20.3%	0.112
Sepsis	29	34.1%	6	15.8%	35	28.5%	0.037
Liver Cell Failure	0	0.0%	7	18.4%	7	5.7%	<0.001
Drug Induced (OHA/Insulin)	37	43.5%	1	2.6%	38	30.9%	<0.001
Alcohol Intoxication	1	1.2%	5	13.2%	6	4.9%	0.004
Other Causes							
Carcinoma							
Duodenum	0	0.0%	2	5.2%	1	1.6%	0.001
Idiopathic	0	0.0%	5	13.2%	5	4.1%	
Insulinoma	0	0.0%	1	2.6%	1	0.8%	

DISCUSSION

In our study Hypoglycemia was more common in known diabetics than non-diabetic population which is attributed to the fact that most of the patients were on medications for Diabetes Mellitus.

The prevalence of Type 2 Diabetes Mellitus is more than Type 1 Diabetes Mellitus and this was evidenced by the fact that 95.3% were diagnosed Type 2 Diabetes Mellitus and 4.7% were Type 1 Diabetes Mellitus.This was consistent with a retrospective study done by Jordi Caballero, *et al* at Hospital Universitario de Bellvitge in Emergency Room 81.9% episodes occurred in type 2 diabetic and 16.1% occurred in Type 1 Diabetic[10].

Many studies on Hypoglycemia used the study definition of Hypoglycemia as Glucose Random Blood Sugar (GRBS) <40mg/dl. Hence our data of level 2 Hypoglycemia according to International Hypoglycemia Group classification being the most common at 71.5% was inconsistent (Fig 2).

27.6% of total hypoglycemic episodes occurred in the elderly age group of 60-69 years however, among non-diabetics 23.7% episodes occurred in a young age group of 30-39 years. These findings were almost consistent with a study done by Ohenhen Oluwatoyin Abisoye, *et al* at a Tertiary Health Institution at Nigeria in which among diabetics 38% episodes occurred in 55-64 years of age and 31% occurred in 65-74 years of age[11].

Among non-diabetic group there were 27 episodes in less than 60 years of age which is consistent with findings done by Krishnaraj, *et al* in 2010 in which total 108 participants, 61 episodes occurred in less than 65 years of age[12].

In our study the mean age among diabetic group was 63.9 years which was similar with study done by Satish, *et al* on clinical profile of Hypoglycemia in which the mean age of patients ranged from 61.6 years[13]. The mean age among non-diabetic population was 46.1 years. This was comparable with the finding done by Santra, *et al* in which the mean duration among non-diabetics is 42.84 years[14].

52.8% participants were female, however among diabetic group the gender distribution was approximately equal among both genders. In our study among non-diabetes 60.5% were females, which was similar to a study done by Ekpebegh et al among 26 non-diabetic patients out of which 65.4% were females[15].

31.8% participants among known Diabetics Mellitus,had an episode during early morning hours which was in conformity with a study done by Ohenhen Oluwatoyin Abisoye, *et al* among diabetic patients, 51.7% had hypoglycemic episodes in the early morning hours[11]. In our study among the 38 non-diabetics, 39.5% had a hypoglycemic event in noon hours. This is a new finding as no much studies had been done on the time of presentation of non-diabetic hypoglycemia which needs further studies.
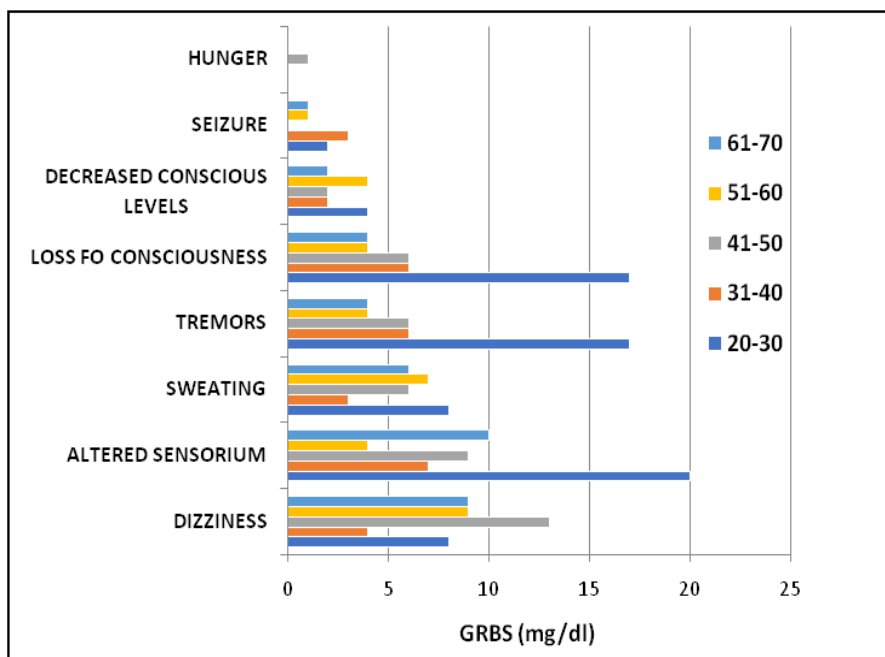

Fig 2 — Association of GRBS with Symptoms of Hypoglycemia

The mean GRBS value among diabetic was 39.7 mg/dl, this value was similar with the study conducted by Satish et al in which the mean GRBS was 37.12 mg/dl[13].

40.7% patients presented with altered sensorium which indicates that neuroglycopenic symptoms are the most common presenting symptoms of Hypoglycemia which was consistent with study done by Kumar, *et al* in which 59.3% presented with decreased conscious levels[2].

Among 123 participants on comparing the onset of symptoms with different ranges of GRBS values 54.1% presented with a neuroglycopenic symptom, altered sensorium within range of 20-30mg/dl. However autonomic symptoms such as sweating were common in patients with GRBS value >30mg/dl. This implies the importance of counter regulatory hormones in the pathophysiology of Hypoglycemia, which helps to counsel the patients regarding various symptoms onset.

Another than Diabetes Mellitus, among 51% systemic Hypertension was associated comorbidity, which was similar to the study done by Caballero et al who found in 73.3% systemic hypertension was the most associated comorbidity[10].

Among the non-diabetic population malignancy was the most common underlying comorbid conditions. However, in the studies done on non-diabetic Hypoglycaemia, have emphasized on the fact that Hypoglycemia can present as undiagnosed malignancy.

Among non-diabetic group autonomic symptom such as sweating were common at 39.5%. This finding in conformity with a study done Gharbi, *et al* among 40 non-diabetic patients, 82.5% presented with autonomic symptoms[16].

In our study among 123 participants,30.9% had a hypoglycemic event secondary to anti-diabetic medication, this finding is consistent with the study done by Kumar, *et al* among 320 diabetics out of which 59.81% were diagnosed drug-induced hypoglycemia[2].

Among the drug-induced Hypoglycemia 32.5% were OHA user's, followed by 20.3% were on OHA's and insulin, this was consistent with the study done by Ohenhen Oluwatoyin Abisoye, *et al* 60.7% were on OHA drugs and 32.6% were both OHA plus insulin users[12]. Among OHA user's 39% occurred among the diabetics who were on monotherapy, out of which 14.6% were on sulphonylureas closely followed by 13.8% on biguanides which was similar to the study conducted by Eren, *et al* among 225 patients,64 subjects were using oral hypoglycemic drugs out of which 43 were on sulphonylureas[17].

In our study among the non-diabetic group 28.9% of hypoglycemic event was due to inadequate food intake due to fasting among 32% of participants followed by Liver Cell Failure. This was inconsistent with the study done by Ekbepegh, *et al* in which the main cause for Hypoglycemia was hypercortisolism attributed to underlying retroviral status of the patient[15].

In our study by correlating the most common time of presentation of Hypoglycemia being the noon hours and the most common cause being inadequate food intake secondary to fasting the possibility of underlying impaired glucose tolerance among non-diabetic group was found. This is a new finding and further studies are needed regrading Hypoglycemia among non-diabetic population.

In this study among 28.5% the cause of hypoglycemic event was sepsis, out of which 34.1% was in the diabetic group which is inconsistent to the fact that infections are the most common cause for Hypoglycaemia among non-diabetes[12]. This can be due to a smaller number of non-diabetic patients were included in this study. However, considering the focus of Sepsis 32.4% was diagnosed urosepsis, which is consistent with the study done by Indu, *et al* in which among the 10 patients diagnosed Hypoglycemia secondary to infection most common was urosepsis diagnosed in three patients[18]. Also among the causes of sepsis 5.9% had hypoglycemic event due to COVID-19 during the pandemic.

38.5% of them had a previous episode of Hypoglycemia among the 85 already diagnosed Diabetes Mellitus in past 12 months and all had a Modified Clarke's score of more than four indicating that there was impaired awareness of hypoglycemic symptoms and thus this episode is a recurrence of Hypoglycemia. This was correlating with study done by Geddes, *et al* showed strong association between Modified Clarke's score and impaired awareness thus recurrent Hypoglycemia[9].

In 55.3% patients the outcome from Emergency Room was admission for further management It was also noted that in non-diabetic group discharged against medical advice was most common outcome. There were two deaths,with sepsis accounting for 1.6%. This is consistent with the study done by Makoto, *et al* among patients with Sepsis had increased mortality among hypoglycemic group[19].

Limitations :

- It is a single center study.
- Difficulty in taking history from the patient himself, more reliability on the attender's history which

can be a source for information bias.

• Among the non-diabetic with hypoglycemia most of them went discharge against medical advice which attributes to missing out the etiology.

CONCLUSION

71.5% presented at level 2 Hypoglycemia and above, but considering the non-diabetics level 1 Hypoglycemia was the commonest. Neuroglycopenic symptoms occurred in Capillary Blood Sugar levels of 20-40 mg/dl while autonomic symptoms were the presenting symptom above 30mg/dl. Sulphonylurea induced hypoglycemia was the most common cause for hypoglycemia among the diabetics. In the non-diabetic group, it was evident that more hypoglycemic episodes occurred during noon hours which raise the concern for pre-existing impaired glucose tolerance. Hypoglycemia among the non-diabetic population needs further studies. Hypoglycemia was also the presentation for COVID-19 in diabetic population. The Modified Clarke's scoring system evaluated in patients proved that a score of more than 4, indicates impaired awareness and recurrent Hypoglycaemia. The overall death was 2.6% in Emergency Room due to Multiorgan Failure due to Sepsis.

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