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Original Research

Incidence and risk factors of hypoglycemia among Type 2 diabetic patients in a South Indian hospital

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ABSTRACT

Aim: The study was aimed at assessing the cumulative incidence of hypoglycemia and precipitating risk factors among type 2 diabetes mellitus in-patients of a tertiary care hospital in South India.
Methods: The prospective cross sectional study spanning 14 months was conducted in a tertiary care hospital in Kerala. All T2DM patients who were administered any form of insulin during the length of hospital stay was monitored for assessing the hypoglycemic episodes. Any patient with a GRBS value less than 70 mg/dL was defined to be hypoglycemic as per the ADA guidelines. The statistical analysis of collected data was performed using SPSS 18 for windows version.
Results: Of the 1650 subjects enrolled in the study, 204 subjects developed hypoglycemia. The sample composed of 60.8% females and 39.2% males and the difference was significant with $p = 0.02$. A significant positive correlation was observed between HbA1c values and GRBS value, with a 2 tailed Pearson correlation coefficient of 0.027. On stratifying as per the modality of insulin dose prescribed, 72.5% of the hypoglycemic patients were found to have been administered fixed dose insulin.
Conclusion: The cumulative incidence of institutional hypoglycemia among type 2 diabetic inpatients was gauged as 12.36%; among which, 26.96% had asymptomatic episodes.

1. Introduction

Optimal glycemic control can subdue the complications and mortality manifested by hypoglycemia in patients admitted to healthcare facilities. However, there has been widespread debate on the optimal blood glucose level in hospitalized patients [1]. As per American Diabetes Association (ADA), hypoglycemia is defined as abnormally low plasma glucose concentration below the threshold level of 70 mg/dL; exposing the patient to probable harm [2]. Contrastingly, hypoglycemic definition of the European Medicines Agency (EMEA) advocates a lower threshold of <60 mg/dL [3]. Ramifications of the lack of a common consensus have obscured the estimation of the exact prevalence of hospital hypoglycemia and its risk factors.

Hypoglycemia often remains undetected and is conceivably the most common adverse event confronted during diabetes care. To achieve a favourable shift in the glycemic triad of HbA1c, fasting plasma glucose level and post-prandial blood glucose level; wide array of drugs has become available. However, the therapeutic strategies aimed at elevating plasma insulin concentration ineluctably possess risk of intermittent hypoglycaemia. This is prominently evident in patients with Type 1 diabetes mellitus (T1DM) and those with chronic insulin therapy for type 2 diabetes mellitus (T2DM) [4]. Iatrogenic hypoglycemia is an outcome of complex interplay amongst absolute or relative insulin surplus and defective glucose counter-regulation.

There is global variation in the reported incidence of hypoglycemia attributed to the diversity in both regional diabetic and therapeutic patterns. A population-based study of health service resource use, employing DARTS (Diabetes Audit and Research in Tayside Scotland)/MEMO (Medicines Monitoring Unit) Collaboration as data source, estimated hypoglycemic prevalence of 7.1% in type 1 diabetes mellitus patients and 7.3% in type 2 diabetes mellitus patients on insulin [5]. The most frequent hypoglycemia precipitating factors include increasing age, diabetes medications including insulin and sulphonylureas, renal

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dysfunction and hepatic impairment [6]. As per the Endocrine Society clinical practice guideline, about 90% of all patients who receive insulin experience hypoglycemic episodes [7]. A recent South Indian study in diabetic old age home inmates has estimated the prevalence of hypoglycemia at 33.86% among which, 56.14% patients were on insulin monotherapy or combination therapy [8].

The hypoglycemic prevalence and episode frequency are usually under-estimated because accurate estimations require continuous blood glucose monitoring. Any decline in the plasma glucose level below threshold, in the absence of hypoglycemic symptoms may therefore go unnoticed in the absence of such stringent monitoring strategies. Research has reported the impact of hypoglycemia on the patient's health-related quality of life, cost of diabetic therapy and treatment contentment [9,10]. Hypoglycemia is a major hindrance in the achievement of optimal glycemic control and has the potential to precipitate vascular events in addition to other detrimental effects. Recognition and appraisal of hypoglycemic risk factors, appropriate treatment regimen selection, and enhancing the awareness among patients and healthcare practitioners can aid in maintain good glycemic control, minimize the risk of hypoglycemia, and prevent long- term complications [11].

The following study was aimed at assessing the incidence and risk factors for hypoglycemia among T2DM in-patients of a tertiary care hospital in South India.

2. Materials & methods

This prospective cross-sectional study of 14-month duration (January 2014 to March 2015) was conducted in a tertiary care hospital in South India. A data collection form was designed to capture aspects which included patient demographics, medical history, medication history, plasma glucose level indicators, route of food intake and specifics of insulin administered. This information was obtained through patient or by-stander interview and patient medication record evaluation. All T2DM patients who were administered any form of insulin during the length of hospital stay was monitored for assessing the hypoglycemic episodes. Patients were routinely monitored using general random blood sugar (GRBS) test to evaluate the response to insulin therapy. Any patient with a GRBS value less than 70 mg/dL was defined to be hypoglycemic as per the ADA guidelines. A glucometer (Accu-Check® 2014) working on biamperometric principle was used to estimate the blood glucose levels on a daily basis. The glucose dehydrogenase in the strip converted the glucose in the blood sample to gluconolactone. The reaction generates electrons; whose number is proportional to the concentration of glucose in the solution. The patients having blood glucose level below the threshold of 70 mg/dL were further evaluated to appraise the risk factors responsible for precipitation of hypoglycemia. The minimum required sample size was estimated at 1270 using the following equation.

$$n = \frac{4pq}{d^2}$$

Where, n= minimum required sample size, p = prevalence of hypoglycemia among type 2 diabetic patients (taken as 7.3%) [5], $q = 1 - p$ and d is the precision (taken as 20% of p).

Microsoft Excel 2010 was used for data entry and IBM SPSS 22.0 for windows version was used for statistical analysis.

3. Results

An aggregate of 1650 subjects were enrolled in the study of whom, 204 subjects were found to have developed at least 1 hypoglycemic episode during the length of hospital stay. Thus the hypoglycemic cumulative incidence was estimated as 12.36% in the study sample. The mean age of the study sample was 59.94 ± 12.63 years. The sample composed of 60.8% females and 39.2% males and the difference was found to be significant with $p = 0.02$. The mean age of the females was estimated as 58.45 ± 13.58 years and that of males as 60.9 ± 11.93 years. There was found to be non-significant difference of age distribution between male and female patients with $p = 0.219$. Almost half of the patients (49%) belonged to the age group 40–59 years with 60–79-year group closely trailing with 45.1% subjects (Fig. 1). The mean HbA1c value of the study sample was realized as 8.7 ± 1.2%. A significant positive correlation was observed between HbA1c values and GRBS value, with a 2 tailed Pearson correlation coefficient of 0.027. Average time for onset of hypoglycaemia was estimated to be 15.01 h ± 6.51 h after the initial insulin dose. There was significant difference ($p < 0.001$) in the distribution of hypoglycemic incidents among various departments, with major share of hypoglycaemic cases reported from the Nephrology and General Medicine department of the institution, accounting together to 41.3%. 33.3% patients developed hypoglycemia between 18 to 24 h after the first dose of insulin. Only 3.9% patients contracted hypoglycemia 24 h past the initial insulin dose (Table 1). The difference in distribution of patients within each time group, calculated with respect to first dose insulin, was significant with $p < 0.001$. 51% patients had GRBS level between 30 to 50 mg/dL and 35.3% had the level between 50 to 70 mg/dL. 5.9% patients had severe hypoglycemia with GRBS less than 30 mg/dL (Table 2). The patient distribution in various GRBS ranges were appraised as significant with $p < 0.001$. The number of asymptomatic

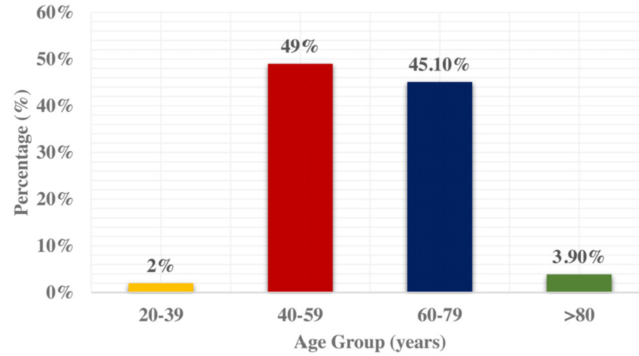

Fig. 1. Bar graph representing the distribution of hypoglycemic subjects in different age groups.

Table 1
Latency of hypoglycemic onset after first dose of insulin.

Time of Onset (hours)	Frequency (no of patients)	Percentage (%)
<6 h	40	19.6
6 to 12 h	24	11.8
12 to 18 h	64	31.4
18 to 24 h	68	33.3
>24 h	8	3.9

Table 2
Stratification of patients with respect to hypoglycemic intensity as per GRBS grades.

GRBS value (mg/dL)	Frequency (no of patients)	Percentage (%)
<30	12	5.9
30–50	104	51.0
50–70	72	35.3
70–90	12	5.9
>90	4	2.0