Naser AY, Alwafi H, Alsairafi Z. Cost of hospitalisation and length of stay due to hypoglycaemia in patients with diabetes mellitus: a cross-sectional study. Pharmacy Practice 2020 Apr-Jun;18(2):1847.
https://doi.org/10.18549/PharmPract.2020.2.1847

Original Research

Cost of hospitalisation and length of stay due to hypoglycaemia in patients with diabetes mellitus: a cross-sectional study

Abdallah Y. NASER, Hassan ALWAFI, Zahra ALSAIRAFI.
Received (first version): 18-Feb-2020 Accepted: 24-May-2020 Published online: 25-May-2020

Abstract

Objective: This study aims to estimate the length of stay and hospitalisation cost of hypoglycaemia, and to identify determinants of variation in the length of stay and hospitalisation cost among individual patients with type 1 or 2 diabetes mellitus.

Methods: A cross-sectional study was conducted using inpatients records for patients with diabetes mellitus who had been hospitalised due to hypoglycaemic events in two private hospitals in Amman, Jordan between January 2009 and May 2017. All hospitalisation costs were inflated to the equivalent costs in 2017. Hospitalisation cost was estimated from the patient's perspective in Jordanian dinars (JOD). Descriptive analyses and correlation between sociodemographic or clinical characteristics with the cost and length of stay were explored. Predictors of hypoglycaemic hospitalisation cost and length of stay were determined using logistic regression.

Results: During the study period a total of 126 patients with diabetes mellitus were hospitalised due to an incident of hypoglycaemia. The mean patient age was 64.2 (SD=19.6) years; half were male. Patients admitted for hypoglycaemia stayed in hospital for a median duration of two days (IQR=2 days). The median cost of hospitalisation for hypoglycaemia was 163.2 JOD (USD 230.1) (IQR=216.3 JOD). We found that the Glasgow coma score was positively associated with length of stay (0.345, p=0.008), and older age was correlated with higher hospitalisation cost (0.207, p=0.02). Patients with a family history of diabetes had higher hospitalisation costs and longer duration of stay (0.306 and 0.275, p<0.05). In addition, being a male patient (0.394, p<0.05) and with an absence of smoking history was associated with longer duration of stay (0.456, p<0.01), but not with higher hospitalisation cost.

Conclusions: Costs associated with the incidence of hypoglycaemic events are not low and constitute a large cost component of managing and treating diabetes mellitus. Male patients and patients having a family history of diabetes should receive extra care and education on the prevention of hypoglycaemic events, and a treatment de-intensification approach should be considered if necessary, so we can prevent its associated hospitalisation costs and length of stay.

Keywords

Hospital Costs; Length of Stay; Hospitalization; Diabetes Mellitus; Hypoglycemic Agents; Hypoglycemia; Incidence; Logistic Models; Cross-Sectional Studies; Jordan

INTRODUCTION

Diabetes mellitus (DM) is considered one of the most common life-threatening conditions due to its association with various fatal chronic and acute complications.[1] In 2015, DM affected around 415 million patients worldwide; this figure is expected to reach 642 million by 2040.[2] The majority of patients with DM are diagnosed with type 2 DM, making up around 90% of cases.[2,3] The estimated cost of treating diabetic patients in 2015 had reached USD 673 billion and is expected to reach USD 802 billion by 2040.[2] The costs of diabetes include direct medical costs such as hospital inpatient care, emergency department visits, diagnostic tests, and prescription drugs; indirect costs such as productivity losses related to morbidity and mortality, in addition to other direct non-medical costs and intangible costs.[4]

One of the main problems encountered in the treatment of DM is the incidence of hypoglycaemic events.[5,6] Hypoglycaemia is a serious adverse event in patients with DM. Although the risk of hypoglycaemia is higher among patients with type 1 DM, patients with both type 1 DM and type 2 DM are prone to hypoglycaemic events due to their use of antidiabetic medications such as insulin in type 1 DM and type 2 DM, and intensive antidiabetic therapy, commonly associated with insulin secretagogues, and intensive antidiabetic therapy.[6,7] Previous studies have found that the hypoglycaemia incidence rate among patients who are on oral antidiabetic medications ranges between 16% and 39% [8, 9]. Prevalence of hypoglycaemia was 45.0% (95%CI 0.34 - 0.57) for mild/moderate events, and 6.0% (95%CI 0.05 - 0.07) for severe events.[10] Incidence of hypoglycaemic episodes per person-year for mild/moderate and for severe episodes was 19.0 (95%CI 0.00-51.08) and 0.8 (95%CI 0.00-2.15), respectively.[10]

Costs associated with the incidence of hypoglycaemic events are not low, and constitute a large cost component of managing and treating diabetes.[11-14] Costs associated with hypoglycaemia involve direct, indirect, and intangible costs, which differ significantly according to the severity of the hypoglycaemic event experienced by the patient.[15] Estimating the economic impact of hypoglycaemia on healthcare services is important as it helps in the development of effective interventions that improve diabetes management and the overall process of patient care.[16] This study aimed to estimate the length of stay and cost per hypoglycaemia episode, and to identify

Abdallah Y. NASER. Department of Applied Pharmaceutical Sciences and Clinical Pharmacy, Faculty of Pharmacy, Isra University. Amman (Jordan). abdallah.naser@iu.edu.jo
Hassan ALWAFI. Faculty of Medicine. Umm Al Qura University. Mecca (Saudi Arabia). Hassan.alwafi.16@ucl.ac.uk
Zahra ALSAIRAFI. Department of Pharmacy Practice, Kuwait University. Kuwait (Kuwait). ucnvzka@ucl.ac.uk

determinants of variation in length of stay and hospitalisation cost among individual patients with either type 1 or type 2 DM.

METHODS

Study design

This study employed a cross-sectional study design of patients with DM and confirmed diagnosis of hypoglycaemic events for the period between January 2009 and May 2017. Hypoglycaemic events can be broadly defined as either severe, when the patient is admitted to hospital because of hypoglycaemia; moderate, when the patient seeks medical attention for hypoglycaemia but is not admitted to hospital overnight; or mild, when the patient requires no medical attention and needs only assistance from family or friends.[17] In this study, we defined hypoglycaemia as an event that required hospitalisation or admission, which included only severe and moderate hypoglycaemic events.

Study population

Inclusion criteria for this study were: 1) patients were required to have been diagnosed with either type 1 or type 2 DM, and 2) visited the emergency department of a hospital because of a hypoglycaemic episode during the study's time frame (from January 2009 to May 2017). Patients who did not meet the inclusion criteria mentioned above were excluded.

Study site

Two private hospitals in Amman, the capital of Jordan, were selected as the sites of data collection for this study. The two hospitals have a total capacity of 285 beds, providing advanced inpatients and outpatients health care services for the Jordanian population, with more than 700 physicians from different specialities.[18,19]

Data extraction

Data were obtained from the electronic database at each hospital as well as from medical records for each eligible patient. Patients' records were identified using the diagnostic codes E16.0, E16.1, E16.2 from the 10th version of the International Statistical Classification of Diseases (ICD) system. Data collected includes patient demographics, medical history, DM-specific information (such as type of DM, duration of the disease, and family history of the disease), medications use history (including antidiabetic medications and other prescribed medications), patient-specific clinical information (such as history of previous surgery, engagement in daily exercises, living status and their dependency in activities of daily living "degree of help they need to perform their daily activities"), patient admission-related information (such as behaviour during admission, mental health status, communication barrier, admission time, length of stay, and status on discharge), patients' health score at the time of admission (such as Glasgow coma scale, venous thromboembolism risk factor score, and Braden risk assessment score), and hypoglycaemia-specific information (such as the time of the event and blood glucose level (mg/dL) at the time of the event).

Study outcomes

Study outcomes included the median cost of hospitalisation and length of stay, and rate of mortality. The mortality rate of patients admitted for hypoglycaemia was calculated by dividing the number of patients who died during their admission by the total number of admitted patients.

Costs estimation

Direct costs were identified as the costs of the management of hypoglycaemic events such as hospitalisation and emergency department services.[20] Data on individual patient treatment costs were obtained from the financial departments of the participating hospitals, where it was presented as total cost per admission. Hospitalisation costs included: a) emergency management care such as ambulance service, emergency department visit, and the cost of the observation period by healthcare professionals, costs of medical procedures and medications provided, and b) hospital stay cost for admitted patients.

Hospitalisation cost was estimated in Jordanian dinars (JOD) (exchange rate is USD 1.41) as reported by the central bank of Jordan.[21] All costs were inflated to costs in 2017; the inflation rate was averaged as 5.3% from 1977 until 2017, as reported by the Department of Statistics in Jordan.[22] The following formula was used to calculate the inflated cost:

$$Inflated\ cost = Initial\ cost * (1 + inflation\ rate)\text{^}n$$

Initial cost: the cost in any year before 2017; inflation rate: average inflation rate during the years of interest (which is 0.053); n: number of years before 2017.

Costs of hospitalisation that were associated with the hypoglycaemic event were analysed from the patients' perspective, and the average direct economic cost of hypoglycaemic event per patient was estimated. Indirect costs such as productivity losses resulting from lost workdays and direct non-medical costs were not available in patients' records at the hospitals and thus, not considered.

Data quality

The data was extracted by one of the authors (AN) using a pre-designed data extraction sheet. The accuracy and quality of the data entry was checked by a pharmacist to guarantee the accuracy of data entry. Another quality check was performed through a random selection of 20 records and checking the accuracy of the extraction.

Ethics approval

Ethical approval was obtained for this study from the University College of London Research Ethics Committee (Project ID: 7915/001). The study protocol was reviewed and ethics approvals were granted by the Research Ethics Committees of the two hospitals selected as sites of data collection. This was a retrospective analysis of previously collected data, and involved no change in the management of patients. Obtaining individual consent was not feasible, so patient records were anonymised and de-identified before analysis.

Data analysis

Data was analysed using SPSS (version 22). Continuous data were reported as a mean (SD) and median (IQR) for non-normally- distributed variables, and categorical data were reported as percentages and frequencies. Descriptive statistics were used to describe patient demographic characteristics, medication use, and comorbidities. Due to the skewed distribution of hospitalisation cost and length of stay, Spearman's correlation coefficient and the Mann-Whitney test were used as appropriate. Multiple linear regression analysis was conducted after applying log-transformation for the data. In addition, significant predictors of hypoglycaemic hospitalisation cost and length of stay were determined using logistic regression analysis. A confidence interval of 95% ($p<0.05$) was applied to represent the statistical significance of the results. The level of significance was assigned as 5%.

RESULTS

A total of 129 patients were admitted with an incident of hypoglycaemia during the study period. The medical records of all identified patients were reviewed to determine whether they met the inclusion criteria of the study. A total of 126 patients had a clear diagnosis of type 1 or type 2 DM, while one patient was diagnosed as pre-diabetic and two did not have a clear diagnosis of DM, and thus were excluded from the study.

A total of 126 patients were included in the analysis, of whom half were male (n=63, 50.0%). The average age was 64.2 (SD=19.6) years. The average BMI of the patients was 28.5 kg/m^2 (SD=6.4). The most common type of diabetes was type 2 DM, contributing to 86.5% (n = 109) of the sample. The average duration of DM was 12.1 (SD=8.4) years. Around 21.4% of the patients had reported a family history of DM. Other characteristics are presented in Table 1.

The glucose level was available for 84 patients out of 126 (66.0%), and their mean glucose level was 39.8 mg/dL (SD 15.07). The majority of the patients (n=96, 76.2%) were suffering from more than one chronic condition and receiving treatment for them. The two most common chronic conditions across the study sample were hypertension and cardiovascular diseases (such as atrial fibrillation, chronic heart failure and ischaemic heart disease), which were affecting around 76.2% and 49.2% of the patients, respectively. Dyslipidaemia and thyroid problems were also prevalent conditions among the patients, contributing to 19.8% and 17.5%, respectively.

The majority of the patients were receiving oral antidiabetic therapy (n=56, 44.4%), followed by the use of insulin injection only (n=34, 27.0%), then the use of a combination of tablets and insulin injection, which contributed to (n=29) 23.0%, and (n=7) 5.6% of the patients were on diet and exercise only. Insulin was the most commonly used antidiabetic therapy (n=34, 27.0%), followed by metformin and sulfonylurea combination therapy (n=23, 18.3%). Combination therapies based on sulfonylurea or insulin medications were the most prevalent therapies, and accounted for 46.0% (n=58) of the patients. In general, 43.7% of the patients were on antidiabetic dual therapy, followed by 7.1% (n=9) for the use of antidiabetic triple therapy and 0.8% (n=1) for the use of quadruple therapy. A total of 54 patients (42.9%) were using antidiabetic monotherapy. Cardiovascular system medications such as aspirin, beta-blockers and diuretics were commonly used by the patients, contributing to 50.8% (n=64), 39.7% (n=50) and 34.9% (n=44), respectively.

Patients admitted for hypoglycaemia stayed for a median duration of two days (IQR=2 days). Some of the patients

Table 1. Demographic and clinical characteristics of patients admitted with hypoglycemic events

Characteristics	Mean (SD)
Age on the day of the event (years);	64.18 (19.6)
	N (%)
Gender	
Male	63 (50.0)
Female	63 (50.0)
Nationality	
Jordanian	106 (84.1)
Non-Jordanian	20 (15.9)
Marital status (n=125)	
Married	114 (91.2)
Unmarried	11 (8.8)
Smoking status	
Non-smoker	95 (75.4)
Ex-smoker	9 (7.1)
Smoker	22 (17.5)
Alcohol consumption status	
Yes	1 (0.8)
No	125 (99.2)
Body mass index (n=87); mean (SD)	28.50 ± 6.4
Type of diabetes mellitus	
Type 1 patients	17 (13.5)
Type 2 patients	109 (86.5)
Duration of diabetes mellitus (years) (n=91)	12.14 ± 8.4
Family history of diabetes	27 (21.4)
Number of comorbidities	
0	13 (10.3)
1	17 (13.5)
2	46 (36.5)
>2	50 (39.7)
Behaviour during admission (n=115)	
Cooperative	100 (87.0)
Uncooperative	2 (1.7)
Anxious	9 (7.8)
Unconscious	3 (2.6)
Sedated	1 (0.9)
Mental health (n=112)	
Normal	109 (97.3)
Dementia	3 (2.7)
Patients with communication barrier (n=106)	10 (9.4)
Living status (n=114)	
Single	1 (0.9)
Spouse	1 (0.9)
With family	112 (98.2)
Activity of daily living (n=115)	
Dependent	37 (32.2)
Independent	52 (45.2)
Need assistance	26 (22.6)
Insured patients	48 (38.1)
Patients performing 30 minutes of exercise daily (n=109)	7 (6.4)
Patients with history of previous surgery (n=121)	79 (65.3)
Patients with history of previous hypoglycaemia admission in the past year	9 (7.1)

*Total number does not add up to 126 because of missing data

Table 2. Median hospitalisation cost and length of stay stratified by patient characteristics

	Cost		Lenght of stay	
	Median (IQR)	**p-value**	**Median (IQR)**	**p-value**
Age		0.320		0.335
Below 18 years	110.9 (187.5)		1 day (2.0)	
19 – 39 years	105.3 (115.6)		1 day (0.5)	
40 – 59 years	158.0 (116.9)		2 days (2.0)	
60 years and above	194.2 (270.4)		2 days (3.0)	
Gender		0.705		0.152
Male	151.2 (223.1)		1 day (2.0)	
Female	184.3 (215.8)		2 days (2.0)	
Type of diabetes		0.163		0.049*
Type 1 DM	123.0 (119.8)		1 day (2.0)	
Type 2 DM	184.3 (250.6)		2 days (2.5)	
Severity of hypoglycaemia		0.099		
Moderate	111.7 (207.1)			
Severe	185.7 (250.9)			

(n=16, 12.7%) only needed to be observed by the medical team for a few hours, and were discharged on the same day. The majority stayed four days or less (n=109, 86.5%). Other patients needed to stay for longer periods because their case deteriorated after admission, or due to the development of further life-threatening complications. This led to a longer stay, up to a maximum of 33 days in one case (Table 2).

On the discharge sheet, the health status of the patient was reported to describe the improvement after the admission period. A total of 118 patients (93.7%) recovered after being admitted for hypoglycaemia and 6.3% (8 patients) had died due to acute complications during their duration of stay.

The study cohort, which comprised 126 patients hospitalised for hypoglycaemia, had a total inflated cost of 40,232 JOD (USD 56,712). The median cost of hospitalisation for hypoglycaemia was 163.2 JOD (USD 230.1) (IQR=216.3 JOD). When we excluded the one outlier patient with 33 days of stay, the median cost of hypoglycaemia hospitalisation reached 160.0 JOD (USD 225.6) (IQR=211.7 JOD). There was no statistically significant difference between different demographic groups (Table 2).

Using Spearman correlation, we found that hospitalisation cost was significantly correlated with length of stay (0.705, $p<0.001$). We further examined correlation between length of stay, hospitalisation cost, and several patients' demographics using Spearman correlation coefficient. Older age was correlated with higher hospitalisation cost (0.207, $p=0.02$), but not with length of stay (0.159, $p=0.076$). We found a positive correlation between Glasgow coma score and length of stay (0.345, $p<0.05$), but not hospitalisation cost (0.241, $p=0.068$). We found a strong correlation between number of comorbidities and length of stay (0.263, $p=0.003$), but not hospitalisation cost (0.143, $p=0.111$). We found no significant correlation between glucose level on admission, duration of diabetes, and length of stay or hospitalisation cost ($p>0.05$). We examined whether length of stay and hospitalisation cost differed based on gender, family history of diabetes, and independence with daily activity using the Mann-Whitney test. We found no significant differences between male and female patients in length of stay or hospitalisation cost. In addition, we found no significant differences between type of insurance and length of stay or hospitalisation cost. On the other hand, we found that patients with a family history of diabetes had a longer length of stay and higher hospitalisation cost ($p=0.008$ and 0.01, respectively). Patients who were dependent in their daily activities were found to have higher length of stay and hospitalisation cost ($p=0.009$ and 0.004, respectively). We did not assess the differences in hospitalisation cost between users of different antidiabetic medications, such as insulin or sulfonylurea users, or the users of different combination therapies. These comparisons were not feasible in our study as we had a small sample size in some subgroups.

Using linear regression models, we found that family history of DM and dependency in daily activities were potential confounders that affected the cost of hypoglycaemia and length of stay.

A multiple linear regression was used to explore determinants of hospitalisation cost and length of stay due to hypoglycaemia. Multiple regression analysis was conducted using two models; the first one was conducted using patients' demographic characteristics (age, gender, and marital status) which we anticipated to have effects on hospitalisation cost and length of stay, and the second one included patients' demographics and other clinical factors (smoking status, type of diabetes, duration of the disease, family history of DM, dependency in daily activities, communication barriers, and exercise practice). We did not find any statistically significant association between age, gender, and marital status and hospitalisation cost or length of stay using the first model ($p>0.05$). The second model showed that patients who had a family history of DM had higher hospitalisation cost and longer length of stay ($p<0.05$). In addition, it showed that being male and without a previous history of smoking was associated with having longer length of stay ($p<0.01$), but not higher hospitalisation cost. For further details about the multiple regression analysis for determinants of hypoglycaemia hospitalisation cost and length of stay, please refer to Online appendix 1 and Online appendix 2.

DISCUSSION

Our study found that hospitalisation due to hypoglycaemic events has a substantial cost in hospital settings. The median hospitalisation cost for a hypoglycaemic event was 163.2 JOD (USD 230), which contributed to the per capita

expenditure for healthcare in Jordan (USD 257 in 2015).[23] The findings of our study confirmed those of previous studies in identifying hypoglycaemia as a costly diabetic complication with a negative impact on the economic resources of the society and the overall healthcare system.[24] However, hypoglycaemia hospitalisation cost is considered low compared to other major health conditions such as acute myocardial infarction, unstable angina, and acute ischaemic stroke.[25]

The costs associated with hypoglycaemia differ significantly according to the severity of the case, which determines the type of medical support needed and ultimately its associated costs. Previous studies mentioned that the highest costs associated with hypoglycaemic events are costs associated with hospitalisation, followed by ambulance cost and emergency room visits.[26-28] Several previous studies using different methodologies have provided results that are in broad agreement with our study findings. A previous study estimated the cost of hypoglycaemic events in three European countries and reported costs that differ slightly from our estimates: EUR 533 (USD 658.83) in Germany, EUR 537 (USD 663.77) in the UK, and EUR 691 (USD 854.13) in Spain.[29] Parekh *et al*. calculated the average cost per episode of insulin-related hypoglycaemia in adults in Spain as EUR 716.82 (USD 885.99) for severe and EUR 7.09 (USD 8.76) for non-severe episodes in type 1 DM, and EUR 680.49 (USD 841.08) and EUR 14.61 (USD 18.06) for severe and non-severe, respectively. It is worth mentioning that the per capita expenditure on health for these three countries is 10 to 20 times higher than that for Jordan, namely USD 4,592, USD 2,354, and USD 4,356 for Germany, Spain and the UK, respectively, whereas in Jordan it is only USD 257.[30]

For type 2 DM the majority of the cost for severe episodes consisted of hospitalisation and ambulance use.[26] Jönsson *et al*. estimated the costs of severe hypoglycaemic events in Sweden to be EUR 3,917.4 (USD 4,841.89) (combined direct costs of EUR 2,806.8 (USD 3,469.19) and indirect costs of EUR 1,110.6 (USD 1,372.70).[17] Jönsson *et al*.'s study considered direct and indirect costs and included hypoglycaemic events that ranged in severity from mild to severe events. Kim *et al*. estimated medical costs per person per hypoglycaemic event in Korea to range from USD 17.28 to USD 1,857.09 for secondary and tertiary hospitals.[15] Kim *et al*. estimated hypoglycaemic event costs through the implementation of modelling techniques that simulate the procedure of managing patients with hypoglycaemia and cross-sectional survey to evaluate the resource usage of patients with hypoglycaemia. Possible reasons for the difference in hospitalisation cost across studies from different countries could include differences in the definition of a hypoglycaemic event, cost analysis perspective, unit costs, the methods used in data collection, drugs/procedures considered, and different patient populations. Another explanation could be that the cost was higher in those countries, which may be related to per capita expenditure for health care; for example in Portugal (USD 1,722), which is almost seven times higher than in Jordan.[23] The length of stay due to admission for hypoglycaemia in our study was less than what has been observed in previous studies in Portugal and Spain: the Portuguese study had reported a mean duration of 8.8 days, and the Spanish one reported a median of 10.82 days, compared to our estimate of 2 days.[31,32] This difference could be due to the variability in the patient population being studied in terms of demographics, different treatment procedures, the varying severity of hypoglycaemic events, and sociocultural factors. For instance, it is very common for old people to live with their families in Jordan, while this is uncommon in European countries, where many people live in care homes when they are old.

Unlike a previous study that reported having a smoking history is associated with higher risk of comorbidities, mortality and length of hospital stay [33], we found that not having a smoking history was associated with longer duration of stay, but this could be due to the small sample size in our study.[33] In addition, due to the cross-sectional study design, we were not able to draw a causal inference. Previous studies reported that marital status can affect the length of stay at hospital; this could be due psychological and social causes, as unmarried patients usually suffer a more severe form of illness compared to married patients. Also, patients who are married usually have better care at home and could be more keen to return home.[34,35] However, in our study there was no significant association between marital status and length of stay or hospitalisation cost.

Patients with higher BMI are at greater risk of developing cardiac problems including atrial fibrillation and other cardiovascular diseases.[36,37] Hypoglycaemia is associated with an increased risk of atrial fibrillation and cardiac complications [38, 39]; it is therefore, reasonable to assume that patients with a higher BMI will have a longer hospital stay time and more severe cases of hypoglycaemia [40]. However, we did not find this association significant in our study, as the BMI value was available for only 87 patients (69.0%).

According to the International Diabetes Federation, in 2017, around 408,100 patients were diagnosed with DM in Jordan [2]. A previous systematic review had reported a prevalence rate of severe hypoglycaemic events of 6.0% (95%CI, 0.05-0.07).[10] Based on the available estimates from the International Diabetes Federation and the systematic review, we can estimate that each year a total of 24,486 patients in Jordan with DM could experience a severe hypoglycaemic event that requires hospitalisation. Applying our median hospitalisation cost to this number means a hospitalisation cost of around 4.0 million JOD (USD 5.6 million) per year. The high estimated costs of hospitalisation due to hypoglycaemia should be taken into consideration by decision-makers in the healthcare sector from both economic and clinical points of view. The findings of our study are of added value and can be used in healthcare economic analyses in Jordan. Our estimates should increase the awareness of the economic impact of this adverse event and the need for adoption of healthcare strategies to decrease its burden, by promoting the individualisation of HbA1c goals in physicians' practices and increasing the patients' awareness and abilities when encountering this adverse event. At the practice level, antidiabetic therapy de-intensification, treatment protocols revisions, and enhancing patients' awareness of symptoms and prevention methods are needed.[41] Regular HbA1c

levels monitoring, and educating patients on how to deal with their hypoglycaemia and how to avoid future hypoglycaemic events, are important approaches to decrease the clinical and ultimately the economic burden of hypoglycaemia. Similarly, at the individual level, patients can follow advice and simple steps to avoid hypoglycaemia such as regular self-monitoring and administration of glucagon or any other sugar component to reverse the hypoglycaemic attack.[42]

Strengths and limitations

To the best of our knowledge, this is the first study conducted within hospital settings performed in Jordan or elsewhere in the Middle East that estimates direct costs related to hospitalisation for hypoglycaemia. Our study has several strengths. First, data collection was done using real-world patients' records for each hypoglycaemic episode admitted to the emergency department. Second, our study estimated the hospitalisation cost for hypoglycaemic events for moderate and severe episodes and was not restricted to severe cases only. Third, we adjusted the costs, inflating them to equivalent costs as per the costs in 2017, to provide more meaningful estimations of the incurred costs.

Our study also has some limitations. Firstly, our study only estimated direct medical costs related to hospitalisation incurred by the patients, and did not include costs related to follow-up visits, treatments after the event and further examination procedures required after discharge, direct non-medical or indirect costs. However, hospitalisation cost is the main cost driver for severe hypoglycaemic events.[24] Secondly, indirect costs such as costs related to loss of productivity or early retirement were not examined in our study. Thirdly, our cost estimation was based on costs incurred within private rather than governmental hospitals, which might differ and limit the generalisability of the results to the private sector only. Private hospitals provide medical care of higher quality for the patients compared to public hospitals, but at the same time, private hospitals charge higher prices to make a profit.[43] Fourth, the use of charges as a proxy to estimate costs is not free from criticism.[44,45] Finally, the sample size was small. Despite these limitations, we believe our paper makes a real contribution to awareness of the hypoglycaemia burden in Jordan. It should also stimulate further research in this area such as studies that adopt a wider perspective and a longer time frame, which would be needed to comprehensively assess the impact of hypoglycaemia on resources utilisation. This should include direct and indirect costs from both the governmental and private sectors to increase the generalisability of the current estimated costs.

CONCLUSIONS

This study confirmed that hospitalisation due to hypoglycaemic events among patients with DM represents a substantial economic burden within hospital settings. Our study findings provide implications for healthcare providers to target patients at high risk of hypoglycaemia such as males and patients with a family history of DM, to avoid their hospitalisation. Targeting such groups through health educational programme and treatment de-intensification (if necessary) approaches could help reduce their propensity to hypoglycaemia and ultimately reduce their length of hospital stay and cost.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414(6865):782-787. https://doi.org/10.1038/414782a
2. International Diabetes Federation, IDF Diabetes Atlas. Available at: https://www.diabetesatlas.org/en/ (accessed Feb 17, 2020).
3. Rathmann W, Giani G. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(10):2568-2569. https://doi.org/10.2337/diacare.27.10.2568
4. Ng CS, Lee JY, Toh MP, Ko Y. Cost-of-illness studies of diabetes mellitus: a systematic review. Diabetes Res Clin Pract. 2014;105(2):151-163. https://doi.org/10.1016/j.diabres.2014.03.020
5. Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358(24):2545-2559. https://doi.org/10.1056/nejmoa0802743
6. Umpierrez G, Korytkowski M. Diabetic emergencies - ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycaemia. Nat Rev Endocrinol. 2016;12(4):222-232. https://doi.org/10.1038/nrendo.2016.15
7. Naser AY, Wong ICK, Whittlesea C, Beykloo MY, Man KKC, Lau WCY, Hyassat DA, Wei L. Use of multiple antidiabetic medications in patients with diabetes and its association with hypoglycaemic events: a case-crossover study in Jordan. BMJ Open. 2018;8(11):e024909. https://doi.org/10.1136/bmjopen-2018-024909
8. Chan SP, Ji LN, Nitiyanant W, Baik SH, Sheu WH. Hypoglycemic symptoms in patients with type 2 diabetes in Asia-Pacific-Real-life effectiveness and care patterns of diabetes management: the RECAP-DM study. Diabetes Res Clin Pract. 2010;89(2):e30-e32. https://doi.org/10.1016/j.diabres.2010.05.008
9. Miller CD, Phillips LS, Ziemer DC, Gallina DL, Cook CB, El-Kebbi IM. Hypoglycemia in patients with type 2 diabetes mellitus. Arch Intern Med. 2001;161(13):1653-1659. https://doi.org/10.1001/archinte.161.13.1653

10. Edridge CL, Dunkley AJ, Bodicoat DH, Rose TC, Gray LJ, Davies MJ, Khunti K. Prevalence and Incidence of Hypoglycaemia in 532,542 People with Type 2 Diabetes on Oral Therapies and Insulin: A Systematic Review and Meta-Analysis of Population Based Studies. PLoS One. 2015;10(6):e0126427. https://doi.org/10.1371/journal.pone.0126427
11. Heller SR, Frier BM, Hersløv ML, Gundgaard J, Gough SC. Severe hypoglycaemia in adults with insulin-treated diabetes: impact on healthcare resources. Diabet Med. 2016;33(4):471-477. https://doi.org/10.1111/dme.12844
12. Liu S, Zhao Y, Hempe JM, Fonseca V, Shi L. Economic burden of hypoglycemia in patients with Type 2 diabetes. Expert Rev Pharmacoecon Outcomes Res. 2012;12(1):47-51. https://doi.org/10.1586/erp.11.87
13. McEwan P, Larsen Thorsted B, Wolden M, Jacobsen J, Evans M. Healthcare resource implications of hypoglycemia-related hospital admissions and inpatient hypoglycemia: retrospective record-linked cohort studies in England. BMJ Open Diabetes Res Care. 2015;3(1):e000057. https://doi.org/10.1136/bmjdrc-2014-000057
14. Harris SB, Leiter LA, Yale JF, Chiasson JL, Kleinstiver P, Saurio L, Out-of-pocket costs of managing hyperglycemia and hypoglycemia in patients with type 1 diabetes and insulin-treated type 2 diabetes. Can J Diabetes. 2007;31(1):25-33. https://doi.org/10.1016/S1499-2671(07)11008-X
15. Kim G, Lee YH, Han MH, Lee EK, Kim CH, Kwon HS, Jeong IK, Kang ES, Kim DJ. Economic Burden of Hypoglycemia in Patients with Type 2 Diabetes Mellitus from Korea. PLoS One. 2016;11(3):e0151282. https://doi.org/10.1371/journal.pone.0151282
16. Foos V, Varol N, Curtis BH, Boye KS, Grant D, Palmer JL, McEwan P. Economic impact of severe and non-severe hypoglycemia in patients with Type 1 and Type 2 diabetes in the United States. J Med Econ. 2015;18(6):420-432. https://doi.org/10.3111/13696998.2015.1006730
17. Jönsson L, Bolinder B, Lundkvist J. Cost of hypoglycemia in patients with Type 2 diabetes in Sweden. Value Health. 2006;9(3):193-198. https://doi.org/10.1111/j.1524-4733.2006.00100.x
18. Hanan Hospital. About us. Available at: http://www.hananhospital.com/about/vision.html (accessed Mar 14, 2017).
19. The Speciality Hospital. About us. Available at: https://www.specialty-hospital.com/ar/home/ (accessed Mar 14, 2017).
20. Veronese G, Marchesini G, Forlani G, Saragoni S, Degli Esposti L, Centis E, Fabbri A; Italian Society of Emergency Medicine (SIMEU). Costs associated with emergency care and hospitalization for severe hypoglycemia. Nutr Metab Cardiovasc Dis. 2016;26(4):345-351. https://doi.org/10.1016/j.numecd.2016.01.007
21. Central Bank of Jordan. Currency prices. Available at: http://www.cbj.gov.jo/ (accessed Apr 12, 2017).
22. Trading economics. Jordan Inflation Rate. Available at: https://tradingeconomics.com/jordan/inflation-cpi (accessed Mar 14, 2017).
23. World Health Organization. Global Health Expenditure Database. Available at: http://apps.who.int/nha/database/Select/Indicators/en (accessed Jan 25, 2018).
24. Laires PA, Conceição J, Araújo F, Dores J, Silva C, Radican L, Nogueira A. The cost of managing severe hypoglycemic episodes in Type 2 diabetic patients. Expert Rev Pharmacoecon Outcomes Res. 2016;16(2):315-325. https://doi.org/10.1586/14737167.2015.1084230
25. Nicholson G, Gandra SR, Halbert RJ, Richhariya A, Nordyke RJ. Patient-level costs of major cardiovascular conditions: a review of the international literature. Clinicoecon Outcomes Res. 2016;8:495-506. https://doi.org/10.2147/ceor.s89331
26. Parekh W, Hoskins N, Baker-Knight J, Ramirez de Arellano A, Mezquita Raya P. The Economic Burden of Insulin-Related Hypoglycemia in Spain. Diabetes Ther. 2017;8(4):899-913. https://doi.org/10.1007/s13300-017-0285-0
27. Giorda CB, Rossi MC, Ozzello O, Gentile S, Aglialoro A, Chiambretti A, Baccetti F, Gentile FM, Romeo F, Lucisano G, Nicolucci A; HYPOS-1 Study Group of AMD. Healthcare resource use, direct and indirect costs of hypoglycemia in type 1 and type 2 diabetes, and nationwide projections. Results of the HYPOS-1 study. Nutr Metab Cardiovasc Dis. 2017;27(3):209-216. https://doi.org/10.1016/j.numecd.2016.10.005
28. de Groot S, Enters-Weijnen CF, Geelhoed-Duijvestijn PH, Kanters TA. A cost of illness study of hypoglycaemic events in insulin-treated diabetes in the Netherlands. BMJ Open. 2018;8(3):e019864. https://doi.org/10.1136/bmjopen-2017-019864
29. 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):281-290. https://doi.org/10.3111/13696990903336597
30. World Health Organization. Global Health Expenditure Database. Available at: https://apps.who.int/nha/database/Select/Indicators/en (accessed May 14, 2020).
31. Conceição J, Dores J, Araújo F, Brodovicz K, Radican L, Nogueira AM. Hipos-ER (Hypoglycemia in Portugal Observational Study - Emergency Room): Clinical Outcomes in Admitted Patients. Value Health. 2014;17(7):A332. https://doi.org/10.1016/j.jval.2014.08.628
32. Zapatero A, Gómez-Huelgas R, González N, Canora J, Asenjo A, Hinojosa J, Plaza S, Marco J, Barba R. Frequency of hypoglycemia and its impact on length of stay, mortality, and short-term readmission in patients with diabetes hospitalized in internal medicine wards. Endocr Pract. 2014;20(9):870-875. https://doi.org/10.4158/ep14006.or
33. Rezaei S, Akbari Sari A, Arab M, Majdzadeh R, Shaahmadi F, Mohammadpoorasl A. The association between smoking status and hospital length of stay: evidence from a hospital-based cohort. Hosp Pract (1995). 2016;44(3):129-132. https://doi.org/10.1080/21548331.2016.1178579
34. Hayes RM, Carter PR, Gollop ND, Uppal H, Sarma J, Chandran S, Potluri R. The impact of marital status on mortality and length of stay in patients admitted with acute coronary syndrome. Int J Cardiol. 2016;212:142-144. https://doi.org/10.1016/j.ijcard.2016.03.066
35. Gordon HS, Rosenthal GE. Impact of marital status on outcomes in hospitalized patients. Evidence from an academic medical center. Arch Intern Med. 1995;155(22):2465-2471. https://doi.org/10.1001/archinte.1995.00430220129014
36. Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX, Eckel RH; American Heart Association; Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2006;113(6):898-918. https://doi.org/10.1161/circulationaha.106.171016

37. Vyas V, Lambiase P. Obesity and Atrial Fibrillation: Epidemiology, Pathophysiology and Novel Therapeutic Opportunities. Arrhythm Electrophysiol Rev. 2019;8(1):28-36. https://doi.org/10.15420/aer.2018.76.2
38. Frier BM, Schernthaner G, Heller SR. Hypoglycemia and cardiovascular risks. Diabetes Care. 2011;34(Suppl 2):S132-S137. https://doi.org/10.2337/dc11-s220
39. Chow E, Bernjak A, Williams S, Fawdry RA, Hibbert S, Freeman J, Sheridan PJ, Heller SR. Risk of cardiac arrhythmias during hypoglycemia in patients with type 2 diabetes and cardiovascular risk. Diabetes. 2014;63(5):1738-1747. https://doi.org/10.2337/db13-0468
40. Zizza C, Herring AH, Stevens J, Popkin BM. Length of hospital stays among obese individuals. Am J Public Health. 2004;94(9):1587-1591. https://doi.org/10.2105/ajph.94.9.1587
41. Naser AY, Wong ICK, Whittlesea C, Alwafi H, Abuirmeileh A, Alsairafi ZK, Turkistani FM, Bokhari NS, Beykloo MY, Al-Taweel D, Almane MB, Wei L. Attitudes and perceptions towards hypoglycaemia in patients with diabetes mellitus: A multinational cross-sectional study. PLoS One. 2019;14(10):e0222275. https://doi.org/10.1371/journal.pone.0222275
42. Evans Kreider K, Pereira K, Padilla BI. Practical Approaches to Diagnosing, Treating and Preventing Hypoglycemia in Diabetes. Diabetes Ther. 2017;8(6):1427-1435. https://doi.org/10.1007/s13300-017-0325-9
43. Alumran A, Almutawa H, Alzain Z, Althumairi A, Khalid N. Comparing public and private hospitals' service quality. J Public Health (Berl). 2020 [Ahead of print]. https://doi.org/10.1007/s10389-019-01188-9
44. Health Information Act Advisory Committee. What is Health Care Cost? Health Information Act Advisory Committee Meeting. 2016.
45. Glick HA, Doshi JA, Sonnad SS, Polsky D. Economic evaluation in clinical trials. Oxford university press: New York; 2007. ISBN: 978-0198529972