JOURNAL OF BIOMEDICAL RESEARCH & ENVIRONMENTAL SCIENCES
ISSN: 2766-2276
SUBJECT AREA(S): PUBLIC HEALTH | DIABETES
DOI: 10.37871

RESEARCH ARTICLE

Incidence and Costs of Hypoglycemia among Type II Diabetes Mellitus Patients in Turkey

Cihan Fidan*, Funda Salgur, Özdemir Efe Kul, Yusuf Bozkus, Gokhan Eminsoy, Fisun Sozen, Altug Kut and Ergun Oksuz*

Baskent University, Faculty of Medicine, Family Medicine, 06490, Ankara, Turkey

ABSTRACT

We aimed to determine the lifetime and one-year incidence of hypoglycemia in adults who had been treated following a diagnosis of Type II Diabetes Mellitus (T2DM), the factors that affected this incidence, and its effect on the use of health care resources. The descriptive cross-sectional cost study included adult T2DM patients who had an outpatient examination. Using a face-to-face interview method, patients were required to complete a questionnaire containing questions about sociodemographic characteristics, T2DM diagnosis and treatment features, and hypoglycemia events. Episode treatment costs of the patients in whom hypoglycemia was observed were calculated as direct cost per episode from the payer perspective. The mean age of the patients (n = 220) was 48.1 ± 11.8 (range 26-79) years, and the mean duration of disease was 4.5 ± 3.0 (range 1-16) years. According to treatment modalities, the frequency of hypoglycemia in the last year was 4.7% in the patients receiving oral antidiabetic drugs and 32.7% in the patients using insulin. In addition, 61.9% of the patients who had a hypoglycemic event in the last year presented to hospital, and 57.7% of these patients were hospitalized because of the hypoglycemic event. The incidence of hypoglycemia was 18 episodes of hypoglycemia per 100 patient years for T2DM patients and 25 severe hypoglycemia episodes per 100 patient years for patients using insulin. Significant predictors of hypoglycemia included insulin therapy (p = 0.000), regular use of medications (p = 0.013), hospitalization in the last year (p = 0.008), and exercise (p = 0.042). The average cost of a hypoglycemic event was calculated as Purchasing Power Parity İn Dollars ($PPP) 1.370.2 ± 1.407.0 (149.8-5,048.8). T2DM complications are the cause of a high economic burden. Hypoglycemia, which is one of these complications, is observed more frequently in patients who receive insulin therapy, who use regular medication, who do not exercise regularly, and who have been hospitalized in the last year.

INTRODUCTION

Diabetes (DM) is a global health problem with gradually increasing severity that causes significant morbidity and mortality. DM is present in approximately 9.3% of the world population. Worldwide, 11.3% of deaths are caused by DM. In 2019, DM accounted for 12.0% of the total health care expenditure for adults with a cost of $760 billion [1]. According to the International Diabetes Federation Diabetes Atlas, Turkey was the country with the highest age-standardized prevalence of DM in the European region in 2019 (11.1%, the national prevalence was 12.0%). In addition, Turkey ranks third in Europe in terms of the number of patients. According to the IDF forecast in terms of the number of diabetic patients in 2045, Turkey will be among the top ten in the world. In 2019, Turkey had the highest ratio of expenditure resulting from DM-related diseases to the total health care expenditure (23.8%) in the European region [1].

According to the Ministry of Health and Social Security Institution (SSI) (National Health Reimbursement Authority) data, the number of patients with diabetes in

***Corresponding author**

Cihan Fidan, Baskent University, Faculty of Medicine, Department of Family Medicine, Ankara Hastanesi, 06490, Ankara, Turkey

E-mail: fidancihan@gmail.com

Ergun Oksuz, Baskent University, Faculty of Medicine, Department of Family Medicine, Baglica Kampusu, 06770, Ankara, Turkey

E-mail: eoksuz@baskent.edu.tr

DOI: 10.37871/jbres1300

Submitted: 30 July 2021

Accepted: 25 August 2021

Published: 27 August 2021

Keywords

- Hypoglycemia
- Diabetes mellitus
- Incidence
- Cost analysis
- Epidemiology
- Therapeutics

MEDICINE GROUP

PUBLIC HEALTH | DIABETES

VOLUME: 2 ISSUE: 8

How to cite this article: Fidan C, Salgur F, Kul ÖE, Bozkus Y, Eminsoy G, Sozen F, Kut A, Oksuz E. Incidence and Costs of Hypoglycemia among Type II Diabetes Mellitus Patients in Turkey. J Biomed Res Environ Sci. 2021 Aug 27; 2(8): 705-712. doi: 10.37871/jbres1300, Article ID: JBRES1300, Available at: https://www.jelsciences.com/articles/jbres1300.pdf

Turkey in 2017–2018 was between 5.8 million (7.3%) and 8.3 million (10.3%) [2]. In 2012, DM accounted for 23.0% of the total health care expenditure paid by the SSI, corresponding to 10 billion Turkish Lira (TRY). Fifty-nine percent of this cost comprised treatment costs and 41.3% comprised drug costs [3,4]. Four and a half billion TRY was spent by the SSI in 2018 for the primary treatment of DM (5.0%) [5].

The most important acute complication in the treatment of DM is iatrogenic hypoglycemia, which is observed more frequently in patients with Type 1 Diabetes Mellitus (T1DM) and advanced T2DM. Hypoglycemia is more common in patients taking Sulfonylurea (SU), glinide, and insulin [6,7]. Common causes of hypoglycemia include increased glucose use (after exercise, etc.), increased insulin sensitivity (due to weight loss, after exercise, etc.), increased insulin levels during exercise (as a result of impaired glucose secretion), impaired counter-regulatory hormone response (especially during sleep), hepatic glucose output inhibition (after alcohol intake, etc.), insulin use in combination with Oral Antidiabetic Drugs (OAD), and previous history of hypoglycemia (hypoglycemia leading to hypoglycemia) [6,8].

Hypoglycemia also has negative effects on the development of cardiovascular complications and mortality in T2DM patients. In large studies, a high cardiovascular risk was found in patients randomized to intensive glycemic control and standard treatment arms [6,9,10]. In the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation study (ACCORD), the mortality rate was found to be higher in patients with one or more hypoglycemia episodes [10]. In the Veterans Affairs Diabetes Trial study (VADT), severe hypoglycemic episode was strongly associated with mortality on day 90 [11].

This study aimed to determine the lifetime and one-year incidence of hypoglycemia in adults who had been treated following a diagnosis of T2DM for at least one year, the factors that affected this incidence, and its effect on the use of health care resources.

MATERIALS AND METHODS

Before the cross-sectional descriptive epidemiological cost study was conducted, a preliminary statistical evaluation study found that at least 246 patients should be included in the study. Study inclusion criteria included having presented to the Endocrinology outpatient clinic of Baskent University Faculty of Medicine, Ankara Hospital because of DM, having agreed to participate in the study, being over the age of 18 years, and using at least one drug for DM for at least one year. There were no study exclusion criteria.

The data of 220 patients (89.5%) aged over 18 years who were followed up in the outpatient clinic throughout the study, who had been using at least one drug for DM for at least one year, and who were selected randomly during the study were analyzed. Participants were informed about the research, and signed informed consent forms were obtained from the patients who agreed to participate. Using the face-to-face interview method, patients were required to complete a questionnaire.

Clinically, hypoglycemia is classified into different types. Severe hypoglycemia is defined as episodes that require another person to actively apply carbohydrates, glucagon, or other corrective actions. The Plasma Glucose (PG) level may not be known during an attack; however, neurological improvement with the PG level returning to normal is considered to be evidence of an attack with a low PG level [12].

Documented symptomatic hypoglycemia means a PG value of 70 mg/dl in association with typical hypoglycemia symptoms. Cases where typical symptoms of hypoglycemia are absent despite a PG value of 70 mg/dl are classified as asymptomatic hypoglycemia. Possible symptomatic hypoglycemia means that typical hypoglycemia symptoms are present, the PG level is not determined, but the symptoms are probably caused by a PG concentration of 70 mg/dl. Pseudo-hypoglycemia is where any of the typical symptoms are present and the measured PG level is close to 70 mg/dl [12].

In the study, the costs were calculated from the payer perspective (the SSI; June 2020). The micro-costing methodology was used to produce the cost data. Non-medical direct expenditure, intangible costs and indirect costs were excluded from the calculation. Costs were calculated in US dollars ($) using 2019 Purchasing Power Parity ($PPP 1 = 1.8 TRY).

The research data were computerized and evaluated using Statistical Package for Social Sciences (SPSS) for Windows 17.0 (SPSS Inc., Chicago, IL, USA). The descriptive statistics were calculated as mean ± standard deviation, median (minimum–maximum), distribution, and percentage. In descriptive statistics, the Pearson Chi-Square Test and Fisher's exact test were used. The compatibility of the variables to normal distribution was examined using visual (histogram and probability graphs) and analytical methods (the Kolmogorov–Smirnov Test). The mean differences between groups were analyzed by Student's t-test. A $p < 0.05$ was considered statistically significant. To estimate the independent effect of each variable on hypoglycemia events, further statistical analysis was carried out by using logistic regression. The corresponding adjusted Odds Ratio (OR) and 95% Confidence Interval (CI) were obtained. The binary logistic regression analysis showed that there was no multicollinearity problem between the variables by checking collinearity statistics (tolerance >0.1 and variance inflation factor >10) and collinearity eigenvalue values in the multicollinearity research for independent variables before analysis. Heteroskedasticity was controlled by White's test.

RESULTS AND DISCUSSION

The mean age of the 220 T2DM patients who participated in the study was 48.1 ± 11.8 (range 26-79) years. The duration of diagnosis of diabetes was 4.5 ± 3.0 years. In addition, 37.7% of patients (n = 83) had at least one hypoglycemic event between the time of diagnosis of T2DM and the time of the study. The participants were divided into two groups: patients with hypoglycemia and patients without hypoglycemia (non-hypoglycemia). A total of 59 hypoglycemia episodes were observed in 42 patients in a calendar year. In the study, 18 hypoglycemia episodes per 100 patient years were detected for T2DM patients, and the incidence of severe hypoglycemia episode in patients using insulin was found to be 25 episodes per 100 patient years.

The mean age of the patients in the hypoglycemia group was 51.0 ± 13.2 years, and the mean age of the patients in the non-hypoglycemia group was 48.1 ± 11.8 years (p = 0.005). In addition, 67.3% (n = 148) of the patients were female. This rate was 66.3% in the hypoglycemia group and 67.9% in the non-hypoglycemia group (p = 0.804). Furthermore, 85.5% of the patients (n = 188) were married. In total, 47.3% of the participants (n = 104) were university graduates and 35.9% were secondary school graduates. The rate of university graduates was found to be 44.6% in the hypoglycemia group and 48.9% in the non-hypoglycemia group (p = 0.315). In addition, 65.5% (n = 144, p = 0.330) of the patients lived in the city center and 65.9% (n = 145) were public officers. Of the total number of patients, 34.1% (n = 75) smoked and 20.5% (n = 45) consumed alcohol. Moreover, 8.6% (n = 19) of the participants were living alone. While 3.6% of the patients in the hypoglycemia group were living alone, 50.6% of the patients were living with their spouse and children, and 45.8% were living with their spouse or children. These rates were 11.7%, 68.6% and 19.7% in the non-hypoglycemia group, respectively (p = 0.000) (Table 1).

In total, 48.6% (n = 107) of the patients were using OAD or OAD combinations, 30.0% (n = 66) were using insulin or insulin combinations, and 21.4% (n = 47) were using a combination of OAD and insulin. Moreover, 79.5% of the patients in the hypoglycemia group were using insulin, and this rate was 51.4% in the non-hypoglycemia group (p = 0.000). Among the patients who were using OAD, 57.0% were using biguanides, 11.5% were using Dipeptidyl Peptidase-4 İnhibitors (DPP4I), 10.6% were using SU, and 11.1% were using other OAD groups; 9.8% of the patients were using a fixed-dose OAD combination. Although the SU group was used more frequently in the hypoglycemia group, the difference was not significant (4.9% *vs.* 24.3%; p = 0.122). Among the patients who were using insulin, 36.5% were using long-acting insulin and 32.9% were using fast-acting insulin. In the hypoglycemia group, the rate of long-acting insulin use was 40.4%, and the rate of fast-acting insulin use was 37.5%, while these rates were found to be 30.2% and 25.4%, respectively, in the non-hypoglycemia group (p = 0.04) (Table 2).

Table 1: Sociodemographic characteristics of the participants according to the presence of hypoglycaemia.

Characteristics	Hypoglycaemia (N = 83)	Non- Hypoglycaemia (N = 137)	Total (N = 220)
	n (%)		
Age (mean, SD)*	**51.0 (13,2)**	**46.4 (10.5)**	**48.1 (11.8)**
Diabetes duration (mean,SD)	**4.4 (3.7)**	**4.6 (2.6)**	**4.5 (3.0)**
Gender			
Male	28 (33.7)	44 (32.1)	72 (32.7)
Female	55 (66.3)	93 (67.9)	148 (67.3)
Marital status			
Married	74 (89.2)	114 (83.2)	188 (85.5)
Single/Divorced	9 (10.8)	23 (16.8)	32 (14.5)
Education level			
Primary school	8 (9.6)	5 (3.6)	13 (5.9)
Middle School	30 (36.1)	49 (35.8)	79 (35.9)
University	37 (44.6)	67 (48.9)	104 (47.3)
Master degree	8 (9.6)	16 (11.7)	24 (10.9)
Working status*			
Blue collar	6 (7.2)	16 (11.7)	22 (10.0)
White collar	50 (60.2)	98 (71.5)	148 (67.3)
Retired	17 (20.5)	18 (13.1)	35 (15.9)
Unemployed	10 (12.0)	5 (3.6)	15 (6.8)

Income level (TRY/monthly)			
<2500	38 (45.8)	52 (38.0)	90 (40.9)
>2500	45 (54.2)	85 (62.0)	130 (59.1)
Municipality			
Rural	32 (38.6)	44 (32.1)	76 (34.5)
Urban	51 (61.4)	93 (67.9)	144 (65.5)
Living at home status*			
w/o spouse or childs	38 (45.8)	27 (19.7)	65 (29.5)
w/o spouse and childs	42 (50.6)	94 (68.6)	136 (61.8)
Alone	3 (3.6)	16 (11.7)	19 (8.6)
Habits			
Smoking	28 (33.7)	47 (34.3)	75 (34.1)
Alcohol	15 (18.1)	30 (21.9)	45 (20.5)

*$p < 0.05$

Table 2: Diabetes treatment and follow-up features of the participants according to the presence of hypoglycaemia.

Characteristics	Hypoglycaemia (*N* = 83)	Non-Hypoglycaemia (*N* = 137)	Total (*N* = 220)	*p* - value
	n (%)			
Treatment patterns				
OAD	17 (20.5)	90 (65.7)	107 (48.6)	0.000
OAD+Insulin	25 (30.1)	22 (16.1)	47 (21.4)	
Insulin	41 (49.4)	25 (18.2)	66 (30.0)	
Oral Antidiabetic Drug Groups*				
Biguanides	38 (54.3)	95 (57.9)	134 (57.0)	0.122**
Sulfonylureas	17 (24.3)	8 (4.9)	25 (10.6)	
DPP4 inhibitors	3 (4.3)	24 (14.6)	27 (11.5)	
Others	8 (11.4)	18 (11.0)	26 (11.1)	
Fixed-dose combination	4 (5.7)	19 (11.0)	23 (9.8)	
Insulin types*				
Long-acting	42 (40.4)	19 (30.2)	61 (36.5)	0.040***
Rapidly-acting	39 (37.5)	16 (25.4)	55 (32.9)	
Combinations	23 (22.1)	28 (44.4)	51 (30.6)	
Chronic diabetic complications				
Present	32 (38.6)	30 (21.9)	62 (28.2)	0.08
SMBG	81 (97.6)	134 (97.8)	215 (97.7)	0.916
Hospitalization in the past year				
Any reason	30 (36.1)	23 (16.8)	53 (24.1)	0.001
Diabetes-related	11 (13.3)	10 (7.3)	21 (9.5)	0.145
Daily medications count				
1-2	4 (4.8)	28 (20.4)	32 (14.5)	0.001
3-4	40 (48.2)	69 (50.4)	109 (49.5)	
>=5	39 (47.0)	40 (29.2)	79 (35.9)	
Exercise	40 (48.2)	86 (62.8)	126 (57.3)	0.034
Diet	46 (55.4)	63 (46.0)	109 (49.5)	0.175
Regular physician control	73 (88.0)	117 (85.4)	190 (86.4)	0.593
Reguler medications	62 (74.7)	122 (89.1)	184 (83.6)	0.005
Get support	33 (39.8)	50 (36.5)	83 (37.7)	0.628

OAD: Oral antidiabetics; DPP4: Dipeptidyl peptidase-4; SMBG: Self-Measurement Of Blood Glucose
*Multiple drug use is available; **Only for those using OADs; ***Only for those using Insulin

Self-measurement of blood glucose was being performed by 97.7% of the patients. In total, 24.1% (n = 53) of the patients had been hospitalized in the last year due to a health problem. This rate was 36.1% for the hypoglycemia group and 16.8% for the non-hypoglycemia group (p = 0.001). In addition, 9.5% of the patients had been hospitalized due to DM in the last year. This rate was 13.3% in the hypoglycemia group and 7.3% in the non-hypoglycemia group (p = 0.145). Furthermore, 14.5% of the patients were using one–two drugs daily. The rate of the patients using three–four drugs per day was 49.5%, and the rate of the patients using ≥5 drugs per day was 35.9%. In the hypoglycemia group, the rate of the patients using ≥5 drugs per day was 47.0%, and this rate was 29.2% in the non-hypoglycemia group (p = 0.001). While 48.2% of the patients in the hypoglycemia group were exercising, this rate was 62.8% in the non-hypoglycemia group (p = 0.034). Moreover, 55.4% of the patients in the hypoglycemia group and 46.0% of the patients in the non-hypoglycemia group were following their regulated diet (p = 0.175). The proportion of the patients who were using their drugs regularly was 74.7% (n = 62) in the hypoglycemia group and 89.1% (n = 122) in the non-hypoglycemia group (p = 0.005). It was reported by 37.7% of the patients that a relative helped with their treatment (Table 2).

Among the patients in whom hypoglycemia was observed, hypoglycemic event was experienced once in 37.3%, twice in 34.9%, and three or more times in 27.8%. Hypoglycemic event was experienced by 19.1% (n = 42) of the patients at least once in the last year. Among the patients in whom hypoglycemia was observed in the last year, hypoglycemic event was experienced once in 71.4%, twice in 21.4%, and three or more times in 7.2%.

According to treatment modalities, the frequency of hypoglycemia was 4.7% in the patients receiving OAD therapy in the last year, while it was 32.7% in the patients using an OAD and insulin combination or insulin alone (p = 0.000).

Patients reported that 42.2% of the previous episodes of hypoglycemia were resolved at home. In previous episodes of hypoglycemia, the rate of hospital admission was 57.8%, and 60.4% of these patients required hospitalization. The mean length of hospital stay was reported to be 1.9 ± 1.3 days (1–8 days) (Table 3).

In total, 61.9% (n = 26) of the patients who had hypoglycemic events in the last year had presented to hospital because of hypoglycemia. This rate was 20.0% in the patients using OAD and 67.5% in the patients using insulin. Seventeen patients (65.4%) had one hospital admission, seven patients (26.9%) had two hospital admissions, and two patients (0.9%) had three or more hospital admissions. There was no hospitalization due to hypoglycemic episode in the patients using OAD. Hospitalization because of hypoglycemic event occurred in 15 of the patients (60.0%) who were using a combination of OAD and insulin, and the mean hospitalization period was 1.6 ± 1.1 days (median 1.0 days, minimum–maximum 1-5 days) (Table 3).

Table 3: Features of hypoglycemic episodes by therapeutic modalities.

	OAD	Insulin	Total	p - value
Any time during the diagnosis of diabetes				
Number of patients with hypoglycaemia n (%)	17 (15.9)	66 (58.4)	83 (37.7)	0.000
Number of hypoglycaemia events mean (SD) (median; min-max)	1.2 (0.4) (1.0 ; 1-2)	2,4 (1.2) (2.0; 1-5)	2.1 (1.2) (2.0 ; 1-5)	
Number of patients				
Self-resolving n (%)	13 (76.5)	22 (33.3)	35 (42.2)	
Requiring health service application n (%)	4 (23.5)	44 (66.7)	48 (57.8)	0.001
Requiring hospitalization n (%)	-	29 (66.0)	29 (60.4)	N/A
Length of stay (days) mean (SD) (median; min-max)	-	1.9 (1.5) (1.0; 1-8)	1.9 (1.3) (1.0; 1-8)	
Last one-year				
Number of patients with hypoglycaemia n (%)	5 (4.7)	37 (32.7)	42 (19.1)	0.000
Number of hypoglycaemia events mean (SD) (median; min-max)	1.4 (0.9) (1.0; 1-3)	1.4 (0.8) (1.0; 1-4)	1.4 (0.8) (1.0; 1-4)	
Number of patients				
Self-resolving n (%)	4 (80.0)	12 (32.5)	16 (38.1)	
Requiring health service application n (%)	1 (20.0)	25 (67.5)	26 (61.9)	N/A
Requiring hospitalization n (%)	-	15 (60.0)	15 (57.7)	N/A
Length of stay (days) mean (SD) (median; min-max)	-	1.6 (1.1) (1.0; 1-5)	1.6 (1.1) (1.0; 1-5)	

OAD: Oral Antidiabetics; SD: Standard Deviation

Significant predictors of hypoglycemia in T2DM patients include insulin therapy (OR 7.9; 95% CI 2.7-22.9; $p = 0.000$), regular use of medications (OR 0.3; 95% CI 0.1-0.8; $p = 0.013$), hospitalization in the last year (OR 3.2; 95% CI 1.4–7.7; $p = 0.008$), and regular exercise (OR 0.4; 95% CI 0.2–0.9; $p = 0.042$) (Table 4).

Cost components in patients who presented to the outpatient emergency department included the following: examination (emergency outpatient examination and Endocrinology/Internal Diseases and/or Orthopedics/Neurosurgery or Cardiology or Neurology/Neurosurgery or Infectious Diseases consultations in 60% of the patients), laboratory and imaging tests, and treatment (intervention, medication and supplies). The average cost of these patients was $PPP 149.8, 8.0% of which was for the examination, 34.7% was for the laboratory and imaging tests, and 57.4% was for the treatment.

The average cost was found to be $PPP 1.008 in the patients who presented to the emergency department and were hospitalized. Among these patients, cardiac complications developed in 4.2%, cerebrovascular complications developed in 2.1%, and infectious complications developed in 2.5%; a total complications rate of 8.8% was included in the calculation. Cost components in this group of patients were as follows: 7.3% was for the examination, 21.0% was for the laboratory and imaging tests, 27.7% was for the inpatient treatment, and 44.0% was for the complications.

From the SSI perspective, the average hypoglycemic event cost was calculated to be $PPP 1,370.2 ± 1,407.0 (149.8–5,048.8) for the patients who experienced a hypoglycemic event and presented to hospital. The average annual cost of hypoglycemia for T2DM patients was found to be $PPP 161.9 ± 650.0 per patient.

In an analysis conducted to determine the incidence, risk factors and effects of hypoglycemia in T2DM patients, the incidence of hypoglycemia was found to be 1%. The main risk factors for hypoglycemia include intensive glycemic control, previous history of hypoglycemia, renal failure, presence of microvascular complication, duration of diabetes, low education level, and history of dementia [13]. In another study, it was found that hypoglycemia was observed at a significantly higher rate in patients who had macrovascular complications of diabetes and who did not perform regular physical activity [14]. In our study, the DM complication rate was higher in the patients with hypoglycemia (21.9% *vs.* 38.6%; $p = 0.08$). However, it was not found to be a significant predictor in regression analysis ($p = 0.857$).

It has been reported that the frequency of severe hypoglycemia ranges from 35 to 70 per 100 patient years in T2DM patients [6,7]. In the UK Hypoglycemia Study Group study, patients were grouped according to the type of treatment they used and duration of treatment. The rate of episodes of hypoglycemia reported by the patient and detected biochemically was 22%. The incidence of hypoglycemia was determined as four episodes per patient year in T2DM patients who had been using insulin for less than two years and seven episodes per patient year in the group who had been using SU or insulin for less than two years [7]. In a study in Scotland that included T2DM patients using insulin who were selected randomly, there were 16.4 episodes of hypoglycemia in T2DM patients, including five severe hypoglycemia episodes per patient year. The hypoglycemia predictors for T2DM were found to be previous history of hypoglycemia and duration of insulin therapy [6]. In our study, the frequency of hypoglycemia could not be differentiated according to the duration of the treatments, since the duration of treatment was determined as at least one year. In our study, the previous history of hypoglycemia was not different between the patients who had and had not experienced hypoglycemia in the last year.

In a study that included elderly DM patients using SU or insulin, the incidence of hypoglycemia per 100 person years was found to be 1.2 (95% CI 1.1-1.4) in the patients using SU and 2.8 (95% CI 2.5-3.1) in those using insulin. In that study, it was reported that the OR for severe hypoglycemia for the first 30 days after hospitalizations was 4.5 (95% CI 3.5-5.7) against the period after the first year following hospitalizations [15]. In our study, the OR for the patients

Table 4: Results of binary logistic regression on hypoglycaemic events for type 2 diabetes.

Variables	Odds ratio values			
	Value	%95 CI		*p* - value
Insulin therapy	7.889	2.722	22.868	0.000
Using medicines regularly	0.303	0.118	0.773	0.013
Hospitalization in the last year	3.237	1.361	7.697	0.008
Regularly exercise	0.387	0.155	0.965	0.042
Having diabetes complications	1.148	0.435	3.034	0.780
Age	0.978	0.928	1.031	0.404
Diabetes duration	0.955	0.813	1.122	0.578
Total number of drugs	0.975	0.745	1.277	0.855
Living alone	0.635	0.102	3.955	0.635
Active working	0.376	0.118	1.198	0.098
Constant	1.258			0.883

CI: Confidence İnterval; $N = 220$; $R^2 = 0.378$ (Nagelkerke); $R^2 = 0.235$ (Cox&Snell); Hosmer and Lemeshow Test: $X^2 = 7.175$; $p = 0.518$; Percentage Correct 83.6% Model: $X^2(10) = 59.036$, $p = 0.000$

who had hospitalizations was found to be 3.1 (95% CI 1.3-7.4; $p = 0.009$). Since the patients in our study were evaluated within a period of one year, it was not possible to evaluate the hypoglycemia episodes that could be observed after the first year following hospitalization.

There are studies showing that the rate of patients with hypoglycemia presenting to hospital is between 5% and 23%, and 95% of episodes require a health care intervention [9,16-20]. In our study, although the rate of emergency admission for patients using OAD was close to these rates, it was observed that 67.5% of hypoglycemia episodes in patients using insulin were resolved in the emergency room. In an analysis of emergency admissions over a period of 12 years in the USA, it was determined that 25% of hypoglycemia admissions resulted in hospitalization. The rate of admission to hospital with hypoglycemia was reported as 34 (95% CI 30-37) per 1,000 DM patients [21]. The length of hospital stay of the patients who were hospitalized for hypoglycemia was 5.5 days [22]. The mean hospitalization times were 9.8 days for patients using OAD and 8 days for patients using insulin [23]. In our study, the annual hospitalization rate due to hypoglycemia was calculated to be 6.8 for patients using insulin.

In a cost study involving Germany, Spain, and the UK that investigated the cost of severe hypoglycemia in DM patients and was conducted with 639 patients over the age of 16 years (T1DM 319 and T2DM 320) who developed hypoglycemia one or more times in the previous year, the highest cost element was found to be hospital treatment. The average cost of severe hypoglycemia was found to be higher in T2DM patients than in T1DM patients for all three countries. The cost of T2DM patients was €533 for Germany, €691 for Spain, and €537 for the UK. In the study, one or more hypoglycemia episodes in the previous 12 months occurred with a rate of 44.2% in T1DM patients and with a rate of 18.8% in T2DM patients in Germany. These rates were found to be 28.8% and 14.5% in Spain and 38.8% and 12.9% in the UK. In total, 43% of the hypoglycemia episodes in T2DM patients were treated in the hospital [19].

Our study has some limitations. The first of these is that the sample was chosen from a central university hospital. The cost calculation may represent the whole of Turkey as it was calculated from the SSI perspective; however, it should be kept in mind that resource utilizations may be different and more complicated patients may be treated in tertiary care hospitals. The mean age of our patients with T2DM was lower than the mean value of Turkey. Thus, the overall duration of DM treatment may be considered shorter compared to the mean value of Turkey. Therefore, the changes that may be caused over time by a chronic disease such as DM may not be reflected sufficiently in our study. In addition, it should be taken into consideration that the positive or negative conditions that might be caused by a treatment pattern were ignored, as we did not consider the current treatment periods of the patients in our study. In our study, we analyzed T2DM patients for a calendar year. This should be considered as a factor that prevented us from reflecting long-term results. Another limitation is that we did not investigate the symptoms at the time of presentation to the emergency room in the episodes of hypoglycemia experienced by the patients, and therefore, we could not evaluate the clinical features of hypoglycemia.

CONCLUSION

T2DM complications are conditions that cause a high economic burden. Hypoglycemia, which is one of these complications, is observed more frequently in patients who receive insulin therapy, who use regular medication, who do not exercise regularly, and who have been hospitalized in the last year. Severe hypoglycemia is a complication that leads to a significant hospital cost per episode.

AUTHOR CONTRIBUTIONS

Ergun Oksuz, Cihan Fidan, Ozdemir Efe Kul, Yusuf Bozkus, contributed to study conception and design; contributed to data acquisition, data analysis and interpretation, and writing of article; contributed to editing, reviewing and final approval of article.

Funda Salgur, Gokhan Eminsoy, Fisun Sozen, Altug Kut contributed to study conception and design; contributed to resources&materials acquisition, literature search and critical review of article.

INSTITUTIONAL REVIEW BOARD STATEMENT

Baskent University, Faculty of Medicine, Research and Ethics Committee and approved with project number KA17/202.

References

1. International Diabetes Federation, IDF, Diabetes Atlas 9e. 2019; Brussels: International Diabetes Federation.
2. Turkish Public Health Institution, Sagliknet Online Database, T.P.H. Institution., Editor. 2017; Ankara.
3. Ministry of Health General Directorate of Primary Health Care, Turkey Diabetes Prevention and Control Program Action Plan 2011-2014. 2011; Ankara.
4. Turkish Public Health Institution, Turkey Diabetes Program 2015-2020. 2014; Ankara.
5. SSI covered 8.3 million people's diabetes treatment costs in 2018. Anadolu Agency, 2019.
6. Donnelly LA, Morris AD, Frier BM, Ellis JD, Donnan PT, Durrant R, Band MM, Reekie G, Leese GP; DARTS/MEMO Collaboration. Frequency and predictors of hypoglycaemia in Type 1 and insulin-treated Type 2 diabetes: a population-based study. Diabet Med. 2005 Jun;22(6):749-55. doi: 10.1111/j.1464-5491.2005.01501.x. PMID: 15910627.
7. UK Hypoglycaemia Study Group. Risk of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. Diabetologia. 2007 Jun;50(6):1140-7. doi: 10.1007/s00125-007-0599-y. Epub 2007 Apr 6. PMID: 17415551.
8. Cryer PE. The barrier of hypoglycemia in diabetes. Diabetes. 2008 Dec;57(12):3169-76. doi: 10.2337/db08-1084. PMID: 19033403; PMCID: PMC2584119.
9. Leiter L, Yale JF, Chiasson JL, Harris S, Kleinstiver P. Assessment of the Impact of

Fear of Hypoglycemic Episodes on Glycemic and Hypoglycemia Management. Can J Diabetes. 2004;29(3):1-8.

10. Bonds DE, Miller ME, Bergenstal RM, Buse JB, Byington RP, Cutler JA, Dudl RJ, Ismail-Beigi F, Kimel AR, Hoogwerf B, Horowitz KR, Savage PJ, Seaquist ER, Simmons DL, Sivitz WI, Speril-Hillen JM, Sweeney ME. The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. BMJ 2010;340.
11. Duckworth W, Abraira C, Moritz T, Reda D, Emanuele N, Reaven PD, Zieve FJ, Marks J, Davis SN, Hayward R, Warren SR, Goldman S, McCarren M, Vitek ME, Henderson WG, Huang GD; VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. 2009 Jan 8;360(2):129-39. doi: 10.1056/NEJMoa0808431. Epub 2008 Dec 17. Erratum in: N Engl J Med. 2009 Sep 3;361(10):1028. Erratum in: N Engl J Med. 2009 Sep 3;361(10):1024-5. PMID: 19092145.
12. Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, Heller SR, Rodriguez H, Rosenzweig J, Vigersky R. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. Diabetes Care. 2013 May;36(5):1384-95. doi: 10.2337/dc12-2480. Epub 2013 Apr 15. PMID: 23589542; PMCID: PMC3631867.
13. Bloomfield HE, Greer N, Newman D, MacDonald R, Carlyle M, Fitzgerald P, Rutks I, Wilt TJ. Predictors and Consequences of Severe Hypoglycemia in Adults with Diabetes - A Systematic Review of the Evidence [Internet]. Washington (DC): Department of Veterans Affairs (US); 2012 Apr. PMID: 23256228.
14. Alvarez Guisasola F, Tofé Povedano S, Krishnarajah G, Lyu R, Mavros P, Yin D. 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. doi: 10.1111/j.1463-1326.2008.00882.x. PMID: 18435671.
15. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Incidence and risk factors for serious hypoglycemia in older persons using insulin or sulfonylureas. Arch Intern Med. 1997 Aug 11-25;157(15):1681-6. PMID: 9250229.
16. Cobden D, Lee WC, Balu S, Joshi AV, Pashos CL. Health outcomes and economic impact of therapy conversion to a biphasic insulin analog pen among privately insured patients with type 2 diabetes mellitus. Pharmacotherapy. 2007 Jul;27(7):948-62. doi: 10.1592/phco.27.7.948. PMID: 17594200.
17. Leese GP, Wang J, Broomhall J, Kelly P, Marsden A, Morrison W, Frier BM, Morris AD; DARTS/MEMO Collaboration. Frequency of severe hypoglycemia requiring emergency treatment in type 1 and type 2 diabetes: a population-based study of health service resource use. Diabetes Care. 2003 Apr;26(4):1176-80. doi: 10.2337/diacare.26.4.1176. PMID: 12663593.
18. Sarkar U, Karter AJ, Liu JY, Moffet HH, Adler NE, Schillinger D. Hypoglycemia is more common among type 2 diabetes patients with limited health literacy: the Diabetes Study of Northern California (DISTANCE). J Gen Intern Med. 2010 Sep;25(9):962-8. doi: 10.1007/s11606-010-1389-7. Epub 2010 May 18. Erratum in: J Gen Intern Med. 2010 Nov;25(11):1258. PMID: 20480249; PMCID: PMC2917655.
19. Hammer M, Lammert M, Mejías SM, Kern W, Frier BM. Costs of managing severe hypoglycaemia in three European countries. J Med Econ. 2009;12(4):281-90. doi: 10.3111/13696990903336597. PMID: 20001570.
20. Holstein A, Plaschke A, Egberts EH. Incidence and costs of severe hypoglycemia. Diabetes Care. 2002 Nov;25(11):2109-10. doi: 10.2337/diacare.25.11.2109. PMID: 12401771.
21. Ginde AA, Espinola JA, Camargo CA Jr. Trends and disparities in U.S. emergency department visits for hypoglycemia, 1993-2005. Diabetes Care. 2008 Mar;31(3):511-3. doi: 10.2337/dc07-1790. Epub 2007 Nov 19. PMID: 18025407.
22. Greco D, Pisciotta M, Gambina F, Maggio F. Severe hypoglycaemia leading to hospital admission in type 2 diabetic patients aged 80 years or older. Exp Clin Endocrinol Diabetes. 2010 Apr;118(4):215-9. doi: 10.1055/s-0029-1241823. Epub 2010 Jan 12. PMID: 20072965.
23. Fadini GP, Rigato M, Tiengo A, Avogaro A. Characteristics and mortality of type 2 diabetic patients hospitalized for severe iatrogenic hypoglycemia. Diabetes Res Clin Pract. 2009 Jun;84(3):267-72. doi: 10.1016/j.diabres.2009.01.019. Epub 2009 Feb 27. PMID: 19250694.

How to cite this article: Fidan C, Salgur F, Kul ÖE, Bozkus Y, Eminsoy G, Sozen F, Kut A, Oksuz E. Incidence and Costs of Hypoglycemia among Type II Diabetes Mellitus Patients in Turkey. J Biomed Res Environ Sci. 2021 Aug 27; 2(8): 705-712. doi: 10.37871/jbres1300, Article ID: JBRES1300, Available at: https://www.jelsciences.com/articles/jbres1300.pdf