

**Research Article**

HBA1C Levels, Lipid Profile and Thyroid Profile in Patients Admitted with Severe Hypoglycemia in Type 2 Diabetes Mellitus

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Abstract

Objective: We studied the association between HbA1c level, Lipid profile and Thyroid profile in patients admitted with hypoglycemia in type 2 diabetes mellitus. **Materials and methods:** Patients admitted with severe hypoglycemia (<50mg/dl) are included in this observational study from 4 hospitals from January 2013 till January 2015. HBA1C, Lipid profile and Thyroid profile recorded during admission are the points of interest in this study. Demographic and clinical variables were recorded to evaluate the relative risk (RR) of severe hypoglycemia across HbA1c levels. We also studied comorbidities associated with DM. **Results:** Among 1200 patients enrolled, mean age was 58.6±11.7 years. 83% of patients were above 50 years of age of which 50% were in 50-59 years age group. Mean Glycated hemoglobin was 8.3±2.09. Patients admitted with hypoglycemia constitute 118(9.83%), 64(5.33%), 200 (16.6%), 624(52%) and 194(16.16%) in HbA1c categories <6, 6-6.9, 7-7.9, 8-8.9, and >9% which is statistically significant (P value<0.01). Abnormal lipid profile was found in 96.5 % (1158) of the study population and abnormal Thyroid profile in 11.6%. **Conclusions:** Hypoglycemia can occur at any level of glycated Hemoglobin but high risk is found with HBA1c of <6% and >8%. Elderly population should not be subjected for stricter control of blood sugars which can do more harm than good. Patients with mean duration of diabetes more than 10 years are at higher risk of recurrent hypoglycemia.

Keywords: Glycated Hemoglobin (HBA1c); Thyroid profile; Chronic Kidney disease (CKD); Ischemic Heart disease (IHD); Hypoglycemia; Dyslipidemia

Academic Editor: Ge Li, PhD, Weill Cornell Medical College, United States

Received: August 4, 2015; **Accepted:** April 18, 2016; **Published:** May 25, 2016

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Hypoglycemia is a medical emergency caused by reduction in plasma glucose concentration causing symptoms or signs such as altered mental status and/or sympathetic nervous system stimulation due to abnormalities in the mechanisms involved in glucose homeostasis [1]. Incidence of hypoglycemia with diabetes varies in compared to people without diabetes [2-4]. In type 1 diabetes, hypoglycemia is caused due to interplay of insulin excess and inadequate glucose counter regulation rather than insulin excess alone [5]. 2-4% of deaths of people with type 1 diabetes mellitus are estimated to be caused due hypoglycemia [6].

Hypoglycemia is the commonest side effect of treatment of diabetes and is associated with adverse health outcomes (dementia [7], falls [8], fall-related fractures [9], cardiovascular events [9], poor health-related quality of life [10], and increased mortality [11], [12]). Hemoglobin A1c reflects average blood glucose concentration over the course of the RBC lifespan in normal individuals. Lower hemoglobin A1c values, has been shown to delay the onset and slow the progression of diabetic retinopathy, nephropathy, and neuropathy in Diabetes [13].

According to Diabetes Control and Complications Trial (DCCT) hypoglycemia risk is highest among patients with the lowest HbA1c levels. , which reported an inverse relationship between HbA1c levels and the occurrence of severe hypoglycemia in participants with type 1 diabetes [13]. Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial indicated an increased hypoglycemia risk in type 2 diabetic participants with poorer glycemic control compared with subjects with desirable HbA1c levels [14].

Diabetes mellitus increases risk of dyslipidemia, common pattern is elevated triglyceride levels and decreased HDL cholesterol levels [15]. Thyroid dysfunction is found to be prevalent than normal population in Diabetes Mellitus, one meta-analysis reporting 11% prevalence [16]. Major cause of thyroid-dysfunction associated diabetes mellitus is found to be auto immunity with complex biochemical, genetic, and hormonal malfunctions in this pathophysiological association [17].

Eventhough Diabetes is prevalent in India, large studies are lacking to find out the differences between western and Asian populations risk of hypoglycemia with glycated Hemoglobin levels, Dyslipidemia and Thyroid abnormalities. Eventhough it is a hospital based study, we believe that it provides the necessary insight into the problem. Our study is done to test the following hypothesis in Indian population.

1) Risk of hypoglycemia is more prevalent in elderly population. 2) Risk of hypoglycemia is increased with higher and lower HBA1C levels. 3) History of recurrent attacks of hypoglycemia is common with lower HBA1C levels. 4) Risk of hypoglycemia is associated with longer duration of diabetes. 5) Hypoglycemia is more common in patients using insulin and polypharmacy (>4 drugs). 6) High triglyceride levels and decreased HDL cholesterol levels are found in Diabetic patients. 7) There is high prevalence of Thyroid dysfunction in Diabetes.

Materials and Methods

Study population:

Patients admitted with severe hypoglycemia (<50mg/dl) are included in this observational study from 4 hospitals. Identification of Diabetic patients was done by history, Discharge summary details and investigations. Informed and written consent is obtained. History including socio-demographic factors, examination, investigations is noted. Data from type 1 diabetes patients was collected but not included in this study. Previous history of hypoglycemia was assessed by Stanford Hypoglycemia Questionnaire [18]. A total

of 1200 patients were enrolled in the study from January 2013 till January 2015.

Primary outcome of the study was the occurrence of severe hypoglycemia based on plasma Blood glucose levels. History was obtained regarding previous hypoglycemic attacks. HbA1C, Lipid profile and Thyroid profile recorded during admission are the points of interest in this study. HbA1c was divided into five categories i.e. near-normal glycemia (<6%) and very good (6–6.9%), good (7–7.9%), suboptimal (8–8.9%), or very poor (>9%) to find relationship between HbA1c and hypoglycemia. Classification is based on clinical practice guidelines and The Diabetes and aging study [19].

Data was collected regarding covariates of Age, duration of diabetes, Ischemic Heart disease, Chronic kidney disease, cerebrovascular disease, lung disease, drugs used.

Results

Out of 1200 patients enrolled in the study 600 were male and 600 were female. Mean age was 58.6 ± 1.7 years. 83% of patients were above 50 years of age of which 50% were in 50-59 years age group [Figure 1]. Mean Glycated hemoglobin was 8.3 ± 2.09 . Mean HbA1c was higher among those who reported previous history of hypoglycemia ($8.5 \pm 2.7\%$) compared with those who did not ($7.7 \pm 1.5\%$, P value < 0.01).

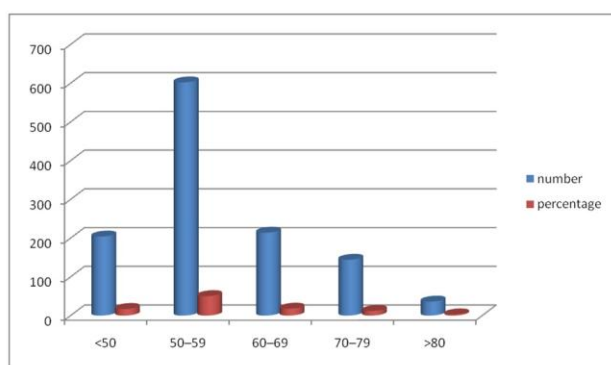


Figure 1 Age distribution

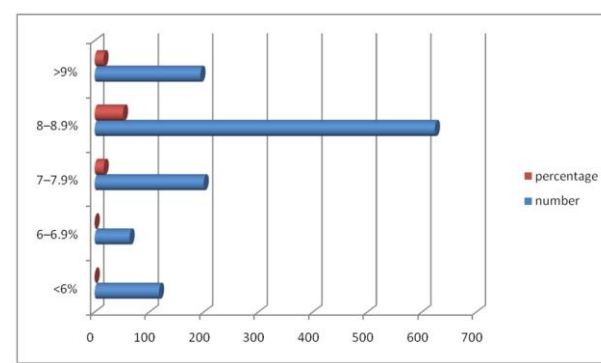


Figure 2 Glycated Hemoglobin

Patients admitted with hypoglycemia constitute 118(9.83%), 64(5.33%), 200 (16.6%), 624(52%) and 194(16.16%) in HbA1c categories <6, 6–6.9, 7–7.9, 8–8.9, and >9% which is statistically significant (P value<0.01)[Figure 2]. Patients with strict control of blood sugar i.e. HbA1c <6% and poor control of Blood sugar HbA1c > 8% constitute around 78% which is significant. Patients with mean duration of diabetes more than 10 years constitute 33% of study population. They are at higher risk of recurrent hypoglycemia compared to persons with lesser duration of diabetes.

Patients taking 4 or more drugs for diabetes constitute 33.83 % (406) of the population. Commonest drugs used are metformin (931, 77.58%) and Glimepiride (897, 74.75%). Patients with insulin therapy are at higher risk for hypoglycemia, 52% of study population constituted. Patients admitted with hypoglycemia and Type 2 diabetes have higher association with Chronic kidney disease (glomerular filtration rate (GFR) <60 ml/min/1.73 m² constitute 14.66%)[Figure 3], Ischaemic Hear disease (17.16%), Congestive cardiac failure (11.16%), cerebrovascular disease (13.66%) and Chronic obstructive pulmonary disease (8.83%)[Figure 4].

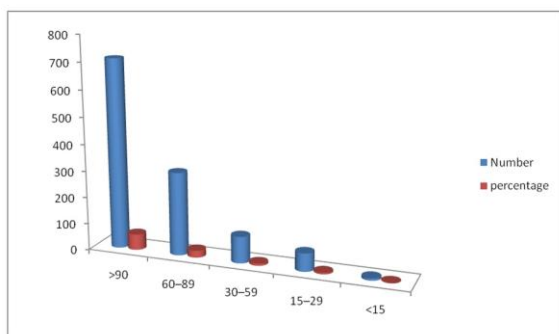


Figure 3 Kidney disease eGFR

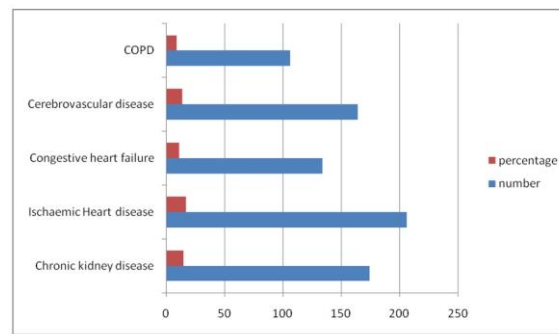


Figure 4 Co-morbidities

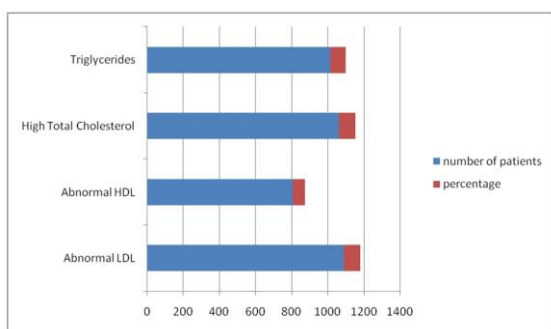


Figure 5 Dyslipidemia

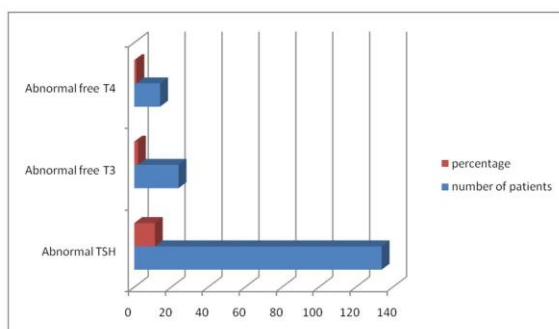


Figure 6 Abnormal thyroid profile

Abnormal lipid profile [Figure 5] was found in 96.5 % (1158) of the study population with Total cholesterol> 200mg/dl in 88.66 % (1064), LDL cholesterol> 100mg/dl in 90.83% (1090), HDL<40mg/dl in 67.16% (806) and hypertriglyceridemia in 84.5% of study group. Thyroid abnormalities were found in 11.16% (134) of study group [Figure 6].

History from patients found that only 25 % (300) of the study groups are taking statins and 90% of population did not get lipid profile checked in past one year.

Discussion

The top 10 countries with diabetes population are currently India, China, the United States, Indonesia, Japan, Pakistan, Russia, Brazil, Italy, and Bangladesh. According to The International Diabetes Federation, people living with diabetes will to rise from 366 million in 2011 to 552 million by 2030 [20].

Hypoglycemia episodes were frequently associated with intensive therapy of diabetes as reported by large studies such as UKPDS, ACCORD, ADVANCE, and VADT. Our study suggests that risk of hypoglycemia is high with intensive therapy of diabetes i.e. HBA1c < 6%, However our study also suggests that hypoglycemia occurs in all HBA1c levels and there is increased association if HBA1c > 8% constituting 78% of study group.

Our study suggests that elderly people are at risk of hypoglycemia with strict control of blood sugars. American Geriatrics Society [21] recommendation that the use of medications other than metformin to lower HbA_{1c} to less than 7.5% in persons older than 65 years is not warranted because of the potential for harm

relative to benefit. Our study found that mean HBA1c values are higher for patients with recurrent hypoglycemic attacks which suggests that poor control is a risk factor for hypoglycemic attacks.

Patients taking insulin are found to have more risk to present with hypoglycemia as per our study. Patients with hypoglycemic attacks and Type 2 DM are at high risk of Ischemic Heart disease, COPD, CCF and CKD as per our study. 96.5% of study group had dyslipidemia and only 25% are on statins and regular exercise which shows that awareness is to be increased regarding complications of Diabetes. 90% of study group did not get lipid profile checked in past year suggests that more affordable health care diagnostics are to be made available for the population below poverty line in India. Patients with abnormal thyroid profile constitute 11.6% of study population which is significant (p value<0.001). Patients with diabetes should be monitored for other autoimmune diseases.

Conclusion

Hypoglycemia can occur at any level of glycated Hemoglobin but high risk is found with HBA1c of <6% and >8%. Elderly population should not be subjected for stricter control of blood sugars which can do more harm than good. Diabetes is associated with higher risk of IHD, CKD, COPD and CCF. Patients should be regularly evaluated for lipid profile and thyroid profile. Awareness of complications and need for testing is to be emphasized in general population.

Severe hypoglycemia, requiring third-party assistance, is a public health issue that affects the quality of life of millions of persons with diabetes mellitus. Overtreatment and under treatment should be minimized.

Conflict of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Stedman, Thomas Lathrop (December 2005) [1911]. "Stedman's Medical Dictionary" (28th ed.). Baltimore: Lippincott Williams & Wilkins. p. 2100.
2. Hill NR, Thompson B, Bruce J, et al. Glycaemic risk assessment in children and young people with Type 1 diabetes mellitus. *Diabet Med.* 2009, 26(7):740-743
3. Turnbull FM, Abraira C, Anderson RJ, et al. Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia.* Aug 5 2009
4. Prolonged Nocturnal Hypoglycemia Is Common During 12 Months Of Continuous Glucose Monitoring In Children And Adults With Type 1 Diabetes. *Diabetes Care.* Mar 3 2010
5. Cryer, Philip E. *Hypoglycemia: pathophysiology, diagnosis, and treatment.* Oxford University Press. 1997
6. Laing SP, Swerdlow AJ, Slater SD et al. The British Diabetic Association Cohort Study, II: cause-specific mortality in patients with insulin-treated diabetes mellitus. *Diabet Med.* 1999, 16 (6): 466–71.
7. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP Jr, Selby JV. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. *JAMA.* 2009;301:1565-1572

8. Schwartz AV, Vittinghoff E, Sellmeyer DE, et al. Health, Aging, and Body Composition Study. Diabetes-related complications, glycemic control, and falls in older adults. *Diabetes Care*. 2008, 31:391-396
9. Johnston SS, Conner C, Aagren M, Ruiz K, Bouchard J. Association between hypoglycaemic events and fall-related fractures in Medicare-covered patients with type 2 diabetes. *Diabetes Obes Metab*. 2012, 14:634-643
10. Johnston SS, Conner C, Aagren M, Smith DM, Bouchard J, Brett J. Evidence linking hypoglycemic events to an increased risk of acute cardiovascular events in patients with type 2 diabetes. *Diabetes Care*. 2011, 34:1164-1170
11. Green AJ, Fox KM, Grandy S; SHIELD Study Group. Self-reported hypoglycemia and impact on quality of life and depression among adults with type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 2012, 96:313-318
12. McCoy RG, Van Houten HK, Ziegenfuss JY, Shah ND, Wermers RA, Smith SA. Increased mortality of patients with diabetes reporting severe hypoglycemia. *Diabetes Care*. 2012, 35:1897-1901
13. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progressions of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993, 329:977-986
14. Miller ME, Bonds DE, Gerstein HC, et al.; ACCORD Investigators. The effects of baseline characteristics, glycaemia treatment approach, and glycated haemoglobin concentration on the risk of severe hypoglycaemia: post hoc epidemiological analysis of the ACCORD study. *BMJ*. 2010, 340:b5444
15. Mooradian, AD (2009) Dyslipidemia in type 2 diabetes mellitus. *Nat Clin Pract Endocrinol Metab*. 5: 150-159
16. Kadiyala R, Peter R, Okosieme OE. Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. *Int J Clin Pract*. 2010, 64(8):1130-1139
17. Brenta G, Danzi S, Klein I. Potential therapeutic applications of thyroid hormone analogs. *Nature Clinical Practice Endocrinology and Metabolism*. 2007, 3(9):632-640
18. Piette JD. Patient education via automated calls: A study of English and Spanish speakers with diabetes. *Am J Prev Med*. 1999, 17:13138-41
19. HbA_{1c} and Risk of Severe Hypoglycemia in Type 2 Diabetes: The Diabetes and Aging Study *Diabetes Care* November 2013 36:11 3535-3542; published ahead of print July 30, 2013, doi:10.2337/dc13-0610.
20. One adult in ten will have diabetes by 2030. International Diabetes Federation. November 14, 2011. Available at <http://www.idf.org/media-events/press-releases/2011/diabetes-atlas-5th-edition>.
21. American Geriatrics Society. Five things physicians and patients should question: Choosing Wisely: an initiative of the American Board of Internal Medicine. <http://www.choosingwisely.org/doctor-patient-lists/american-geriatrics-society/>. Accessed August 5, 2013