

Prevalence of Hypoglycemia Among type 2 diabetes mellitus (T2DM) patients attending the National Center for Diabetes Endocrinology and Genetics Amman, Jordan.Nisser M Alhroub^{1*}, Ali Alzubi²¹Al Neelain University Faculty of Nursing Sciences, Department of Community health Nursing.²Jordan University Faculty of Nursing Sciences

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Abstract: Hypoglycemia and recurrent hypoglycemia may be associated with a significant increase in the risk of major macrovascular and microvascular events and recurrent hypoglycemia was associated with arise in mortality, morbidity. The objectives of this study are to estimate the prevalence of hypoglycemic episodes in T2DM patients attending the National Center for Diabetes, Endocrinology and Genetics and to estimate the rate of hypoglycemic unawareness in these patients and to determine the risk factors associated with hypoglycemic episodes. Across-sectional study was carried out at the National Center for Diabetes ,Endocrinology and Genetics (NCDEG) in Amman-Jordan, conducted from 1st of November 2012 to 1st of March 2013 .A total of 1055 patients with type 2 diabetes according to (ADA) and on one or more hypoglycemic agents .Data collected on the severity and frequency and symptoms of hypoglycemic episodes in the 3 month prior to enrollment based (Hypoglycemic Health Assoc. of Australia Questionnaire). of 1055patients with type 2 diabetes mellitus who aged between 21-85years 499males 47.3% and 556 females 52.7%,25.6%had controlled HBA1c, 67.7%were on insulin treatment, 39.8%of them are having type 2 DM for more than 10 years, 57.7% of them were obese with a mean (SD)of the BMI 31.2kg/m²(4.9).Prevalence of hypoglycemia was 46.6% for patients with hypoglycemic symptoms .Logestic regression analysis revealed that occupation, duration of diabetes , HBA1C level , diabetic nephropathy, diabetic foot and type of medication were significant correlated with hypoglycemic episodes . Hypoglycemia is common among Jordanian patients with type 2 DM attending the NCDEG, to maintain glycemic control and prevent hypoglycemia attack should be designed schedule for education concerning self monitoring of blood glucose, diet, medication, and lifestyle. Encourage patients to treat hypoglycemia episodes if showed immediately and don't delay in treating hypoglycemia.

INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from defect in insulin secretion and/or insulin resistance (Wild S, 2004). Diabetes mellitus type 2 (T2DM) is common problem worldwide. The prevalence of T2DM among persons aged more than 20 years has been

estimated to increase between 2010and 2030from 6.4 %(285million) to 7.7 % (439millions) (Shaw J,2010),. The prevalence of T2DM in Jordan has increased from 13%to 17%over the past decade (Ajlouni K,et al 2008).

Hypoglycemia is the most common complication of intensive diabetes therapy

and was important limiting factor in the treatment and serious problem among patients with diabetes mellitus.(Cryer PE ,2002) The prevalence of hypoglycemia is dependent on type of diabetes therapy; mainly the sulfonylureas that stimulate the pancreas to release insulin and insulin therapy. However, there may be important differences in hypoglycemic risk, depending upon the type and duration of diabetes. (UK hypoglycemia, 2007) study group.

United Kingdom Prospective Study found that 31% of patients with type 2 on oral hypoglycemic agents (OHA) experienced mild hypoglycemic symptoms in the first year of the study(UKPDS,1998) , and other studies reported the prevalence hypoglycemia among T2DM is 63% (Elizabeth Marret ,et al 2011),in US national health and wellness survey and reached 24.5%in African American population with type 2 diabetes (Christopher D, et al 2001) . Symptoms of are due to sympathoadrenal activation symptoms (sweating ,sensation of warmth ,anxiety, tremor, nausea ,hunger, palpitation, and tachycardia)which are considered minor symptoms, and symptoms of neuroglycopenia (fatigue, dizziness, drowsiness, confusion , seizure, loss of consciousness) which are considered severe symptoms that need assistance (Amiel SA ,et al,2008) .

Recent studies have shown that severe hypoglycemia and recurrent hypoglycemia may be associated with a significant increase in the risk of major macrovascular and microvascular events and recurrent hypoglycemia was associated with arise in mortality ,morbidity (MacLeod KM, Hepburn DA, Frier BM, 1993), lower quality of life, (Fernando Alvarez ,2010)limitations of skilled tasks such as driving or operating machines and equipment(Lundkvist J,2005), and utilization of health care resources and increased treatment cost whether hospital

cost and indirect cost due to inability to work in those living alone with no one to provide assistance(Linus Jonsson,2006) .

Also hypoglycemia is clearly an important limiting factor in the glycemic management of patients with diabetes, and a significant barrier to adherence to medication which in turns leads to deterioration in glycemic control (Linus Jonsson,2006) .

After searching in literature, there are no studies in Jordan that investigated the prevalence of hypoglycemia.

Therefore, the aim of this study was to estimate the prevalence of hypoglycemia among T2DM patients attending the National Center for Diabetes, Endocrinology and Genetics (NCDEG).This study aimed to:

- Estimate the prevalence of hypoglycemic episodes in T2DM patients attending the National Center for Diabetes, Endocrinology and Genetics (NCDEG).
- Estimate the rate of hypoglycemic unawareness in T2DM patients attending the National Center for Diabetes, Endocrinology and Genetics (NCDEG).
- Determine the risk factors associated with hypoglycemic episodes in T2DM patients attending the National Center for Diabetes, Endocrinology and Genetics (NCDEG).

MATERIALS AND METHODS

Study design

A cross sectional study will be conducted during the period between 1st November 2012 to 1stFebruary 2013 on diabetic patients attending the national center for diabetes, endocrinology and genetics (NCDEG) in Amman, Jordan.

Setting

The National Center for Diabetes, Endocrinology and Genetics (NCDEG), was established in Amman 1996.

Sampling population:-

All patients with type2 diabetes attending the national center for diabetes, endocrinology and genetics (NCDEG) in

Amman, Jordan during the study period will be the sampling frame from which the sample will be selected.

Inclusion/Exclusion criteria:-

Patients with type 2 diabetes mellitus were eligible for the study. Patients with type 1 diabetes, pregnant women, and any patient who didn't signed the informed consent or the questionnaire is not completely answered, and with first visit to the center, were excluded from study.

Sampling technique:

A face to face structured interview started there by the researcher in front of the participant with maintaining privacy, reading the questions loudly and clearly to him/ her, then writing participant's answers on the questionnaire form. Finishing the interview with the first one on the list, the next patient invited, until finished either the clinic or the list, which ever finished first.

Sample size:-

The sample size will be calculated using the following equation ($n = (Z_{\alpha/2})^2 Pq / \Delta^2$) with a confidence level of 95%, expected prevalence of 45%, and margin error of 3%, which was found to be 1055 participants.

Ethical consideration:-

Consent forms were handed for each of those who accepted to participate in the study. The study was conducted after it has been approved by the ethical committee in the National Center for Diabetes, Endocrinology and Genetics. Participants will be assured confidentiality of information and their names will be kept confidential, and can withdraw at any time.

Data collection:-

The data were collected by using the following sources:-

1-Medical records:

The medical records were used to collect the following data:

Weight in kilograms , Height in meters. BMI (will be obtained by dividing the

weight in kilogram on the square of height in meters). Hemoglobin (HbA1c) last three reading, the last reading of blood pressure, last reading kidney function test

2- Structured questionnaire:

A face to face structured interview questionnaire which were administered while waiting for their turn with their treating physician.

Statistical analysis

Statistical analysis were carried out using the statistical package for social sciences (SPSS, version 17.0), under the guidance and supervision of a biostatistician. Descriptive statistics were obtained such as mean values for continuous and proportions for categorical variables. Chi-square was used to test for independent distribution of categorical variables where appropriate. Multiple logistic regression were used to examine the net effect for each of the proposed variables on hypoglycemic episode P-value less than 0.05 were considered statistically significant.

RESULTS

Table (1). This study included a total of 1055 patients with type 2 diabetes mellitus (499 males 47.3% and 556 females 52.7%), aged between (21-85) years with a mean age (SD) of 57.5(±9.45) years.

Table (2) also showed (32.3%) of participants were on oral hypoglycemia agents (metformin, glibenclamide, glimepiride, gliclazide MR, repaglinide), 67.7% were on insulin treatment (basal insulin, premixed insulin, basal/bolus insulin).

Table (3). Chi-square and its p-value of distribution of hypoglycemia by Socio-demographic and clinical characteristics. The overall frequency of hypoglycemia in the study participants was 46.6 %.

Table (4) shows that patients on insulin therapy were 1.79 times more likely to have

hypoglycemic attack than those on oral hypoglycemic agents ($t(p\text{-value}=0.001)$)

Discussion

This study aim to assess the prevalence of hypoglycemia episodes and assess hypoglycemia unawareness and associated factor among T2DM patients who attended the out patients clinics at the National Center for Diabetes, Endocrinology and Genetics (NCDEG).

As a national center receiving patients from all over the kingdom either directly or indirectly through referrals from other clinics or hospitals in Jordan, we believe that patients with diabetes mellitus who were included in this study may be representative of all diabetic patients in Jordan.

Approximately half of patients (46.6%) reported having hypoglycemia episodes in the 3 months prior to enrollment; 36.2% had mild level of hypoglycemia, 33.8% had moderate level of hypoglycemia and 30% had a severe level of hypoglycemia.

Sympathoadrenal activation and counter regulatory hormones play an important role in restoring the normoglycemia during the episodes of hypoglycemia through metabolic changes. hypoglycemia leads to hemodynamic and hematologic changes in patients with diabetes who had already developed an endothelial dysfunction, that increase risk of tissue ischemia and release of inflammatory cytokines. white cell activation, vasoconstriction and vascular events, which explain the high risk of cardiovascular disease among patients with hypoglycemia.

The prevalence of hypoglycemia in this study is higher than previously reported in the US population by Miller (24%) (Christopher D, et al 2001) and lower than (63%) reported by Zhang and (Elizabeth Marret, et al 2011) also higher than reported in seven European countries by Alvarez-Guisasola (38%) (Alvarez Guisasola F, et al, 2008) and by pettersson (34%) in Sweden (Billie Patterson, et al, 2011) ⁽¹⁵⁾.

These difference in reported the prevalence of hypoglycemia across study are clear, due to different study design, definitions of hypoglycemia and difference of cut point determine of hypoglycemia, treatment modalities and population.

In this study, hypoglycemia was defined by reporting the symptoms of low blood glucose in the previous 3 months, rather than being defined by self monitoring of blood glucose level.

Our study indicated that patients with longer duration of diabetes and glycemic uncontrolled had increased risk for hypoglycemia the probably presents more profound beta cell failure leading to decrease the ability to counter regulate glucose changes made by anti hyperglycemic medication leading to neuroglycopenia, in potentially unsuccessful attempts to lower their high level of HBA1C.

Patients who reported severe level of hypoglycemia were 30% comparing to that reported by WHH, (Sheu WH, et al 2012). in the Asia pacific region through the 2007 in the RECAP-DM study during the 6 months prior to enrollment in which 20.8% of patients who experienced hypoglycemia; reported severe level of hypoglycemia.

Table (1) Frequency distribution of study sample by socio- demographic characteristics (N=1055)

Variables	n	%
Gender		
Male	499	47.3%
Female	556	52.7%
Age, mean $\pm$ SD(57.51 $\pm$ 9.45)		
<45	96	9.1%
45-65	738	70%
>65	221	20.9%
Education		
Illiterate	213	20.2%
School	388	36.8%
University	454	43%
Occupation		
Not employed	426	40.4%
Employed	271	25.7%
Retired	358	33.9%
Marital status		
Married	951	90.1%
Single	43	4.1%
Divorced/ Widow	61	5.8%
Income		
500<	568	53.8%
500-1000	423	40.1%
>1000	64	6.1%
Smoking		
Smoker	216	20.5%
Ex smoker	215	20.4%
Nonsmoker	624	59.1%
Duration		
<5	320	30.3%
5-10	315	29.9%
>10	420	39.8%
BMI		
Normal	117	11.7%
Over weight	329	31.2%
Obese	609	57.7%
Compliance to treatment		
Yes	903	85.6%
No	152	14.4%

Table (2) Frequency distribution of study sample by Clinical and Laboratory Characteristics (N=1055)

Variable	No	%
HBA1C, mean $\pm$ SD(8.11 $\pm$ 1.48)*		
Controlled	270	25.6%
Uncontrolled	785	74.4%
Cardiovascular diseases		
YES	115	10.9%
NO	940	89.1%
Cerebrovascular diseases		
Yes	20	1.9%
No	1036	98.1%
Retinopathy		
Yes	66	6.3%
No	989	93.7%
Nephropathy		
Yes	53	5%
No	1002	95%
Neuropathy		
Yes	56	5.3%
No	999	94.7%
Diabetic foot		
Yes	46	4.4%
No	1009	95.6%
Hypertension		
Yes	819	77.6%
No	236	22.4%
Dyslipidemia		
Yes	873	86.7%
No	182	13.3%
Medication		
Oral hypoglycemic agents		
Yes	341	32.3%
No	709	67.7%
Insulin treatment		
Yes	709	67.7%
No	341	32.3%
Site of injection	No (709)	
Thigh	22	3.1%
Arm	30	4.2%
Abdomen	657	92.6%
Frequency of insulin doses		
1	263	24.9%

2-3	435	41.2%
>3	11	1%
Lipohypertrorhy (among insulin treatment)	)709(	
Yes	140	13.3%
No	569	53.9%
Hypoglycemia		
Yes	490	46.6%
No	565	53.4%
Frequency of hypoglycemic episodes		
One time	111	10.5%
Two time	151	14.3%
Three times	128	12.1%
>3times	171	16.2%
Nocturnal hypoglycemia		
Yes	398	37.7%
No	657	62.3%
Hypoglycemia unawareness		
Yes	59	5.6%
No	996	94.4%
Severity of hypoglycemia		
Mild	236	36.1%
Moderate	221	33.8%
Severe	147	22.5%
Very severe	49	7.5% ^o
Self blood glucose monitoring		
Yes		
No	939	89%
	116	11%
Frequency self monitoring		
Once daily	231	21.9%
Twice daily	55	5.2%
Three times daily	61	5.8%
Once weekly	491	48.5%
Once monthly	104	9.9%

*HBA1C=control if <7%and uncontrolled≥7%

Table (3) Chi-square and its p-value of distribution of hypoglycemia by Socio-demographic and clinical Characteristics.

VARIABLE	ALL patients N=1055	With hypoglycemia (490)	P value
Gender			
Male	499(47.3%)	231 (46.3%)	0.92
Female	556(52.7%)	259(46.6)	
Age, mean $\pm$ SD(57.48 $\pm$ 9.5)			
<45	96(9.1%)	38(39.6%)	0.44
45-65	738(70%)	342(46.3%)	
>65	221(20.9%)	110(49.8%)	
Education			
Illiterate	213(20.2%)	111(52.1%)	0.06
School	388(36.8%)	185(47.7%)	
university	454(43%)	194(42.7%)	
Occupation			
Not employed	426(40.4%)	222(52.1%)	0.005
Employed	271(25.7%)	123(45.4%)	
Retired	358(33.9%)	145(40.5%)	
Marital status			
Married	951(90.1%)	441(46.4%)	0.7
Single	43(4.1%)	23(53.5%)	
Divorced/Widow	61(5.8%)	26(42.6%)	
Income			
500<	568(53.8%)	270(47.5%)	0.6
500-1000	423(40.1%)	189(44.7%)	
>1000	64(6.1%)	31(48.4%)	
Smoking			
Smoker	216(20.5%)	104(48.1%)	0.7
Ex smoker	215(20.4%)	95(44.2%)	
Nonsmoker	624(59.1%)	291(46.6%)	
Duration			
<5	320(30.3%)	96(30%)	0.000
5-10	315(29.9%)	138(43.8%)	
>10	420(39.8%)	164(39%)	
BMI*, Mean $\pm$ SD(31.2 $\pm$ 4.93)			
Normal	117(11.7%)	53(45.3%)	0.43
Over weight	329(31.2%)	144(43.8%)	
Obese	609(57.7%)	293(48.1%)	
Compliance to treatment			
Yes	903(85.6%)	405(44.9%)	0.01
No	152(14.4%)	85(55.7%)	
HBA1C, mean $\pm$ SD(8.11 $\pm$ 1.48)			
Controlled	270(25.6%)	69(25.6%)	0.000
Uncontrolled	785(74.4%)	421(53.6%)	
Cardiovascular diseases			
YES	115(10.9%)	72(62.6%)	0.000.
NO	940(89.1%)	418(44.5%)	
Cerebrovascular diseases			
Yes	20(1.9%)	12(60%)	0.22
No	1036(98.1%)	478(46.2%)	
Retinopathy			
Yes	66(6.3%)	38(57.6%)	0.06
No	989(93.7%)	452(45.7%)	

Nephropathy Yes No	53(5%) 1002(95%)	39(73.6%) 451(45%)	0.000
Neuropathy Yes No	56(5.3%) 999(94.7%)	32(57.1%) 458(45.8%)	0.09
Diabetic foot Yes No	46(4.4%) 1009(95.6%)	30(65.2%) 460(45.6%)	0.009
Hypertension Yes No	819(77.6%) 236(22.4%)	395(48.2%) 95(19.9%)	0.030
Dyslipidemia Yes No	873(82.7%) 182(13.3%)	418(47.9%) 72(39.6%)	0.04
Medication			
Oral hypoglycemic agents Insulin treatment	341(32.3%) 709(67.7%)	99(29%) 390(55%)	0.000
Frequency of insulin doses 1 2-3 >3	263(24.9%) 435(41.2%) 11(1%)	126(47.9%) 257(59.1%) 7(63.6%)	0.014
Lipohypertrophy Yes No	140(13.3%) 569(86.7%)	91(65%) 299(52.5%)	0.000

*BMI=considered normal <25kg/m², over weight 25-29.9kg/m², obesity ≥30kg/m²

Table (4) multiple logistic regression analysis of the effect socio-demographic ,laboratory and clinical factors on hypoglycemia

Variable	OR*	p_value
Occupation		
Retired	1	
Not employed	1.5	0.003
Employed	1.6	0.006
Duration		
<5	1	
5-10	1.78	0.001
>10	3.39	0.000
Compliance to treatment		
Yes	1	
No	1.33	0.17
1CHBA,mean±SD(8.11±1.48)		
Controlled	1	
Uncontrolled	2.75	0.000
Cardiovascular diseases		
NO	1	
YES	1.52	0.053
Nephropathy		
No	1	
yes	2.33	0.01
Diabetic foot		
No	1	
yes	1.97	0.03
Hypertension		
No	1	
yes	1.03	0.82
Dyslipidemia		
No	1	
Yes	1.26	0.07
medication		
OHA**	1	
Insulin	1.74	0.001
Lipohypertrophy		
No	1	
Yes	1.44	0.16
Frequency of insulin doses		
1	1	
2-3	1.01	0.6
>3	1.31	0.97

*OR= Odds Ratio

**OHA= Oral Hypoglycemic Agents

Our study is recall of the occurrence of hypoglycemia episodes may be inaccurate, especially for the mild symptoms that may be unreliable to recall in the previous 3 months. Better methods of classifying the severity level of hypoglycemia are needed, especially mild level that may be occurs due to another reason (headache, fatigue, and hypotension) other than low blood glucose level. However, hypoglycemia episodes were not verified by documentation the measurement of blood glucose level, just reported by a group of low blood glucose symptoms. Impact of hypoglycemia on the questionnaire score may be minimal, because it is a subjective measurement tool. To prevent long-term complications and avoid hypoglycemic episodes and maintain glycemic control should be designed schedule for education concerning self monitoring of blood glucose, diet, physiological insulin replacement, medication, and lifestyle. We recommended for patients keep your blood glucose meter and easily-consumable glucose with you at all times. and test your blood glucose before a high risk situation, such as driving a car or operating heavy machinery and prolonged exercise. Encourage patients to treat hypoglycemia episodes if showed immediately and don't delay in treating hypoglycemia. Subtle symptoms may occur and then get better temporarily. If you have any subtle or possible symptoms, test your blood glucose. If you can't test, treat it like a hypoglycemia.

CONCLUSION

Based on the results of the current study was conclude that.

- Prevalence of hypoglycemia among patients with type 2 diabetes mellitus in our study 46.6 % (499 male, 556female),
- According the frequency of hypoglycemia episodes 16.2%had more than three hypoglycemic episodes, 12.1%had three

hypoglycemic episodes, and 14.3% had two hypoglycemic episodes.

-According to the severity of hypoglycemic episodes 36.1% were mild, 33.8% were moderate, 22.5% were severe, and 7.5% were very severe.

-There is a significant association between hypoglycemic episodes and duration of diabetes, occupation, HBA1C level and diabetic nephropathy, diabetic foot and type of medication.

REFERENCES

- Ajlouni K, et al. An increase in prevalence of diabetes mellitus in Jordan over 10 years. J Diabetes Complications 2008 Sep-Oct;22(5):317-24. Epub 2008 Apr 16.
- Alvarez Guisasola F,et al,2008. Hypoglycaemic symptoms, treatment satisfaction, adherence and their associations with glycaemic goal in patients with type 2 diabetes mellitus: findings from the Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) Study. [Diabetes Obes Metab.](#) 2008 Jun;10 Suppl 1:25-32.
- Amiel SA ,et al:Hypoglycemia in type 2diabetes.Diabet Med 2008;25:245-254.
- Billie Patterson, et al.Self reported experience of hypoglycemia among adult with type 2 diabetes mellitus (Exhypo).Diabetes research and clinical practice 92(2011) 19-25.
- Christopher D, et al .Hypoglycemia in Patients With Type2 Diabetes Mellitus . Arch Intern Med.2001 ;161:1653-1659.
- Cryer PE. Hypoglycemia: The limiting factor in the glycemic management of type I and type II diabetes. Diabetologia 2002;45:937-48.
- Elizabeth Marret ,et al .Assessment of severity and frequency of self reported hypoglycemia on quality of life in patients with type 2 diabetes treated with oral anti hyper glyceimic

agents :Asurvey study .BMC research notes
2011,4:251.

Fernando Alvarez-Guisasola,Donald D
Yin,Gonzalo Nocea, Ying Qie, Panagiotis
Mavro.Association of hypoglycemia
symptoms with patients rating og their health
related quality of life state : a cross sectional
study . Health and Quality of life Outcome
2010, 8:86.

Linus Jonsson, Björn Bolinder, Jonas Lundkvist:
Cost of hypoglycemia in patients with Type 2
diabetes in Sweden .Mendeley 2006, 9:193-
198.

Lundkvist J,BerneC,Bolinder B,Jonsson L:the
economic and quality of life impact of
hypoglycemia . Eur J Health Econ 2005,
6:197-202.

MacLeod KM, Hepburn DA, Frier BM 1993
Frequency and morbidity of severe
Hypoglycemia in insulin-treated diabetic
patients. Diabet Med 10:238–245.

Shaw JE, Sicree RA, Zimmet PZ. Global
estimates of the prevalence of diabetes for 2010
and 2030. Diabetes Res Clin Pract 2010;87:4-
14

Sheu WH,et al. Hypoglycemia is associated with
increased worry and lower quality of life
among patients with type 2 diabetes treated
with oral antihyperglycemic agents in the
Asia Pacific region.Diabetes Ris Clinic
Pract.2012Jan20.

UK hypoglycemia study group. Risk of
hypoglycemia in types 1 and 2 diabetes:
effects of treatment modalities and their
duration. Diabetologia 2007;50:1140-7

United Kingdom Prospective Diabetes Study
(UKPDS) Group. Intensive blood-
glucose control with sulphonylureas or
insulin compared with conventional
treatment and risk of complications in
patients with type 2 diabetes (UKPDS
33). Lancet. 1998;352:837–53.

Wild S,Rolic G,Green A. Global prevalence of
diabetes :estimate for the year 2000 and
projections for 2030.Diabetes Care 2004;
27:1047-53.