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Clinical profile of hypoglycemiain type 2 diabetes mellitus patients

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I. Introduction

Currently, we are experiencing an epidemic growth in the number of people with diabetes worldwide.[1] An estimated 366 million people, corresponding to 8.3% of the world's adult population, have diabetes today, but the prevalence is expected to grow to 552 million by 2030, corresponding to 9.9% of the adult population.[2] This increase goes hand in hand with "westernization" of lifestyle, with consumption of more energy-dense food and decreasing physical activity.[2] Driven by this development, diabetes affects more and more young people. These changes have driven a huge increase in T2DM —the most common form of diabetes, particularly in young people, especially in their working age.[3] The medical burden is rising as patients with diabetes are developing a growing number of metabolic and cardiovascular comorbidities.[4] The growing economic burden in complex socioeconomic structures becomes obvious.[5] The continuation of the diabetes epidemic is predicted, and the World Economic Forum foresees the epidemic as a disaster likely to continue to worsen in the foreseeable future with a significant impact on global economic growth at least similar in scale to the recent banking crisis.[6] The glycosylated hemoglobin goal according to ADA guidelines is below 7.0% but should be individualized based on factors such as age and life expectancy, co-morbid conditions, and hypoglycemia unawareness.

Exercising during the evening hours increases the risk of nocturnal hypoglycemia, which may occur up to 4 to 6 hours after an exercise bout.[4] To decrease the likelihood of this response during the night (or day), the patient with diabetes may need to reduce his or her insulin dose or increase carbohydrate intake before or after exercise.[5] Recognize the signs and symptoms of hypoglycemia. These include heart palpitations, confusion, weakness, and visual disturbances. If hypoglycemia is left untreated, it could lead to unconsciousness or convulsions. To reduce the likelihood of complications, patients with diabetes should always carry a form of fast-acting carbohydrate (e.g., juice, candy, and glucose tablets), exercise with a partner, and wear a diabetes identification tag. Monitor for symptoms of hyperglycemia. These include excessive thirst; frequent urination; blurred vision; itchy, dry skin; and a fruity odor or breathe. Hyperglycemia can lead to diabetic coma.[6]

The pursuit of strict glucose control is frequently hampered by concerns over hypoglycemia. Hypoglycemia requiring third-party assistance is common in the course of type 2 diabetes therapy and occurs with a frequency of approximately 35 episodes per 100 patient-years among insulin-treated patients.[7] Hypoglycemia occurring during treatment has been associated with several adverse events, including increased mortality,[8,9] higher risk of dementia,[10] falls,[11,12] fall related fractures,[13] cardiovascular events,[14] and poor health-related quality of life.[15] In particular, the relationship between hypoglycemia and subsequent cardiac events warrants attention. There are a number of plausible mechanisms by which acute hypoglycemia may trigger ischemia, arrhythmia, and cardiovascular events.[16] Hypoglycemia increases the levels of counter regulatory hormones, such as epinephrine and norepinephrine, which may induce increased cardiac rate and/ or contractility, heightening myocardial oxygen consumption, while also precipitating vasoconstriction and platelet aggregation.[16] Acute hypoglycemia in the presence of hypokalemia prolongs cardiac repolarization, increases the QT interval, favoring a proarrhythmic state. One study of type 1 and type 2 diabetic patients who presented to the hospital with severe hypoglycemia documented frequent hypokalemia, QT prolongation, and severe hypertension during the hypoglycemic events.[17]

Type 2 diabetes mellitus patients between age group 30-65 years admitted as in patients in SMVMCH with other associated factors are assessed for their hypoglycemic episodes and the frequency of hypoglycemia are correlated with other parameters. This study is mainly done in the view of "Hyperglycemia is a serious problem, Hypoglycemia is a fatal condition".

II. Materials And Methods

A hospital based cross sectional study conducted at a tertiary health care setup of Sri Manakula Vinayagar Medical College and Hospital in the department of General Medicine located at Kalitheerthakuppam in Puducherry, for a period of 6 months (April 2019 to September 2019). This study had been cleared by the institutional research and ethics committee.

Study participants

Type 2 diabetes mellitus patients diagnosed to have hypoglycaemic episodes either by blood glucose level or using clarke's questionnaire and with other associated factors like hepatic failure, cardiac failure, renal failure and sepsis in the age group of 30-65 years admitted as in-patient in SMVMCH. The type 2 diabetes mellitus patients with hypoglycemic episodes in age group of 30-65 years which includes the patients taking both oral hypoglycemic agents and insulin therapy associated with other factors like cardiac disease, hepatic disease, renal failure and sepsis.

III. Methodology

Type 2 diabetes mellitus patients admitted as in patient in Sri Manakula Vinayagar Medical College and Hospital, their hypoglycemic episodes were diagnosed by measuring blood glucose level less than 80 mg/dl or by using Clarke's questionnaire[18] and other investigations for associated factors were obtained.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version Software. Categorical data was represented in the form of Frequencies and proportions. Chi- square was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. MS Excel and MS word was used to obtain various types of graphs such as bar diagram.

IV. Results

A total of 47 patients with type 2 diabetes mellitus were taken into study. The mean age of the participants were 59.32±11.44 years; IQR=53 (34, 87). Among them 37 were males and 10 were females (Table 1). Majority of the participants had giddiness (42%) followed by excessive hunger (36.84%), fatigueness (15.79%) and fainting in about 5%. Out of 47 patients with type 2 diabetes mellitus 34% had 1-2 episodes of hypoglycemia in a week followed by 36% having 3-4 episodes in a week and 6% around 5 times in a week. Around 40% needed assistance in our study. Majority of them have skipping meals as a reason, and 42% are not aware and 6% due to over exercise. Out of 47 patients with type 2 diabetes mellitus 68% were having medication and about 23% of them are actually aware of their hypoglycemic symptoms.

Table 1: Demographic profile of study participants (N=47)

Slno	Variable	Frequency	Percentage
1	Age		
	30-40	3	6.4
	41-50	8	17.0
	51-60	17	36.2
	61-70	13	27.7
	71-80	3	6.4
	81-90	3	6.4
2	**Gender**		
	Male	37	78.72
	Female	10	21.28
3	**Symptoms of Hypoglycemia***		
	Excessive hunger	28	36.84
	Fainting	4	5.26
	Giddiness	32	42.11
	Fatigue	12	15.79
4	**Number of episodes in a week**		
	Nil	11	23.40
	1-2	16	34.04
	3-4	17	36.17
	5	3	6.39
5	**Assistance**		
	Yes	19	40.42
	No	28	59.57
6	**Reason**		

	Skipping Meals	24	51.06
	Over exercise	3	6.38
	Not aware	20	42.55
7	**Medication**		
	Yes	32	68.09
	No	15	31.91
8	**Awareness**		
	Yes	11	23.40
	No	36	76.60

*Multiple responses

Table 2 shows the distribution of biochemical profile. Median values are, urea 30 (IQR-114), creatinine 1.00 (IQR-5.00), Hemoglobin 11.25 (IQR-8), WBC 8300(IQR 20000), random blood sugar 71.50 (IQR-280), TB 0.80 (IQR-14.10), DB 0.30 (IQR- 7.7), SGOT 19.00 (IQR-217), SGPT 17.50 (IQR-91), cholesterol 141.00 (IQR- 337), and triglycerides 80.00 (IQR-336).

Table 2: Distribution of biochemical profile of the study participants (N=47)

Slno	Variable	Mean	SD	Median	IQR	Minimum	Maximum
1	Urea	36.74	24.35	30	114	15	129
2	Creatinine	1.27	0.87	1.00	5.00	0.60	5.60
3	Hemoglobin	10.84	1.98	11.25	8	6	14
4	WBC count	9214.89	4356.15	8300	20000	400	20400
5	Random blood sugar	79.02	47.18	71.50	280	37	317
6	TB	1.32	2.31	0.80	14.10	0.60	14.70
7	DB	0.62	1.39	0.30	7.7	0.20	7.90
8	SGOT	30.59	38.32	19.00	217	10	227
9	SGPT	24.70	19.73	17.50	91	10	101
10	Cholesterol	163.26	70.04	141.00	337	100	437
11	Triglycerides	106.53	77.54	80.00	336	50	386

Figure 1: Distribution of study participants according to their mode of treatment (n=38)

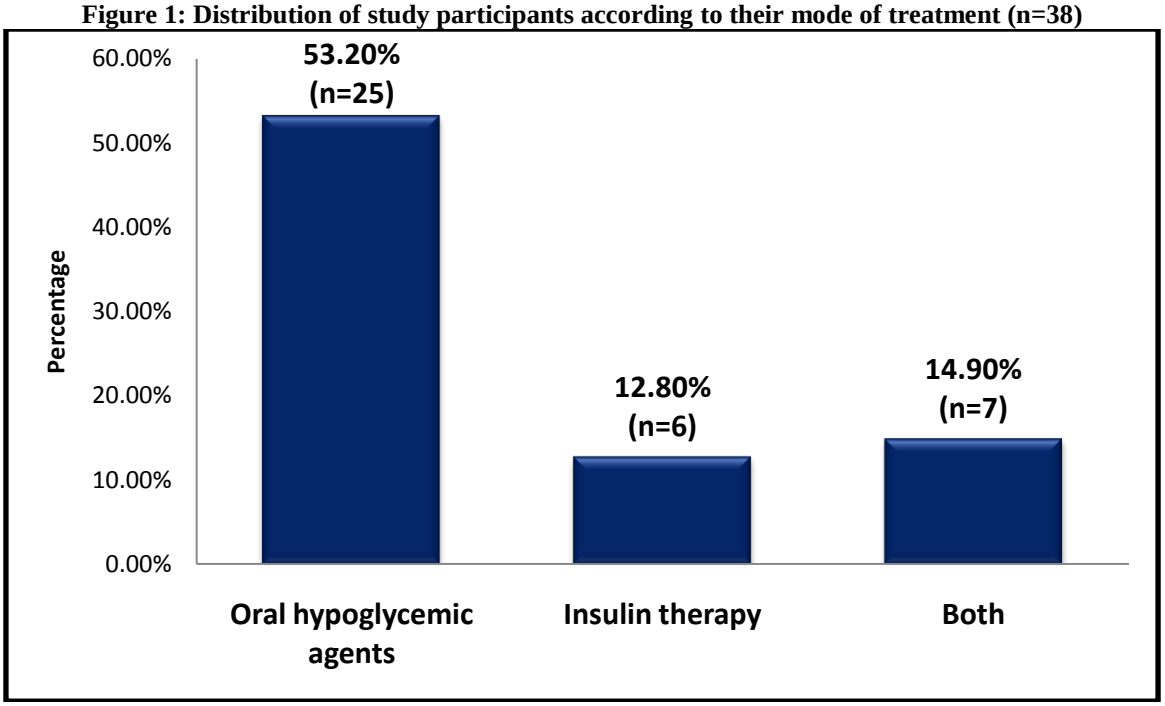
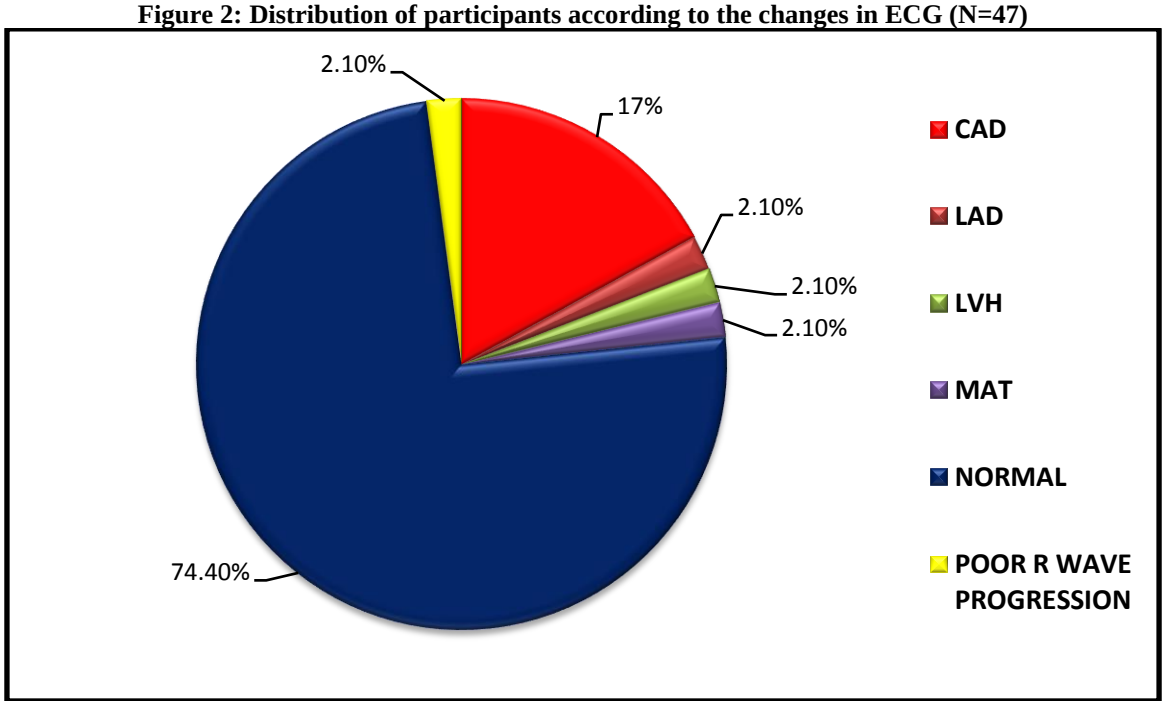


Figure 1 shows the distribution of patients according to their mode of treatment received earlier. Around 53% were on oral hypoglycemic agents followed by 14.9% on both oral hypoglycemic agents and insulin therapy, and 12.80% exclusively on insulin therapy.

Figure 2: Distribution of participants according to the changes in ECG (N=47)



In ECG, 74% of the study participants were having normal ECG. Around 17% had CAD. About 2.1% with LAD, LVH, MAT and poor R wave progression. (Figure 2)

Table 3: Distribution of co morbidities among the study participants (N=47)

Slno	Co-morbidities	Frequency*	Percentage
1	Cardiac disease	11	23.40
2	Liver disease (Alcoholics)	5	10.64
3	Kidney disease (CKD)	7	14.89
4	Sepsis	22	46.81
5	Hypertension	18	38.30
6	Pulmonary Tuberculosis	10	21.28
7	Acute CVA/Chronic CVA	7	14.89
8	Thyroid disorders	2	4.26

*Multiple responses

Among those participants having type 2 diabetes mellitus who were admitted with hypoglycemia had certain co morbidities. Majority of them had sepsis followed by hypertension, cardiac disease and pulmonary tuberculosis.

V. Discussion

This study was done to find out the factors associated with hypoglycemia on patients with type 2 diabetes mellitus. UK Prospective Diabetes Study (UKPDS) group clinical trial data consistently shows that assignment to an intensive glucose control strategy is associated with a twofold to threefold higher risk of hypoglycemia compared with standard care.[19] In trial settings, hypoglycemia requiring third-party assistance occurred with a frequency of 0.6 to 12 events annually per 100 patients in the intensive therapy group and 0.2 to 4 events in the standard therapy group—much less frequently than in the community setting.[19] Whereas, around 40% needed assistance in our study. Although the relationship between intensive therapy and hypoglycemia appears clear, the relationship between achieved level of glycemic control and hypoglycemia is more complex. In the Diabetes Control and Complications Trial (DCCT), an inverse relationship between HbA1c level and serious hypoglycemia was noted, with the number of events logically increasing with decreasing HbA1c.[20] In contrast, however, detailed post hoc analyses of ACCORD participants with type 2 diabetes showed that patients with poorer glycemic control had a higher risk of hypoglycemia, irrespective of treatment assignment.[21]

In our study around 53% were on oral hypoglycemic agents followed by 14.9% on both oral hypoglycemic agents and insulin therapy, and 12.80% exclusively on insulin therapy. Even in patients who do not choose tight glycemic targets, multiple medications to lower glucose are often required with increasing duration of the disease, as beta cell function declines. The relative importance of various adverse effects of medications may vary from patient to patient. In general, drug reactions increase in frequency with the use of multiple medications. Addition of another medication to lower glucose may also pose a financial burden and

significantly increase time and effort required to manage diabetes (including, potentially, capillary blood glucose monitoring). In our study majority of them had associated co morbidities such as sepsis followed by hypertension, cardiac disease and pulmonary tuberculosis.[20]

Patients, who started out with higher baseline HbA1c levels and were unable to reduce their blood glucose levels, appeared to be at the highest risk for this complication. Moreover, participants with persistently elevated HbA1c levels above 7% after initiation of the intensive strategy had a higher mortality risk than that achieving lower glycemic levels.[21] In our study out of 47 patients with type 2 diabetes mellitus 68% were having medication and about 23% of them are actually aware of their hypoglycemic symptoms. A shared decision-making process stresses a partnership between the patient's values and preferences and the physician's knowledge of clinical evidence and judgment. Decisions are highly individualized, based on available evidence. As an example, more intensive glycemic control in a patient already struggling with a complex regimen may lead to an overburdened patient who is unable to cope with his or her disease.[20] Indeed, somewhat paradoxically, pushing forward with intensive antihyperglycemic therapy may decrease adherence to other more evidence-based therapies.[21] On the other hand, a patient whose most important goal is prevention of diabetes complications may choose to take on the additional burden of insulin therapy or multiple medications to control blood glucose levels with high intensity.

VI. Conclusion

The optimal strategy for individual patients to reduce hypoglycemic episodes is still unknown. Despite decades of study, we remain largely ignorant of the benefits and risks of anti hyperglycemic therapy as it relates to cardiovascular disease risk. Based on existing data, patients with high levels of co-morbidity may derive less cardiovascular benefit from intensive glucose control, and most guidelines suggest higher glycemic targets for older patients with longer duration of diabetes, established cardiovascular disease, and high risk of hypoglycemia. Research in the coming decade needs to provide us with better information so that patients can make decisions about glucose targets and anti hyperglycemic strategies that optimize their outcomes.

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