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HYPOGLYCAEMIA

FREQUENCY OF HYPOGLYCAEMIA IN DIABETIC PATIENTS WITH NEPHROPATHY AT NATIONAL INSTITUTE OF DIABETES AND ENDOCRINOLOGY (NIDE) DOW UNIVERSITY OF HEALTH SCIENCES (DUHS), KARACHI

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ABSTRACT... Objectives: Find out the hypoglycaemia in patients with diabetic nephropathic patients. **Study Design:** Cross sectional study. **Setting:** National Institute of Diabetes & Endocrinology at Dow University Hospital, Ojha Campus, Karachi. **Duration of Study:** For the period of one year, from October 2014 to November 2015. **Methodology:** Known "diabetic patients" with nephropathy which were present at National Institute of Diabetes & Endocrinology, Dow University Hospital, Ojha Campus, Karachi Patients presenting with signs and symptoms of hypoglycemia are diagnosed cases of "diabetes mellitus with nephropathy", age 30 and above, Type-I and type-II diabetes mellitus, on oral hypoglycemic agents I insulin were included in this study. Questions regarding the time period for which patient has been using these drugs and if the patient is suffering from illness which may be acute or chronic, should be asked regarding the relevant disease & its association with hypoglycaemia be mentioned, & patients urine D/R & Serum Creatinine & Urea are measured by sending to the appropriate laboratory. Patients with severe malnutrition and starvation, chronic liver disease, alcoholics, chronic disease as tuberculosis, patients with renal diseases without diabetes, any other malignancy patients were excluded from this study. **Results:** Depending upon the selection of 200 patients, the result concluded in our study consisted of 54% male patients and 46% were females, out of which 11% had type I and diabetes and type II diabetics constituted 89%. Most of the patients age between 60 to 75 years of age. The average duration of diabetes was 12.20 + 6.14 years. Out of 24 hypoglycaemic patients, 6 (25%) had type-I diabetes in which 4 were male and 2 was female while 18 (75%) had type-II diabetes in which 10 were male and 8 were female patients. **Conclusion:** Observed that hypoglycaemia was common in diabetic patients, who developed renal failure due to diabetic nephropathy.

Key words: Nephropathy, Renal failure, Diabetes mellitus, Hypoglycaemia.

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INTRODUCTION

Diabetes is associated with altered metabolism of carbohydrates, proteins & fats. There are two main types of diabetes which are referred to as type 1 and type 2. Previously the diabetes was known by juvenile onset and adult onset diabetes & also depending upon the insulin requirements as depending on insulin or non-insulin dependent. Among the various symptoms of diabetes, the common symptoms include polyuria, polydypsea, fatigue & increased satiety.[1]

There are 171 million people worldwide suffer from diabetes, & the estimation is more prevalent by 2030 especially with respect to the prevalence of type 2 diabetes in developed countries worldwide.[2] Diabetes mellitus includes the disorders of carbohydrate metabolism which is manifested by hyperglycaemia in the long run & resulted in microvascular& macrovascular complication of diabetes leading to diabetic nephropathy as a microvascular complication.[3]

"Diabetic nephropathy" is a chronic renal disease with collection of symptoms which constitutes albuminuria, declining glomerular filtration rate (FGR). As the excretion of protein increases, as a microvascular complication, the kidneys

progressively detoriates its functioning ability.[4] There are various tests which can be used for detecting diabetic nephropathy but the most sensitive of all is albuminuria which can be micro albuminuria (20-200micrograms/min.) or macro albuminuria (>200 micrograms/min.) or labelled as overt proteinuria.[5] Eventually the end stage is renal failure.

There is predisposition of Asian population in various studies in which it is stated that Asians are prone to diabetic nephropathy because of various factors leading to diabetic predisposition, increased BMI, increased body Fat composition & uncontrolled Diabetes. Various factors which predispose to microvascular complications such as diabetic retinopathy which is proliferative variety, accompanies nephropathy along with hypoglycaemia.[6]

There is high prevalence of diabetes in Pakistan. Greater than 10% of the adult population suffers from diabetes. In Pakistan, 5.54 million people had diabetes in 1995 but in 2000 about 6.99 million people had diabetes with a prevalence of 4.66%, however it is estimated that in 2025, it will be 14.5 million with a prevalence of 6.76%. Pakistan will be the fourth country in the world with diabetes by 2025 after India, China and the USA respectively.[7] Another study conducted in Lahore, showed, type1 to type-2 diabetes ratio of 1:3.[8] A survey conducted in rural areas of North West Frontier Province (NWFP) by Pakistan National Diabetes Survey has shown prevalence of 11.1% and 9.4% for diabetes and IGT respectively. Prevalence of type-2 diabetes and IGT was 9.2% for men and 11.6% for women.[6] The prevalence rates are higher in men (11.6% urban, 10.3% rural) as compared to women (10.6% urban, 4.8% rural). Various studies have emphasized the need for diabetes education at all levels, both for the patients as well as the health care providers to counter the pandemic of diabetes related complications globally. As per WHO recommendation, there should be prioritization regarding the education programmes which are required to educate the patients a better knowledge, prevention, and to prevent complications, and premature morbidity & mortality concerned with patients suffering fromdiabeest.[10]

SUBJECTS AND METHODS

Known "diabetic patients" with nephropathy which were present at National Institute of Diabetes & Endocrinology, Dow University Hospital, Ojha Campus, Karachi Patients presenting with signs and symptoms of hypoglycemia are diagnosed cases of "diabetes mellitus with nephropathy", age 30 and above, Type-I and type-II diabetes mellitus, on oral hypoglycemic agents I insulin were included in this study. For these patients if blood sugar level was found below "45- 50mg/dl". Firstly "hypoglycemic patients" were treated. Detailed history; specific information regarding duration of diabetes and anti-diabetic drugs which were used by the patient was collected. Moreover questions regarding the time period for which patient has been using these drugs and if the patient is suffering from illness which may be acute or chronic, should be asked regarding the relevant disease & its association with hypoglycaemia be mentioned, & patients urine D/R & Serum Creatinine & Urea are measured by sending to the appropriate laboratory. Patients with severe malnutrition and starvation, chronic liver disease, alcoholics, chronic disease as tuberculosis, patients with renal diseases without diabetes, any other malignancy patients were excluded from this study.

RESULTS

Patients were of the average age of 61.28 ± 10.34 years (95% CI; 59.23 to 63.33). Patients mostly belonged to the age group of 60 to 75 years. The average duration of diabetes was 12.20 ± 6.14 years (95% cr. 10.98 to 13.42). The average with 95% confidence interval, median with IQR and minimum & maximum observation& variables such as weight, along with blood pressure recordings along with respiratory rate of the patients are also presented in table-I.

Out of 100, 54% were males and 46% were female patients making male to female ratio of 1.2:1. 11% had type-I diabetes & 89% were associated with type-II diabetes. The average blood sugar of

Variables	Mean ± SD	95% CI	Median (IQR)	Max-Min
Age (years)	61.28 ± 10.34	59.23 to 63.33	60 (14)	82 – 30
Duration of diabetes (years)	12.20 ± 6.14	10.98 to 13.42	12 (10)	25 – 2
Weight (Kg)	73.34 ± 8.55	71.64 to 75.04	76 (11)	88 – 46
Pulse	93.76 ± 11.75	91.43 to 96.1	92 (20)	120 – 68
SBP, mmHg	146.75 ± 19.95	142.79to 150.7	150 (20)	210 – 90
DBP, mmHg	82.90 ± 11.72	80.57 to 85.23	85 (15)	120- 50
Respiratory rate	17.03 ± 3.06	16.42 to 17.64	16 (04)	28 – 12

Table-I. Descriptive statistics of study variables (n=200)

diabetes patients was 161.0 ± 12.8mgldl (95% CI; 137 to 185.3). The average proteinuria 1154.6 + 482.3mg/dl (95%CI: 1058 to 1251), blood urea 53.7 - 14 (95% CI: 137 to 185.3.7 14) and serum creatinine 2.73 _ 1.7 (95%CR.4 to 3.1) are presented in table-II. The signs and symptoms presented in accordance with their percentages are 72% of the patients presented with "tremor"s, followed by "dizziness" 71%, "palpitations" "55%, sweating" "49%, confusion" "42%, slurred speech" "23%, intense hunger10%"&"loss of conscious 4".

From 200 patients, 12% were suffering hypoglycemia (blood sugar <45 -50mg/dl) where as 88% were non-hypoglycemic patients. Out of 24 hypoglycaemic patients, 6 (25%) were in type-I diabetes patients in which 4 were male and one was female while 18 (75% were in type-II diabetes patients in which 10 were male and 8 were female as shown in table-III.

Palpitations, dizziness, tremors, intense hunger, slurred speech were not significant between hypoglycaemic patients than non-hypoglycaemic patients while sweating, confusion and loss of conscious were significantly high in hypoglycaemic patients than non-hypoglycaemic patients as shown in table-IV.

Variables	Mean ± SD	95% CI	Median (IQR)	Max-Min
Blood Sugar (mg/dl)	161.2 ± 12.8	137 to 185.3	114.5 (16)	476 – 30
Proteinuria (mg/dl)	1154.6 ± 482.3	1058 to 1251	1075 (782)	2368 – 153
Blood urea	53.7 ± 14.0	50.7 to 56.7	56 (24)	84 – 28
Serum creatinine	2.73 ± 1.7	2.4 to 3.1	2.1 (2.1)	8.2 – 0.9

Table-II. Descriptive statistics of investigation of the patients (n=200)

Diabetes Mellitus	Male	Female	Total
Type-I	4	2	6 (25%)
Type-II	10	8	18 (75%)
Total	**14 (58.3%)**	**10 (41.7%)**	**24**

Table-III. Hypoglycaemia patients according to gender and type of diabetes mellitus (n=24)

DISCUSSION

This purpose of this study was aimed to observe the "frequency of hypoglycemia in diabetic patients with nephropathy". As in diabetic patients "hypoglycaemia" which is the major factor in limiting the glycaemic control to an extent that limits strict control & this leads to complications & neurological manifestations[11] of 200 patients of type-1 and type-2 were observed in this study that had nephropathy, both male and female gender based on common autonomic and neuroglycopenic symptoms.

Eleven percent (11%) of the total patients constituted of type-1 diabetes, type-1 and type-11 diabetes ratio is almost the as observed in rest of the world including Pakistan (around 10%).[12] There is male preponderance in diabetics with nephropathy were observed which might be related to smoking & central obesity more

Clinical presentation	Hypoglycaemic patients (n=24)	Non-Hypoglycaemic patients (n=176)	P – value
Sweating	24 (100%)	74 (42%)	0.0001*
Palpitations	18 (75%)	92 (52.3%)	0.134
Dizziness	14 (58.3%)	128 (72.2%)	0.303
Confusion	18 (75%)	66 (37.5%)	0.014*
Tremors	22 (91.7%)	122 (69.3%)	0.106
Intense hunger	4 (16.7%)	16 (9.1%)	0.412
Slurred speech	8 (33.3%)	38 (21.6%)	0.365
Loss of conscious	6 (25%)	2 (1.1%)	0.0001*

Table-IV. Clinical presentation of hypoglycaemic and non-hypoglycaemic patients
**Significant*

common in male gender. more prevalence of nephropathy in male gender has been shown in study carried out by Gross JL et al.[13] In our study type-I diabetic patients were 22 in which 6 patients (25%) presented with hypoglycemia in one year.

Leese GP[14] et al conducted a population survey in a Scotland region in which all episodes of severe hypoglycaemia were attended at emergency medical service provider around the clock over the period of 12 months. In those, 160 patients were recorded for hypoglycaemia, the total episodes of them were around 244. If we take into consideration the Incidence rates for the patients who were treated with insulin was as low as 11.5 to 11.8 events per 200 patients presented or registered in one year time period. The risk factors for severe hypoglycemia were identified as Age, duration and socioeconomic status. In our study patients with poor socioeconomic condition and type- II diabetes mostly presented with longer duration of diabetes. If we take into consideration for further evaluation of type-2 diabetics for those who consumed metformin were appx. 2.4%, sulfonylurea were taken by appx. 3.3% & 11.2% of those were reported for being having hypoglycaemia which were on insulin regime. So, the incidence was highest in patients using Insulin treatment.

In Diabetes Control and Complications Trial (DCCT) it was estimated that if we do tight glycaemic control, with intensive intervention, the follow up of these patients showed that 65% of those underwent severe hypoglycaemic episode as compared to UKPDS Study, which was done on new diagnosed patients with poor glycaemic control. The frequency of hypoglycemia in type – 2 diabetes was well underestimated by UKPDS data.[15]

It was observed by Molitch ME[16] et al that around 20-40% of both types of diabetes develop nephropathy at certain period of their life in the long runs if not treated properly >75% after 20 years of uncontrolled diabetes. According to Rossing K[17] et al overt nephropathy was diagnosed in approximately 3% of newly diagnosed type-2 diabetic patients.

Study was done by Earle KK[18] et al who explained in which various patients were admitted here for renal replacement, among which 30-40% patients from diabetic nephropathy. The incidence was higher in type 2 diabetics than type 1 diabetics with reference to occurrence of nephropathy & was concluded that was 10 times higher. The incidence was also greater in “Indo-Asian” and “African Caribbean” origin if we compared those to “Caucasians”. Detoriated rate of renal functions accelerated in “Indo-Asian subjects” The significance of our study is that we can demonstrate the difference in relation to the type of diabetes in association with nephropathy & its consequences on hypoglycaemia separately if we do compare to other studies.

Renal failure impairs the metabolism of insulin

and other oral hypoglycemic drugs, causing frequent hypoglycemic attacks in these patients. Rashid K[19] et al conducted a study in Pakistan in which it was observed that a reduction in insulin requirement of about 28.2 -60% in type-I diabetic and about 35.2% of patients who were diagnosed with type-2 diabetes do not need insulin as there is progressive renal failure as a consequence of nephropathy. In Germany study was conducted in which the incidence of hypoglycemia was estimated in patients with type-2 diabetics who were enrolled in a study over the duration of 4 years. According to the study 148 patients with type 2 diabetes had severe hypoglycemia for which they attended the emergency department.

In insulin treated type 2 diabetes, the annual rate of severe hypoglycemia was 1.5 episodes per 200 patients if we do compare them with a rate of 0.4 episodes per 200 patients for the overall group of type-2 diabetic patients. Various factors were considered in our study with Advanced age (76+/-12 years) & detoriated renal function in 54% of patients (80 /148 patients) which are considered the most frequent contributing factor leading to hypoglycacmia in type-2 diabetic patients.

The patients who were suffering from type-2 diabetes were middle aged or were mostly elder; if we do accurately measure the frequency of hypoglycaemia in this age group there was usually underestimation with regards to the frequency of hypoglycaemia as a consequence of nephropathy.[20] Numerous patients suffering from type-2 diabetes have little knowledge of symptoms and proper treatment of hypoglycemia. Same was experienced by us during our study. Considering above discussion it is found that there was a great difference with respect to the frequency of hypoglycemia if we do consider the results as shown in them.

It was observed through this study, taking into consideration of various symptoms 12% of those had actual hypoglycemia, 88% of those were euglycaemic. Major patients were of old age group & It was also found through examination and history of patients that the majority if these patients were also lost to follow & for that reason they were receiving treatment for a long period of time without change in dose and medications. These patients had major problem with drug compliance. Some patients try to maintain strict glycemic control and neglecting their renal function. There is wide variation of hypoglycaemia in various studies worldwide, & there was a wide variability In various studies worldwide it was found, there is a wide variation of hypoglycemic episodes in diabetic patients due to multiple factors; & we did mention few important problems out of those.[21]

Patients suffering from nephropathy were selected in this study on the basis of signs and symptoms of hypoglycemia by not taking into account the stage of nephropathy or renal failure As most of the patients were elderly the accuracy of this study is doubtful. Particular types of diabetes were not selected in this study and during this study neither the duration of diabetes nor was particular class of drug patients were using taken into account.

CONCLUSION

Therefore it is concluded through this study that “diabetic patients suffering from nephropathy” will be exposed to “hypoglycemia” as a greater predisposing factor. As these patients are much prone to undergo end stage renal disease which is the contributing factor for Renal Failure as a consequence, the various medications which may contribute to renal impairment. So, these high risk patients should be considered for regular follow up & renally adjusted doses should be prompted at the earliest possible time to prevent the complications.

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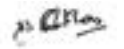
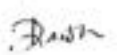
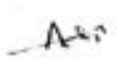
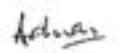
1	Dr. Muhammad Umar Khan	Conception and design, Statistical expertise,	
2	Dr. Darshan Kumar	Critical revision of the article for important	
3	Dr. Adil Faraz	intellectual content. Data Collection	
4	Syed Muhammad Adnan	Drafting of the article Data collection	
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