



## Original Research Article

# Hypoglycemia unawareness index in the Indian population

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### ABSTRACT

India is fast catching on, to be the world's capital for Diabetes. With this, comes the burden of setting, and maintaining glycemic goals individually, which is seemingly impossible. Intensive therapy can predispose to episodes of hypoglycemia, which can in fact be fearful for the individual experiencing them itself. This fear, can then hamper the ability of clinicians to assist the client, in achieving their apt glycemic goals. It is reported that a six-fold increase in deaths due to diabetes has been attributed to patients experiencing severe hypoglycemia in comparison to those not experiencing severe hypoglycemia. Repeated episodes of hypoglycemia can lead to impairment of the counter-regulatory system with the potential for development of hypoglycemia unawareness.<sup>1</sup>

The lack of adequate Indian Data on Hypoglycemia unawareness incited the need for this study.

**Materials and Methods:** This prospective observational study, was conducted utilising Modified Clarke's questionnaire.<sup>2</sup> After clearance from the Ethical committee of AJIMS and RC, 92 consenting subjects were recruited.

**Results:** Of the 92 participants in the study, 72 subjects were found to have hypoglycemia unawareness based on a validated questionnaire. Individuals with a higher level of education, were able to interpret their symptoms to be those of hypoglycemia. Most individuals are aware that eating something when recognizing a first sign of low sugars, will help alleviate symptoms, the next step being reducing their insulin dose. Almost 40% of the study population worried about having a severe hypoglycemia in public.

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## 1. Introduction

Diabetes, a lifestyle disorder due to disarrayed glucose metabolism, i.e. defects in insulin secretion, insulin action, or both. It is quickly catching on in India, with more than 77 million diabetic individuals currently diagnosed with the disease.<sup>3</sup>

Hypoglycemia, especially iatrogenic, is a fearful occurrence in individuals with diabetes, and it impairs its management. Reduced neurogenic symptoms, a key feature of hypoglycemia unawareness, are largely the result of reduced sympathetic neural responses to falling glucose levels.<sup>4</sup>

In view of no available statistics in the population in this area, it would be not only interesting, but imperative to conduct a study to determine the incidence of the same and whether or not symptoms occur during the episode of hypoglycemia. The role of diabetes education in this juncture is very important. Explaining to patients about hypoglycemia symptoms, correction and possibility of HAAF in individuals with long standing diabetes can help reduce its occurrence and therefore reduce morbidity in patients who insist of relaxed glycemic goals in fear of severe hypoglycemia.

## 2. Materials and Methods

This prospective interventional study was conducted after ethical committee clearance, in AJ Institute of Medical

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sciences and Research Centre. 92 consenting individuals were recruited on a basis of a score, achieved, from Modified Clarke’s Questionnaire to reveal clinically, Hypoglycemia unawareness. Individuals with hepatic, renal or other known autonomic disturbances were excluded, as were pregnant ladies and individuals on beta blockers.

### 2.1. Statistics

The collected data was analyzed using mean, mode for demographic data and frequency percentage for the analysis of the clinical data. Statistical analysis was done using SPSS software version 23.0. A ‘p’ value less than 0.05 ( $p < 0.05$ ) is considered significant. The various measures of central tendencies and graphical representations were used to analyze the data.

### 3. Results

Over a period of one year, a total of 92 subjects with diabetes Mellitus were assessed clinically, then objectively for hypoglycemia. Of these, 72 were found to have hypoglycemia unawareness as per the modified Clarke’s questionnaire. 62 then underwent 72 hours Continuous Glucose monitoring, to objectively confirm episodes of asymptomatic hypoglycemia. A hypoglycemia index done, then showed that for every 3 symptomatic episodes of hypoglycemia, 5 episodes were asymptomatic.

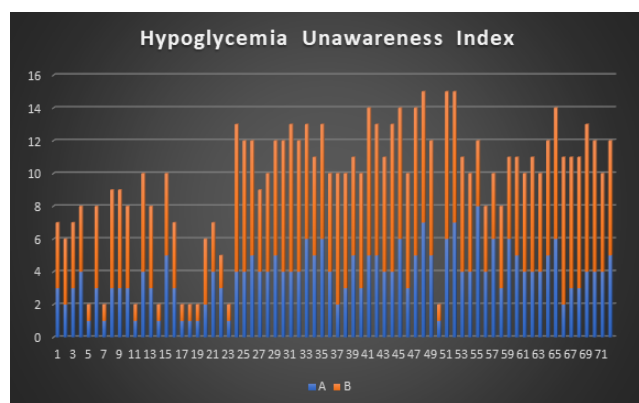


Fig. 1: Hypoglycemia unawareness Index

#### 3.1. Behavioral modifications with respect to hypoglycemia

Although an individual with diabetes adapts multiple measures to prevent hypoglycemia, the most common behavior practiced by individuals with diabetes was to consume something when they feel the first sign of low sugars, followed by reducing their insulin dose. The least common strategy was to keep their sugars on the higher side.

1. Eat large snack at bed time

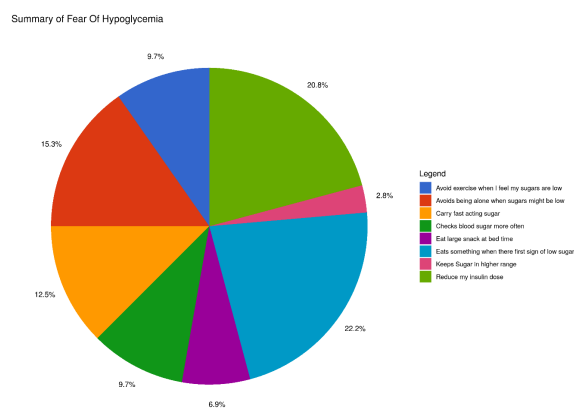


Fig. 2: Behavioural changes when encountering hypoglycemia

2. Avoids being alone when sugars might be low
3. Checks blood sugar more often
4. Keeps Sugar in higher range
5. Eats something when there first sign of low sugar
6. Reduce my insulin dose
7. Carry fast acting sugar
8. Avoid exercise when I feel my sugars are low

#### 3.2. Concern about not being able to self correct low sugars

Only two individuals were worried about not having any aid to self correct low sugars if they have symptoms. 54% were not at all worried about being able to reach for sugars when having symptoms of low sugars. This on further prompting was found to be due to lack of awareness about how to self correct - use of glucose, checking with glucometer etc.

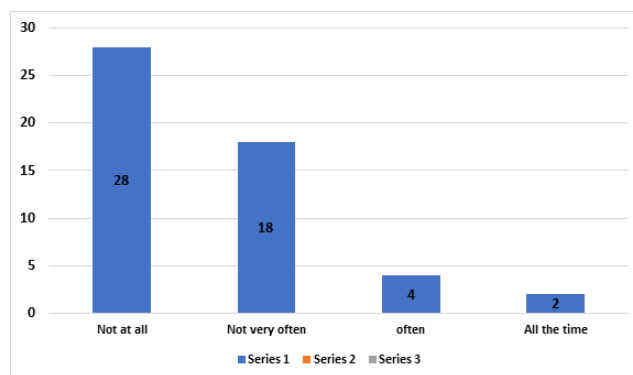


Fig. 3: Concern about not having food/juice when I have a low sugar

#### 3.3. Concern about severe hypoglycemia

39% of the population with hypoglycemia were not concerned about having an severe hypoglycemia in public,

whereas 8% were often worried that they may feel dizzy due to low sugars.

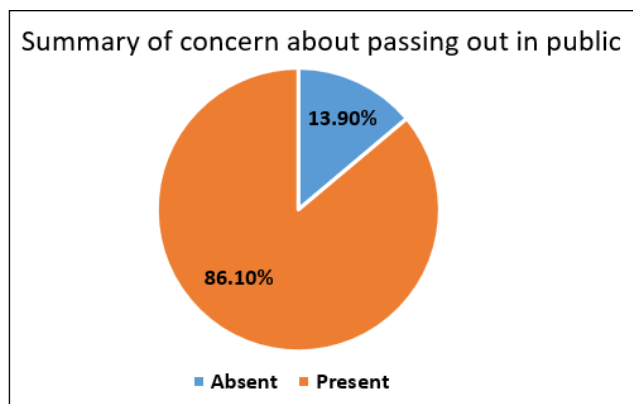


Fig. 4: Concern about severe hypoglycemia

### 3.4. Concern about having low sugars

35% of the population was not worried at all about having low sugars while asleep but 2.5% was always worried about having low sugars while asleep.

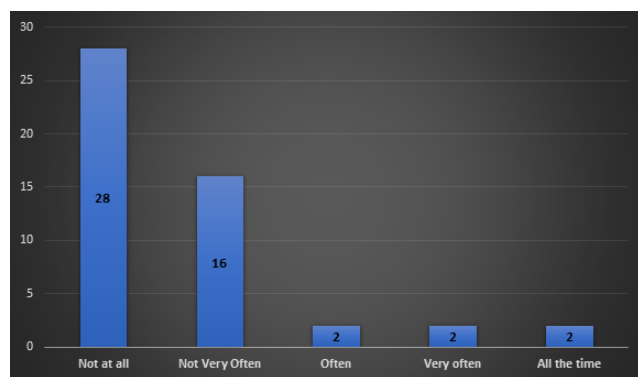


Fig. 5: Concern about having low sugars while asleep

## 4. Discussion

Hypoglycemia is an inevitable part of diabetes mellitus. Clinically the greatest risk occurs after failure of cerebral glucose supply causing progressive cognitive impairment, confusion and unconsciousness. Psychologically, it is fearful, and the burden of having to deal with hypoglycemia in public is all the more difficult to cope with.

Hypoglycemia unawareness and a previous history of episodes of severe hypoglycemia are risk factors for severe hypoglycemia. Hypoglycemia unawareness in turn is also associated with a 6 fold increased risk of severe hypoglycemia in type 1 diabetes.<sup>5</sup>

In a tertiary care center in south India, 40 individuals with type 1 diabetes clinically determined to have hypoglycemia

unawareness were subjected to a CGM Study with which asymptomatic hypoglycemia was confirmed in 25% of these individuals, and 50% were nocturnal. It was concluded that a reasonable individualised glycaemic goal in Type 1 Diabetes Mellitus, should be the lowest A1C that preserves awareness of hypoglycemia, preferably with minimal symptomatic or even asymptomatic hypoglycemia.<sup>2</sup>

The prevalence of Hypoglycemia unawareness in a post-hoc analysis of data collected as part of the UK Hypoglycemia Group study, was found to be 22.1%.<sup>4</sup> Frier et studied 518 subjects with diabetes with a self reported questionnaire. These subjects had retrospectively documented episodes of hypoglycemia by self monitoring of blood glucose. Hypoglycemia unawareness was present of 19.5% of this cohort.<sup>6</sup>

It is known, based on several studies that hypoglycemia can have a major impact on the quality of life. The well-being could be affected by direct effects of hypoglycemia and also indirectly from fear of recurrence.<sup>7,8</sup> As a result of fear, there is a tendency to modify behavior to prevent hypoglycemia, which may contribute to poor glycaemic control and again attenuate their quality of life.<sup>6</sup>

There have also been several studies done to suggest that severe hypoglycemia and cognitive dysfunction go hand in hand. Asvold et al suggested that early exposure to severe hypoglycemia could have clinically relevant effects on cognition many years later. In this study the overall cognitive scores of the nine diabetic children who experienced severe hypoglycemia before age of ten were lower than the eighteen diabetic children without history of severe hypoglycemia.<sup>9</sup>

Hypoglycemia can on the other hand, place an individual at risk of unpleasant situations resulting in social embarrassment.<sup>10,11</sup>

This study has revealed the need for further evaluation on hypoglycemia unawareness in our population in India, and individualised goals. Diabetes education must include recognition of and apt corrective measures for hypoglycemia.

## 5. Conclusion

Overall, the conclusions drawn from this study are:

1. Diabetes Education sessions must regularly highlight hypoglycemia recognition and management.
2. Quality of life (with respect to Fear of hypoglycemia) is impaired
3. Hypoglycemia unawareness should be included as part of assessment during every visit to the clinician
4. Glycaemic Targets need to be individualized based on risk of hypoglycemia

## 6. Limitation

The limitations of the study were

1. The study was done at a tertiary care centre, hence the data may not actually represent the problems of the population at large.
2. The short duration and small sample size as compared to the disease burden.
3. We recommend that
4. To validate this study, a larger number of patient's have to be studied with non-traditional risk factors.

## 7. Source of Funding

None.

## 8. Conflict of Interest

The authors declare that there is no conflict of interest.

## References

1. Kalra S, Mukherjee JJ, Venkataraman S, Bantwal G, Shaikh S, Saboo B, et al. Hypoglycemia: The neglected complication. *Indian J Endocrinol Metab.* 2013;17(5):819–34.
2. Naik D, Shilpa RM, Mahesh DM, Asha HS, Kapoor N, Paul T, et al. Evaluation of hypoglycaemia unawareness in individuals with type 1 diabetes mellitus using continuous glucose monitoring in a tertiary care centre. *Endocr Abstracts.* 2015;p. 271. doi:10.1530/endoabs.38.p271.
3. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: 2019.
4. Galan BD, Schouwenberg BJ, Tack CJ, Smits P. Pathophysiology and management of recurrent hypoglycaemia and hypoglycaemia unawareness in diabetes. *Neth J Med.* 2006;64:269–79.
5. Chan O, Cheng H, Herzog R, Czyzyk D, Zhu W, Wang A, et al. Increased GABAergic Tone in the Ventromedial Hypothalamus Contributes to Suppression of Counterregulatory Responses After Antecedent Hypoglycemia. *Diabetes.* 2008;57(5):1363–70. doi:10.2337/db07-1559.
6. Dunn JT, Cranston I, Marsden PK, Amiel SA, Reed LJ. Attenuation of Amygdala and Frontal Cortical Responses to Low Blood Glucose Concentration in Asymptomatic Hypoglycemia in Type 1 Diabetes: A New Player in Hypoglycemia Unawareness? *Diabetes.* 2007;56(11):2766–73. doi:10.2337/db07-0666.
7. Feyter HD, Mason GF, Shulman GI, Rothman DL, Petersen KF. Increased Brain Lactate Concentrations Without Increased Lactate Oxidation During Hypoglycemia in Type 1 Diabetic Individuals. *Diabetes.* 2013;62(9):3075–80. doi:10.2337/db13-0313.
8. Moheet A, Emir UE, Terpstra M, Kumar A, Eberly LE, Seaquist ER. Initial experience with seven tesla magnetic resonance spectroscopy of hypothalamic GABA during hyperinsulinemic euglycemia and hypoglycemia in healthy humans. *Magn Reson Med.* 2014;71(1):12–8. doi:10.1002/mrm.24663.
9. Chan O, Paranjape S, Czyzyk D, Horblitt A, Zhu W, Ding Y, et al. Increased GABAergic Output in the Ventromedial Hypothalamus Contributes to Impaired Hypoglycemic Counterregulation in Diabetic Rats. *Diabetes.* 2011;60(5):1582–9. doi:10.2337/db10-1579.
10. Zammitt NN, Warren RE, Deary IJ, Frier BM. Delayed Recovery of Cognitive Function Following Hypoglycemia in Adults With Type 1 Diabetes. *Diabetes.* 2008;57(3):732–6. doi:10.2337/db07-0695.
11. Oz G, Kumar A, Rao JP, Kodl CT, Chow L, Eberly LE, et al. Human Brain Glycogen Metabolism During and After Hypoglycemia. *Diabetes.* 2009;58(9):1978–85. doi:10.2337/db09-0226.

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