www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v4i12.66

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Study of 100 Cases of Hypoglycaemia in Elderly Patients of Diabetes Mellitus

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ABSTRACT
Demographic ageing is a global phenomenon. The average life expectancy and the prevalence of diabetes are continuing to rise. Amongst the elderly population, type 2 diabetes mellitus is a growing problem, and a larger proportion of newly diagnosed diabetics are older. As the prevalence of diabetes mellitus increases and as treatment guidelines call for more rigorous glycaemic control, rates of hypoglcaemia are on the rise. Hypoglycaemia is often a risk of diabetes treatment in the elderly. Hypoglycaemia has serious consequences in terms of mortality and morbidity. Globally diabetes mellitus affects 10-20% of the elderly in the age group of 65-74 years & about 40% of the elderly over the age of 80 years. Type 2 DM is characterized by impaired insulin secretion, insulin resistance, excessive hepatic glucose production, and abnormal fat metabolism. Lifestyle factors such as individuals who are obese, who consume diets that are high in saturated fat and low in complex carbohydrates, or are inactive are more likely to develop diabetes as they age. Functional status of the study patients was assessed by using Katz index of activities of daily living. The altered counter regulatory effect may contribute to the altered cognitive response to reductions in blood glucose. Thus, the lower glycemic threshold to Hypoglycaemia in older people may limit the time available to self-treat and thereby increase the risk of developing neuroglycopenia. Additionally, these neurological symptoms of Hypoglycaemia may be misinterpreted in older patients because of coexisting illnesses, such as cerebrovascular diseases or dementia.
Keywords: *Hypoglycemia, elderly, counteregulator hormones, neuroglycopenia.*

INTRODUCTION

Objective of this study is

1. To study the risk factors predisposing to hypoglycaemia in elderly subjects with diabetes mellitus.
2. To identify symptoms occurring during the hypoglycaemic episode.
3. To study the outcome of hypoglycaemia in these patients.

MATERIALS AND METHODS

This study is a case control study conducted in the medical wards of Government general Hospital, Siddhartha Medical College Vijayawada

Inclusion Criteria

1) Age ≥60 years
2) Known case of diabetes mellitus
3) Blood sugar of < 60mg/dl. This included patients who are were admitted with hypoglycaemia and who developed hypoglycaemia in hospital.

Controls

Age and sex matched diabetic patients ≥60 years admitted during the same period.

Number of patients:

No of cases: 50

No of controls: 50

Method of collection of data:

All patients who fulfilled the inclusion criteria were enrolled in the study after taking valid informed consent. Data was filled in according to the proforma. Proforma included details such as age, demographic details, education level, duration of diabetes mellitus, details of treatment of diabetes at the time of hypoglycaemia, details of the hypoglycaemic episode (symptoms, severity, glucose level, risk factors identified, treatment and outcome), comorbidities, polypharmacy, alcohol use and assessment of functional status. Assessment of the functional status was done using Katz score. Data was also collected for the control group which consisted of elderly diabetics who did not develop hypoglycaemia during their hospital stay.

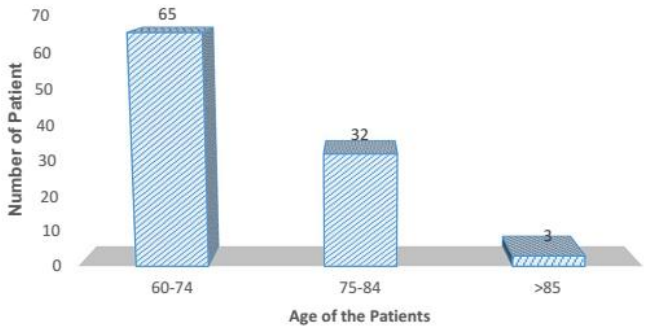
Statistical Analysis

Statistical analysis was conducted using SPSS package and epi info software.

Unpaired 2 tailed t tests were used to compare means between study and control groups and chi square analysis to compare frequency of events between groups. We performed univariate and multivariate logistic regression to determine clinical predictors of hypoglycaemia.

RESULTS

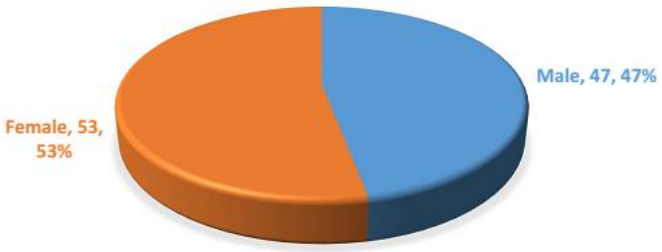
100 diabetic patients diagnosed to have Hypoglycaemia & 100 age & sex matched control diabetic patients without Hypoglycaemia were studied. Study patients included both patients admitted for a hypoglycemic episode as well as those that developed Hypoglycaemia after admission for an inter current problem.



	Mean Age (In Years)	Age Range (In Years)	SD
Age	70.48	65-87	7.801

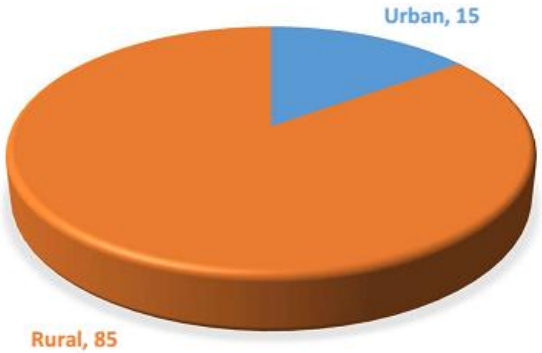
Majority of the patients belonged the Young-old category (60- 74 yrs)

SEX DISTRIBUTION OF STUDY GROUP



Gender	Number of Patients	Percentage
Female	53	53%
Male	47	47%
Total	100	100%

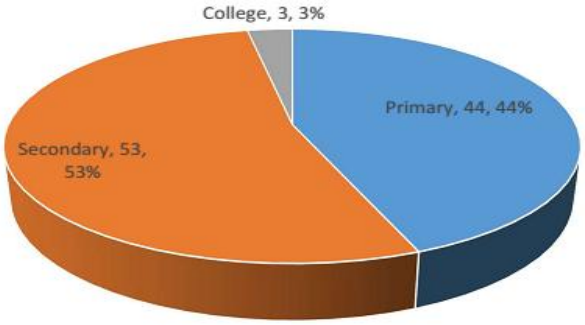
RESIDENCE OF STUDY PATIENTS



Gender	Number of Patients	Percentage
Rural	85	85%
Urban	15	15%
Total	100	100%

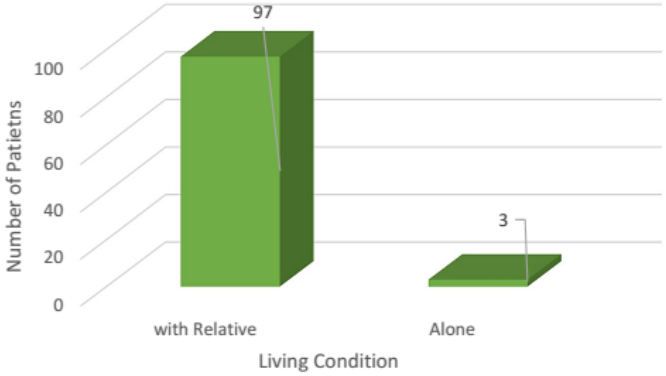
Majority of study patients reside in rural areas 85%

EDUCATIONAL STATUS OF STUDY GROUP:



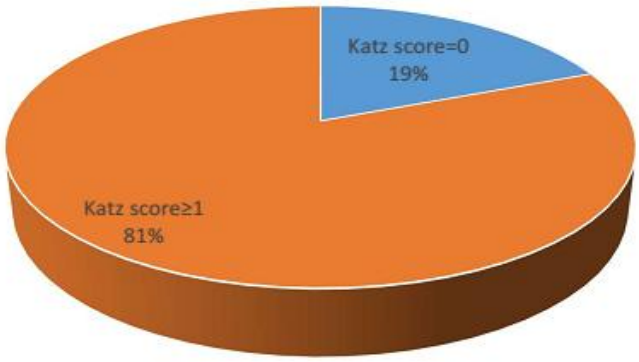
Education	Number of Patients	Percentage
Primary	44	44%
Secondary	53	53%
College	3	3%
Total	100	100%

LIVING CONDITION OF STUDY PATIENTS



97% of patients are living with relatives or spouse & 3% of patients are living alone.

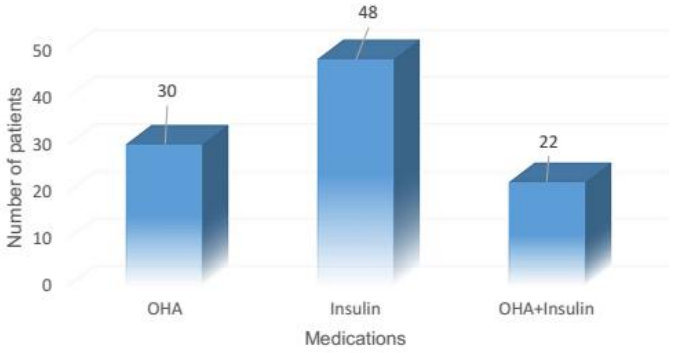
FUNCTIONAL STATUS OF STUDY PATIENTS

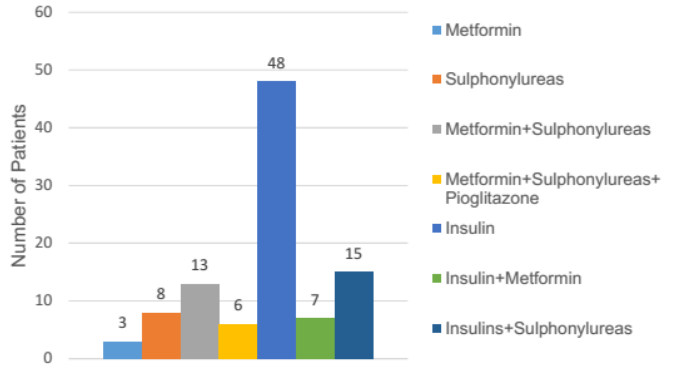


Functional Status	Number of Patients	Percentage
Katz score=0	64	64%
Katz score≥1	36	36%
Total	100	100%

Functional status of the study patients was assessed by using Katz index of activities of daily living. In this study 64 patients out of 100 had a Katz score of 0, meaning that they had to depend on caregivers for all the activities of daily living.

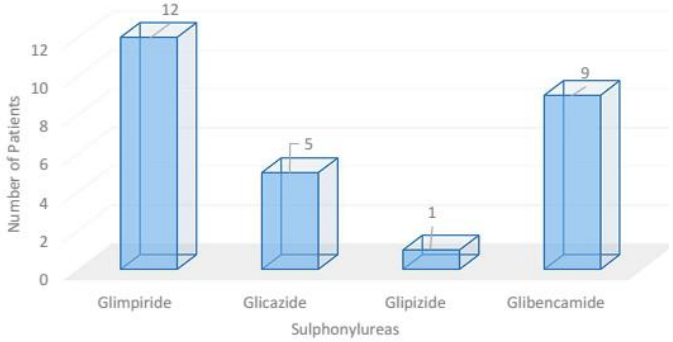
ANTI DIABETIC MEDICATIONS OF STUDY GROUP





30% of the study patients were on OHA, 48% were on insulin and the remaining were on a combination of OHA and insulin.

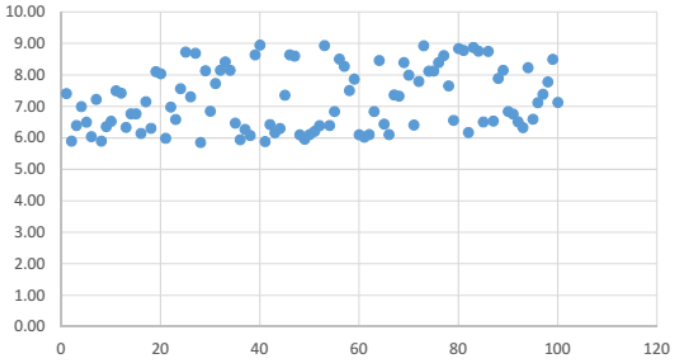
Use of sulphonylureas in study patients



Sulphonylurea	Number of Patients	Percentage
Glimpiride	12	44%
Glicazide	5	19%
Glipizide	1	4%
Glibencamide	9	33%
Total	27	100%

27 out of 100 study population using sulphonylureas. Glimipiride is used by 12 patients and Glibencamide is used by 9 patients.

HbA1c of the study patients



HbA1C	Study group	
<6.0	33	33%
6.1-6.9	35	35%
7.0-7.9	16	16%
8.0-8.9	16	16%
9.0-9.9	0	0%
>10	0	0%
	100	100%

68 % of the study patients had an HbA1c < 7.

RESULTS OF THE HYPOGLYCEMIC EPISODE

Out of the 100 study patients, 53 patients were admitted for hypoglycaemia and 47 patients developed hypoglycaemia during hospital stay. 93 patients had only single episode of documented hypoglycaemia, whereas 13 patients had more than one episode of hypoglycaemia. Blood sugar level of patients during hypoglycaemia

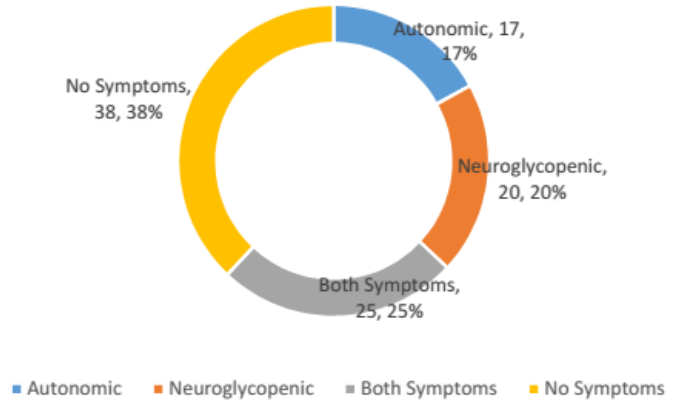
	Mean	Range	SD
Blood Sugar (mg/dl)	46.5	23-67	10.581

Time of occurance of hypoglycaemia in study group

Time of day	Number of patients	Percentage
08.01-12.00 hrs	5	5%
12.01-16.00 hrs	7	7%
16.01-20.00 hrs	20	20%
20.01-00.00hrs	20	20%
00.01-04.00hrs	32	32%
04.01-08.00hrs	16	16%
Total	100	100%

20% of the patients developed hypoglycaemia in the evening and 22% had nocturnal hypoglycaemia (20.00hrs – 8.00 hrs) and 32% developed in early morning.

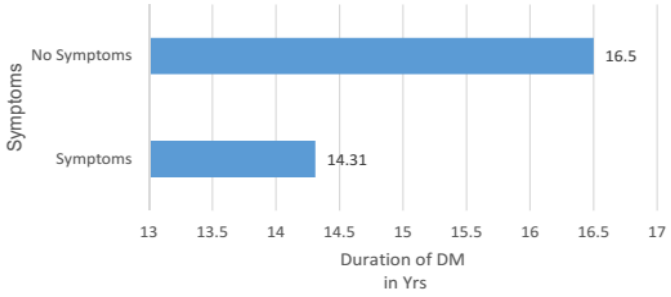
Symptoms of hypoglycaemia in study patients



Symptoms of hypoglycaemia in elderly diabetics

Symptoms	Number of patients	Percentage
Autonomic	17	17%
Neuroglycopenic	20	20%
Both Symptoms	25	25%
No Symptoms	38	38%
Total	100	100%

Duration of Diabetes mellitus and hypoglycemic unawareness



Duration of diabetes and hypoglycaemic unawareness

	Nos	Mean Duration of DM in years	SD	p value	95% CI
Asymptomatic	38	16.5	7.951	0.023	5.276-12.715
Symptomatic	62	14.31	4.721		

In this study, the mean duration of diabetes mellitus was more in the asymptomatic patients rather than in patients with symptoms of hypoglycaemia. This was found to be statistically significant. (p = 0.023)

Treatment given for Hypoglycaemia

Treatment	No of Patients
Venous dextrose	95
Oral Sugars	3
Only change in dose of medication	2

Majority were given intravenous dextrose

Presentation and clinical features:

One half of older patients with diabetes are unaware they have the illness, suggesting that symptoms of hyperglycaemia are rarely present in this patient population. This may be because the renal threshold for glucose increases with age so that no sugar is spilled into urine until the glucose level is markedly elevated. In addition, because thirst is impaired with normal aging, polydipsia is unlikely in elderly patients with diabetes even if they are hyperosmolar as a result of marked hyperglycaemia. If symptoms do occur, they are nonspecific, like confusion, failure to thrive, incontinence etc. Often, diabetes presents for the first time in an elderly patient who is hospitalized with a complication that may be related to diabetes, such as a myocardial infarction or a stroke. In frail elderly nursing home patients, non ketotic hyperosmolar coma may be the first sign of diabetes.

Pathophysiology of hypoglycaemia

Normal physiological response to Hypoglycaemia. The brain depends on a continual supply of glucose and is vulnerable to any glucose deprivation. Unable to synthesize or store this primary source of energy, the brain is one of the first organs affected by lowered blood glucose levels. Once plasma glucose concentrations fall below the physiological range at a glycemic threshold of ~70 mg/dl, a sequence of responses is activated that includes release of neuroendocrine hormones (also called counter regulatory or anti-insulin hormones), stimulation of the autonomic nervous system (ANS), and production of neurogenic and neuro glycopenic symptoms to protect the brain and limit systemic effects of hypoglycaemia.

The normal physiological counter regulatory response to Hypoglycaemia consists of suppression of insulin release and secretion of glucagon and pancreatic polypeptide from the pancreas, epinephrine from the adrenal medullae, norepinephrine from sympathetic postganglionic nerve terminals and adrenal medulla, cortisol from the adrenal cortex, and growth hormone from the anterior pituitary gland. In humans, inhibition of insulin secretion is the initial defence against falling glucose and occurs at a plasma glucose concentration of 80 – 85 mg/dl. Glucagon and epinephrine are the primary fast-acting hormones in the defense against acute Hypoglycaemia. Glucagon acts to increase endogenous glucose production and does so via increases in hepatic glycogenolysis and gluconeogenesis, providing three carbon glucose substrates (lactate, pyruvate, alanine and glycerol). Epinephrine can also acutely increase endogenous glucose production. Epinephrine has effects similar to glucagon on hepatic glucose production but can also stimulate net renal glucose production. Additionally, epinephrine has an important physiological function in reducing insulin-stimulated glucose uptake. During the prolonged Hypoglycaemia that is usually observed in clinical practice, it is the reduced glucose uptake in peripheral tissues that contributes most to the preservation of circulating glucose levels and hence the defense against Hypoglycaemia. Activation of the sympathetic nervous system (via both circulating catecholamines and direct innervation) results in increased lipolysis in adipocytes. The increased release of free fatty acids (FFAs) results in significant glucose sparing (because tissues can oxidize FFAs instead of glucose). In fact, the contribution of FFAs has been estimated to be 25% of the total defense against hypoglycaemia.

Growth hormone and cortisol play a modest role in the metabolic defense against acute Hypoglycaemia but become more important during prolonged Hypoglycaemia. In fact, the counterregulatory actions of growth hormone and cortisol on increasing glucose production and restraining glucose disposal do not become evident until 4 hours after the onset of Hypoglycaemia. Even so, their counterregulatory actions are only 20% compared to that of epinephrine.

Counterregulatory Hormone Responses to Hypoglycaemia in Older Adults

Meneilly et al. have investigated the effects of age on counterregulatory responses during clamped Hypoglycaemia. Older adults with type 2 diabetes demonstrated reduced glucagon and growth hormone responses but increased epinephrine and cortisol responses when compared to age matched nondiabetic control subjects. However, hypoglycaemic symptom scores were similar in both groups at all levels of glycemia. Matyka et al. 25 on the other hand, found differences in hypoglycemic symptom responses when comparing healthy older men aged 60–70 years with younger men aged 22–26 years. During hyperinsulinemic-hypoglycemic clamp studies, neuroendocrine responses subjects and to a greater degree. The usual 10–20 mg/dl plasma glucose difference between the subjective awareness of Hypoglycaemia and the onset of cognitive dysfunction was lost in the older men. This altered counterregulatory effect may contribute to the altered cognitive response to reductions in blood glucose. Thus, the lower glycemic threshold to Hypoglycaemia in older people may limit the time available to self-treat and thereby increase the risk of developing incapacitating neuroglycopenia. Additionally, these neurological symptoms of Hypoglycaemia may be misinterpreted in older patients because of coexisting illnesses, such as cerebrovascular diseases or dementia.

***Definition of hypoglycaemia in elderly*:**

There is no consensus definition of hypoglycaemia in diabetes, and a variety of criteria have been used to define hypoglycaemic events. An early, very practical, definition of hypoglycaemia was the presence of Whipple's triad: decreased plasma glucose concentration, symptoms compatible with hypoglycaemia and rapid attenuation of those symptoms by correction of the low glucose. With the recognition of hypoglycaemia occurring without subjective awareness, this definition requires the addition of 'and signs' to the 'symptoms' of item two, but otherwise remains relevant to current practice. More recent definitions have been provided by the American diabetic association and the Canadian diabetic association. These groups have attempted to define the clinical severity of hypoglycaemia, classify the event according to the presence or absence of a plasma glucose test and identify a threshold level for plasma glucose at which hypoglycaemia is diagnosed. Each group has defined a different level for this threshold, ranging from < 3.9mmol/l down to< 3.0 mmol/l. This lack of consensus makes it difficult to compare studies or quantify the frequency of hypoglycaemia in Type 2 diabetes.

***Canadian Diabetic Association* has defined hypoglycaemia as:**

1) the development of autonomic or neuroglycopenic symptoms
2) a low plasma glucose (PG) level (the Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada propose 4.0 mmol/L as an operational clinical cutoff for patients treated with insulin or an insulin secretagogue)
3) symptoms responding to the administration of carbohydrate.

The ADA Workgroup definition describes a classification of hypoglycemic events based on the above considerations.

A hypoglycemic episode could be:

1) Severe Hypoglycaemia: An event requiring assistance of another person to actively administer carbohydrate, glucagons, or other resuscitative actions. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration.

2) Documented symptomatic hypoglycaemia. An event during which typical symptoms of Hypoglycaemia are accompanied by a measured plasma glucose concentration <70 mg/dl (3.9 mmol/l).

3) Asymptomatic Hypoglycaemia: An event not accompanied by typical symptoms of Hypoglycaemia but with a measured plasma glucose concentration <70mg/dl (3.9 mmol/l). Since the glycemic threshold for activation of glucagon and epinephrine secretion as glucose levels decline is normally 65–70 mg/dl (3.6 – 3.9mmol/l) and since antecedent plasma glucose concentrations of <70 mg/dl (3.9 mmol/l) reduce Sympathoadrenal responses to subsequent Hypoglycaemia this criterion sets the lower limit for the variation in plasma glucose in non diabetic, non pregnant individuals as the conservative lower limit for individuals with diabetes.

4) Probable symptomatic Hypoglycaemia. An event during which symptoms of Hypoglycaemia are not accompanied by a plasma glucose determination- (but that was presumably caused by a plasma glucose concentration <70 mg/dl [3.9 mmol/l]). Since many people with diabetes choose to treat symptoms with oral carbohydrate without a test of plasma glucose, it is important to recognize these events as "probable" Hypoglycaemia. Such selfreported episodes that are not confirmed by a contemporaneous low plasma glucose determination may not be suitable outcome measures for clinical studies that are aimed at evaluating therapy, but they should be reported.

5) Relative Hypoglycaemia: An event during which the person with diabetes reports any of the typical symptoms of Hypoglycaemia, and interprets those as indicative of Hypoglycaemia, but with a measure plasma glucose concentration >70 mg/dl (3.9 mmol/l). This category reflects the fact that patients with chronically poor glycemic control can experience symptoms of Hypoglycaemia at plasma glucose levels >70 mg/dl (3.9 mmol/l) as plasma glucose concentrations decline toward that level.

The lack of consensus regarding definitions makes it difficult to compare rates of hypoglycaemia across studies.

CONCLUSIONS

Hundred cases of elderly diabetic patients with hypoglycaemia & 100 age & sex matched controls were studied for risk factors for hypoglycaemia, symptoms of hypoglycaemia & the outcome. Sixty five percent were in the young old category (60 – 75 years), thirty two percent were in the old old category (75-85) and three percent were in the oldest old category (> 85). Forty seven percent of the patients presented to the hospital with hypoglycaemia whereas fifty eight percent of the patients developed hypoglycaemia in the hospital during their admission for an intercurrent problem. The mean duration of diabetes was longer in the study group (15.14years) than in the control group (10.06 years), though the difference did not reach statistical significance (p = 0.062). The commonest risk factors for developing Hypoglycaemia in our study patients was infection (63%), nutritional discordance (61%), recent change in the dose of medications (50%), polypharmacy (41%), and HbA1c < 6.5 (33%). BMI were significantly lower in the study group than in the control group (p = 0.035). Asymptomatic hypoglycaemia was common in the elderly diabetics. Over one third of the patients in the study group (38%) had no symptoms. In symptomatic patients, neuroglycopenic symptoms were more commonly encountered than autonomic symptoms.

The mean duration of diabetes mellitus was longer in the group of study patients with no symptoms of hypoglycaemia as compared to patients who were symptomatic for hypoglycaemia. Infection was found to be a significant precipitating factor for hypoglycaemia (p =0.007) using multiple logistic regression. Poor functional status was another significant risk factor for hypoglycaemia (p = 0.02) in our patients. Renal failure was found to be a significant precipitating factor for hypoglycaemia on univariate analysis (p = 0.03),

though this was not confirmed on multivariate analysis. Hypoglycaemia was found in patients taking OHA alone, insulin alone and both OHA and insulin. The mode of treatment was not a significant risk factor for hypoglycaemia. Ninty five percent of the patients were treated with intravenous dextrose. This was probably due to the fact that the patients were in the hospital & cannot be interpreted as a requirement. All our patients recovered without any sequelae.

DISCUSSION

This study was designed to study the risk factors, symptoms and outcome of hypoglycaemia in elderly diabetics and compare these patients with age and sex matched diabetic controls who did not develop hypoglycaemia. It was a case-control study which was conducted on 100 patients and 100 controls both were admitted to Government General Hospital, Siddhartha Medical College, Vijayawada.

Demographic details of study patients.

The elderly are classified as young old (60-75 years), old (75-85 years) and oldest old (>85 years). In our study, there were more young old than old old or oldest old. This could be due to the life expectancy in Indians, 62.6 years for males & 64.2 years for females. The risk of hypoglycaemia increases exponentially with age.18 However, this could not be assessed in this study as majority of the patients belonged to the young old group. Many studies have shown that hypoglycaemia is more common in women. In a study done in elderly diabetics in Changi hospital, Singapore, out of 45 cases of hypoglycaemia, 32 were females and 13 were males . Christopher et al, in his study, also showed that females had a higher incidence of hypoglycaemia (71.8% were females).Our study also have more female study population (53%).

Majority of patients coming from rural areas in the study population. Siddhartha Medical College is located in even though located in an urban area., it is a tertiary care institution which draws patients from rural areas of Krishna district. This could explain the majority patient load is from rural areas. In 2007 -2008 the NSSO survey showed that only 50 % of Indian men and 20% of Indian women above 60 years were literate. However in this study, all the patients were literate, with a majority having had primary school education. Elderly who stay alone are more susceptible to severe hypoglycaemia due to various reasons and medication intake may be erratic. There may be none to notice the early symptoms or signs of hypoglycaemia and give them timely help. Our study could not assess this as all of our study patients & most of our controls were staying with their spouse or another relative. Only 3 patients were living alone.

Symptoms of hypoglycaemia

In our study, out of the 100 patients who had hypoglycaemia, thirty eight percent (38%) were asymptomatic, twenty percent (20%) had neuroglycopenic symptoms, seventeen percent, (17%) had autonomic symptoms and Twenty five (25%) percent had both neuroglycopenic and autonomic symptoms. Hence our study showed that *more than one third of our elderly diabetics were asymptomatic during the hypoglycaemic episodes*. Also in our study neuroglycopenic symptoms were more frequent than autonomic symptoms. In a study done in Singapore, out of the 45 episodes of hypoglycaemia in elderly diabetics, all of whom were symptomatic, 40 patients presented with neuroglycopenic symptoms and only 5 patients presented with autonomic symptoms. This is probably due to impaired cognition, reduced autonomic response and reduced adrenergic sensitivity causing hypoglycaemic unawareness. Patients with a longer duration of diabetes are known to have asymptomatic hypoglycaemic episodes due to defect in counter regulatory hormones. In the UKPDS, almost 50% of patients experiencing hypoglycaemia without warning symptoms had diabetes mellitus for 25 years or more. In our study, the mean duration of diabetes mellitus was 16.5 years in the asymptomatic patients as compared to symptomatic patients who had

diabetes for an average of 14.31 years. This was statistically significant (p = 0.023). This study supports the hypothesis that a longer duration of diabetes mellitus is more likely to be associated with 60 asymptomatic hypoglycaemi. This is probably due to diminishing counter regulatory responses with increasing duration of diabetes.

Hypoglycaemic episode

Hypoglycaemia can be classified into mild or severe. Mild Hypoglycaemia is defined as patient report of typical symptoms of Hypoglycaemia that is relieved by eating or patient report of home glucose monitoring values of less than 70 mg/dl, and severe Hypoglycaemia is defined as loss of consciousness or other major alteration of mental status caused by Hypoglycaemia that requires the assistance of another person to treat the condition. The mean blood glucose during the hypoglycaemic episodes among study patients was 46.5 mg/dl with lowest random blood sugar value noted is 23 mg/dl and highest recorded blood sugar value is 67 mg/dl. Ninty five percent (95%) of the hypoglycaemic patients received intravenous dextrose correction and only 2 % had reduction of the dose of anti diabetic medications alone. Thirty eight (38%) percent of the patients in this study had asymptomatic hypoglycaemic episodes, but the majority was treated with parenteral dextrose. This discrepancy is probably because the study has been done in a hospital where sugar monitoring is intense & parenteral dextrose is started as an immediate response to the same. The time at which patient develops hypoglycaemia depends on the pharmacokinetics of the hypoglycaemic agent in use in addition to other factors such as meal composition and timings and time of taking of medications. In this study 16 out of 100 patients (32%) developed hypoglycaemia in the early morning hours (between midnight 12 am and 4.00am). Nocturnal hypoglycaemia (between 8 pm and 8 am) was documented in 68 patients (68%) with most patients developing early morning hypoglycaemia (32%). In literature, various studies have documented different times of day during which hypoglycaemia occurs based on the anti diabetic medication in use were asymptomatic biochemical Hypoglycaemia (Glucometer blood sugar value < 60 mg/dl). The numbers studied were too small to evaluate the causes for these findings, the evening hypoglycemic episodes are probably due to long gap between lunch, supper, and poor living conditions and skipping of meals by patients for various reasons including spiritual reasons. The nocturnal Hypoglycaemia due to meal timings & inappropriate nocturnal dosages of medications. However physicians should be aware of this so that appropriate medications are prescribed & the patients counseled regarding this so that they can take appropriate precautions. Previous hypoglycaemia is a strong predictor for recurrence. In a previous study 40% of the patients had suffered previous hypoglycaemic episodes, 87 whereas in our study this was documented in 35 % of the patients but out of the 35 patients only 7 patients seeked medical care during the episode. The reason could be asymptomatic hypoglycaemia noted in some cases.

Risk factors for hypoglycaemia

Risk factors for the development of hypoglycaemia in elderly diabetics are well documented in literature. These risk factors include HbA1c < 6.5, multiple comorbidities, infection, nutritional discordance, hepatic failure, renal failure, polypharmacy, alcohol, drugs such as nonselective beta blockers and poor functional status. All these risk factors were identified in our study patients. The immediate factors that precipitated hypoglycaemia in our study patients were recent increase in insulin dosage, nutritional discordance, infection, renal failure and hepatic failure. Most patients had more than one precipitating factor. This finding is similar to other studies in literature. Twenty patients developed hypoglycaemia because of recent increase in insulin dosage. One major reason for hypoglycaemia with change in insulin dosage was asynchrony between nutrition delivery, glucose monitoring and insulin

delivery. Nutritional discordance in our study patients was due to nausea, vomiting or anorexia secondary to an intercurrent problem such as an infection & occasionally due to a 'nil per oral' order, without an appropriate modification in the antidiabetic medication. An intercurrent infection was found to be a significant precipitating factor for hypoglycaemia on univariate analysis. Infection is commonly thought to be a risk factor for poor control of sugars and DKA or hyperosmolar hyperglycaemic non ketotic coma. It must be remembered that infection can also precipitate hypoglycaemia in the elderly. Nutritional discordance due to poor appetite, nausea & vomiting is the usual contributory factor. Elderly living alone will be more vulnerable in this situation. Renal dysfunction was another significant precipitating factor for hypoglycaemia on univariate analysis. Most of the antidiabetic drugs are metabolized through the kidney & renal failure brings down the requirement of antidiabetic medications & can trigger a hypoglycaemic episode if appropriate modifications are not made in the medications. Poor functional status was one of the significant factors associated with the risk of hypoglycaemia. This is well documented in literature. These patients, if living alone may not be able to help themselves even if they become aware of the hypoglycaemic symptoms. Hypoglycaemic unawareness is another major problem in these individuals. As documented in our study 33% of the patients did not have symptoms of hypoglycaemia. Fifty percent of the study patients developed hypoglycaemia change in dosage of Insulin. This could be due to attain a strict glycemic control and a recent rise in blood sugar level. Most of rural patient usually take the insulin medication without frequent monitoring of the random blood sugar levels at frequent intervals. The events that precipitated hypoglycaemia were identified in all 100 patients, as compared to other studies, where, the cause of hypoglycaemia was not identified in a few patients.

Outcome of hypoglycaemia in study patients

Morbidity of hypoglycaemic episodes includes strokes, myocardial infarction, ventricular arrhythmias and falls causing fractures. Most of the studies have documented significant morbidity. However, none of our patients developed any such morbidity and all patients recovered completely to the premorbid functional status. This could be because of rapid recognition and correction of hypoglycaemic symptoms. Many of the hypoglycaemic episodes that occurred in hospital were identified from monitoring rather than from symptoms of hypoglycaemia & treatment instituted. Patients that came to the hospital for hypoglycaemia were diagnosed & treated at the emergency department without any delay. This study included patients who were admitted only in the medical wards and casualty.

Comparison of study and control patients

Comparison of demographic details of study and control patients

Residence, educational status and living conditions were not predictors of hypoglycaemia by univariate analysis. Functional status was assessed by Katz score with a score of zero indicating that the patient had to depend on caregivers for all activities of daily living. By univariate and multivariate analysis, this study also showed that a poor functional status was associated with a high risk of hypoglycaemia which is comparable to other studies in literature. Patients with a poor functional status are incapable of feeding themselves even if they experience early symptoms of hypoglycaemia and only a vigilant care giver with a high awareness can avert serious hypoglycaemia. Recent hospitalizations are a risk factor for hypoglycaemia. Poor appetite, changes in the dose of anti diabetic medications, introduction of new drugs with drug- drug interactions are a few of the reasons for this. However, in this study, there was no significant difference in the history of recent previous hospitalization (11% of study patients as compared to 2% of the controls). The numbers

were probably too small to evaluate this. Study patients had a lower BMI than controls which was statistically significant (p = 0.035). This is similar to other studies were frail elderly had a higher incidence of hypoglycaemia.

Duration of diabetes was longer in patients who developed hypoglycaemia as compared to diabetic patients who did not develop hypoglycaemia (p = 0.063). This was similar to other studies.

Anti diabetic medications in study and control patients.

The patients included in this study were on OHA, insulin or a combination of OHA & insulin. There was no significant difference in the prevalence of hypoglycaemia among the various groups. Among patients using sulphonylureas, 44% of the patients were on glimipiride, 33% were on glimencamide and the 19% and 4% patients were on gliclazide and glipizide respectively. There were no patients on chlorpropamide. The large number of patients on glimiperide in the study probably reflects the fact that this drug is becoming the favoured sulfonylurea, because of its pharmacokinetic profile & its low hypoglycaemic potential. Metformin alone has a very low potential for Hypoglycaemia. However, unlike in other studies, none of our study patients were on metformin alone at the time they developed hypoglycaemia. In the elderly, particularly in the presence of co morbid conditions such as infection, renal dysfunction or hepatic dysfunction, even metformin alone can cause Hypoglycaemia. Out of the 100 patients who developed hypoglycaemia, 48% of were on insulin alone and 22% were on insulin and oral hypoglycaemic agents. This trend is different from that of other studies where patients with combination therapy developed hypoglycaemia more frequently. This could be because 58% of the patients were admitted for an intercurrent illness & were switched over to receive insulin alone. There was no significant difference in the frequency of use of oral hypoglycaemic agents and/or insulin between study and control patients both by univariate & multivariate analyses. This implies that study patients were not at a higher risk of developing hypoglycaemia solely because of their treatment when compared to control patients.

Comparison of HbA1c among study and control patients

HbA1c was significantly lower in the study group (mean HbA1c (6.67%) as compared to the control group (mean HbA1c 7.27%) which is statistically significant (p=0.001). This was similar to other studies in literature 52,85,88 & it is well documented that stricter the control of sugars greater the risk for hypoglycaemia.

Polypharmacy among study and control patients

Poly pharmacy was more common in the study patients as compared to the control group and the difference was statistical significance (p = 0.046). It is well documented in literature that poly pharmacy is a strong predictor of hypoglycaemia in the elderly and our study has similar results. Greater the number of medications greater is the chance for medication errors.

Alcohol and Hypoglycaemia

Alcohol was also found be significant factor to the development of hypoglycaemia in this study. Twenty five percent (25%) study group has history of alcohol consumption. Alcohol consumption and development of hypoglycaemia is statically significant (p = 0.005). Alcohol is known to blunt responses to episodes of hypoglycaemia.80 In our study Alcohol consumption and development of hypoglycaemia is statically significant (p = 0.005).

Self monitoring of blood glucose in study and control patients

Self monitoring of blood glucose (SMBG) is known to decrease hypoglycaemic episodes and this has been proven in various studies 90. In our study, Frequency of self monitoring of blood glucose was less in the study group, the difference was statistically significant (p=0.01) Frequent monitoring of sugars would obviously result in

treatment modifications as & when required & prevent the occurrence of hypoglycaemia.

Analysis of precipitating factors of hypoglycaemia by univariate logistic regression

The factors that precipitated hypoglycaemia in study patients were compared with control patients by univariate logistic regression. It was found that infection (p = 0.01) and renal failure (p = 0.03) were significant precipitating factors. Infections, particularly in the elderly cause nutritional discordance due to poor intake & renal failure is well known to reduce the metabolism of most anti diabetic mediations. Hepatic failure was not a predictor for hypoglycaemia.

Analysis of risk factors of hypoglycaemia by multivariate logistic regression

We also performed multivariate logistic regression on certain risk factors and it was found that poor functional status (p = 0.02) and infection (p= 0.007) were significant predictors of hypoglyca-emia. Although renal failure was a predictor of hypoglyaemia by univariate analysis, it was not significant by multivariate analysis. Poor functional status poses a risk for hypoglycaemia in this population as they may not be able to help themselves or even seek help. In the latter situation only an alert caregiver can help avert hypoglyacemia.

Limitations of the study

This study is a hospital based study. Many patients & care givers recognize hypoglycaemia & take corrective measures at home without coming to a health care setting. As hypoglycaemia is an easily treatable condition, many hypoglycaemic elderly would have received treatment in the emergency department and sent home without admission. For these reasons the patients studied here may not reflect the full spectrum of the problem. Many episodes have been detected on 'routine monitoring'. Though this fulfils the criteria for hypoglycaemia the true significance of this, needs to be clarified further. Many of the episodes have been treated with intravenous dextrose probably because the patients were inpatients. These are some of the shortcomings of this study.

SUMMARY

In a developed world, most people can now expect to live up to old age. Diabetes mellitus is the most common metabolic disease in the aging population and is associated with increased morbidity, disability and premature death. As the prevalence of diabetes mellitus increases and as treatment guidelines call for more rigorous glycaemic control, rates of hypoglcaemia are on the rise. Hypoglycaemia was the most frequent metobolic complication noted in elderly diabetics & can have serious consequences in terms of mortality & morbidity. The consequences of hypoglycaemia can be particularly severe in the elderly. There is an increased risk of myocardial infarction, ventricular rhythm disorders and stroke as well as the risk of injury and fractures in a predisposed population. In particular, several severe episodes of hypoglycaemia can cause permanent memory impairment. The burden of elderly diabetes is increasing in India, and hypoglycaemia is one of its most common complications. This study was undertaken as there are very few reported studies from India. The objectives were to study the risk factors predisposing to hypoglycaemia, most common symptoms occurring during hypoglyc-aemia, the treatment required and outcome of hypoglycaemia in elderly diabetics.

It was a case control study done in the medical wards of Government General Hospital, Siddhartha Medical College, Vijayawada. The data collected included details such as age, demographic details, education level, duration of diabetes mellitus, details of treatment of diabetes at the time of hypoglycaemia, details of the hypoglycaemic episode (symptoms, severity, glucose level, risk factors identified and treatment outcome), comorbidities, polypharmacy, alcohol use and assessment of functional status using Katz score. Out of the 100 patients, 47 were males and 53 were females with a mean age of 70.48 years. Most of the patients had completed primary

school and 97 patients out of were staying with relatives. 64 patients who developed hypoglycaemia had a Katz functional score of 0 and a low functional score was a predictor of hypoglycaemia by univariate analysis and multiple logistic regression. The mean duration of diabetes was more in the study group whereas the BMI was low in the study group & both of these were statistically significant. 30% of the study patients were on OHA, 48% were on insulin and the remaining were on a combination of both. BMI were significantly lower in the study group than in the control group .Over 1/3 of the patients in the study group (38%) had no symptoms. Among the symptomatic patients, neuroglycopenic symptoms (20%) were more commonly encountered than autonomic symptoms (17%). Duration of diabetes was longer in the group of study patients who were asymptomatic. The commonest risk factors for developing Hypoglycaemia in our study patients was infection (63%), nutritional discordance (61%), recent change in the dose of medications (50%), polypharmacy (41%), and HbA1c < 6.5 (33%) and alcohol intake (25%).By multiple logistic regressions, infection was associated with significantly higher incidence of hypoglycaemia. Poor functional status was an important risk factor for hypoglycaemia in our patients. All our patients recovered without any sequelae. Ninty five percent of the patents were treated with intravenous dextrose. This was probably because the study was done on inpatients & does not imply that most patients need intravenous dextrose for the correction of hypoglycaemia.

Hypoglycaemia can be prevented in elderly 1)by evaluating the patient for possible risk factors. 2) glycaemic goals should be tailored to individual patient assessing the potential benefits & risks.3), selection of anti diabetic agents should be judicious. Patients and family should be educated to recognize and treat hypoglycaemia. Finally, coordinated care should be provided to identify, treat and prevent hypoglycaemia.

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