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The site of insulin storage inside domestic refrigerators is associated with ketoacidosis and hypoglycemic episodes among patient with diabetes mellitus, in Tabuk City, The Kingdom of Saudi Arabia

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RESEARCH

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ABSTRACT

Background
Insulin storage is vital for use in type 1 diabetes and most patients with type 2 diabetes mellitus. No researchers have investigated the site of insulin storage inside the fridge, the proper rotation of insulin injection sites, and the worsening glucose profile in Tabuk, Saudi Arabia.

Aims
The study aimed to assess the association between storing insulin in different sites of the fridge, rotating insulin injection sites, hypoglycemia, and ketoacidosis.

Methods
This is a cross-sectional study conducted in King Fahd Specialist Hospital, Tabuk, Saudi Arabia during the period from May 2019 to November 2019, 394 participants were approached to collect demographic data, site of insulin storage in domestic refrigerators, number of ketoacidosis and hypoglycaemic attack during the last year, number of insulin injection sites and rotation of injections, and if the patients were regularly checking their glycated haemoglobin.

Results
Of the 349 patients (98 per cent had type 2 diabetes), 98.3 per cent had a hypoglycaemic episode during the last year, and 11.2 per cent were admitted for ketoacidosis, this is mirrored by not properly storing insulin inside the fridge (39.2 per cent), and inappropriately rotating insulin injection sites (87.4 per cent). Patients who were storing their insulin inappropriately had higher rates of both ketoacidosis and hypoglycaemia than their comparators (0.26±0.65 *vs.* 0.11±0.39, and 19.51±19.46 *vs.* 7.07±9.54 respectively, $P<0.05$.

Conclusion
Hypoglycaemia and ketoacidosis were common among patients who inappropriately store insulin inside the fridge and wrongly rotate insulin injection sites. Further larger multi-center studies investigating the patient's behaviour to high and low blood sugar and the rates of lipohypertrophy are recommended.

Key Words
Insulin storage, fridge, hypoglycaemia, ketoacidosis, Saudi Arabia

What this study adds:

1. What is known about this subject?
Wrong insulin storage and rotation of insulin injection sites may lead to both hypoglycaemia and rebound hyperglycaemia. However, this is the first study to

investigate both important issues in diabetes management.

2. What new information is offered in this study?
Storing insulin in the upper and lower shelf of domestic refrigerators were associated with ketoacidosis and hypoglycaemia.

3. What are the implications for research, policy, or practice?
Patients education regarding insulin storage and the proper rotation of insulin injection site need to be included in diabetes holistic care.

Background

Diabetes mellitus is a global health burden. The incidence and prevalence are on the rise despite the prevention programs and the increasing knowledge regarding its risk factors. More than four hundred million are with the disease worldwide and an estimated 193 million people are not diagnosed.[1] According to the recent IDF Atlas, 463 million are suffering from diabetes, 374 million (aged 20–79 years) had impaired glucose tolerance, and three in four of people affected by diabetes live in low and middle-income countries.[2]

The management of diabetes mellitus is based on early detection, diabetes prevention programs, and pharmacotherapy. Insulin therapy is needed for the treatment of both type 1 and types 2 diabetes due to a lack of insulin in the former and the progressive nature of the latter. Insulin is also recommended when the plasma glucose is ≥300mg/dl or the admission glycated haemoglobin is >10.[3]

Even though insulin is a cornerstone in the management of diabetes mellitus. However, the guidelines for its storage are not followed in particular regarding the storage temperature of 2–8°C and keeping the opened vials or pens at room temperature. It is recommended that insulin should be transported without shaking and exposure to temperature >32°C, also, open vials should be kept at room temperature and immersion underwater should be avoided to decrease the loss of potency, contamination and injection abscess formation.[4] According to the European Association for the Study of Diabetes (ESAD) insulin kept in a fridge was out of the ideal temperature range more than insulin carried by the patient, putting insulin at a high risk of losing its potency, the freezing temperature was recorded by 17 per cent of thermometers.[5] Addressing needle phobia that could be a major barrier to insulin use is of paramount significance. Also, the proper needle size, injection sites, and technique should be addressed from the first visit onwards. Insulin is effective only if stored and administered correctly. It is recommended to use the same site of injection for one month separating each injection by 2.5cm, then another site. Failure to rotate within the same site may lead to an increase in the day to day variability of absorption, lipohypertrophy, early postprandial hyperglycaemia, and late hypoglycaemia.[6]

There is an increasing trend in hospital admission for ketoacidosis among patients with both type 1 and type 2 diabetes mellitus.[7] A study published in England showed that hypoglycaemia requiring hospital admission remain static in the period 2009-2013 among young and middle-aged patients, a decreased incidence observed in the elderly population may be attributed to decreased sulphonylureas use.[8,9]

Domestic refrigerators may pose an underestimated risk for insulin quality because insulin may be outside the recommended range in a significant number of cases. The butter container of the fridge is warm, while the lower shelf tends to be cooler. The middle shelf is ideal for insulin storage.[10,11]

To our best knowledge, no researchers have studied insulin storage among patients with diabetes mellitus in Tabuk. Thus, we conducted this survey to assess insulin storage and its associated factors among patients on insulin in Tabuk, Saudi Arabia.

Method

This a cross-sectional study conducted in King Fahd Specialist Hospital, Tabuk City, Saudi Arabia during the period from May 2019 to November 2019. Three hundred-forty-nine consecutive patients with the diagnosis of diabetes were approached. The sample size was calculated assuming that the prevalence is 50 per cent, confidence interval 5 per cent. A structured questionnaire was used to collect: Age, sex, type of diabetes, medications used, the dose of insulin, the number of pens, the maximum period of using the pens, the place of insulin storage (upper, middle or lower shelves of fridge), the site of insulin injection and knowledge regarding injection rotation. Whether the patients are measuring the glycated haemoglobin, the number of admission with ketoacidosis and hypoglycaemia were also recorded. The purpose of the study was explained to the participants, and they were told that participation is voluntary and that all the information collected will be used only for this research. Consent was taken from all the participants before enrolment in the study. Ethical approval

was obtained from the ethical committee of the Medical College, University of Tabuk. The Statistical Package for Social sciences. (SPSS, version 20, New York) was used for data analysis, a P-value of <0.5 was considered significant.

Results

There were three hundred forty-nine patients with diabetes (age ranged from 12–67 years with a mean of 33.91±11.08), the patients were using insulin for 6.64±6.12 years, the dose ranged from as small as three units/day up to 75 units (42.89±13.97/day), the number of insulin pens ranged from one-three with lower duration than the duration of insulin use (5.28±1.22 years). It is to note that the number of hypoglycaemic episodes ranged from 0–19 with a mean of 10.71±14.37 Table 1.

Out of 349 patients (53.6 per cent males), the dominance of type 2 diabetes was obvious, 73.4 per cent were on long-acting insulin (17.8 per cent were also using short-acting insulin), while only 8.9 per cent were on short-acting insulin only, the commonest oral hypoglycaemic medication was metformin followed by sulphonylureas, and DPP-4 inhibitors, (69.9 per cent, 10.3 per cent, and 6.6 per cent). It is interesting to note that 13.2 per cent of patients with diabetes were on lifestyles only. The current data showed that the majority of patients (92.6 per cent) were using the fridge to store their insulin and 70.8 per cent were using the middle shelf. However, a considerable number of patients were using either the upper or lower parts of the refrigerator for insulin storage (18.3 per cent &10.9 per cent respectively. In the current study, in spite of being familiar with the sites of insulin injection, the patients incorrectly rotate the injection sites (87.4 per cent) or not rotating at all (12.6 per cent). Furthermore, some patients with diabetes mellitus (17.5 per cent) were not checking their HbA1c regularly. This implies that the present sample may be prone to lipohypertrophy, poor glycaemic control, and fluctuating insulin levels. The above findings are mirrored by high rates of admission for ketoacidosis (11.2 per cent), and hypoglycaemia (98.3 per cent) during the last year Table 2.

It is interesting to note that, patients who inappropriately stored their insulin had higher rates of both ketoacidosis and hypoglycaemia (0.26±0.65 *vs.* 0.11±0.39, P-value=0.000, and 19.51±19.46 *vs.* 7.07±9.54, P-value=0.007 respectively) Table 3.

Discussion

In the current study, the majority of patients (92 per cent) had type 2 diabetes, and the majority of patients were on metformin in line with the previous literature.[12] It is interesting to note that nearly one in three patients were inappropriately storing their insulin in the upper or lower shelf of the fridge. The upper container of the fridge is warm, while the lower shelf tends to be cooler. A plausible explanation is that the patients are not adherent to the doctor's advice or the physicians are not concentrating specifically on the site of insulin storage inside the domestic refrigerators. This practice may pose great risk regarding insulin quality. Physicians may need to address these issues and incorporate education regarding insulin storage in domestic refrigerators as an essential component of diabetes holistic care. Improper insulin storage observed in the current study is mirrored by a high rate of ketoacidosis admission. A similarly high rate of diabetic ketoacidosis was observed by Besado and colleagues.[13] Also, there is a trend of increasing admission for ketoacidosis in the last two decades.[14] A strong contributor to poor glycaemic control and possible ketoacidosis in the current study could be that nearly one in five of patients were not estimating the glycated haemoglobin regularly, overtreatment of a hypoglycaemic attack may lead to high blood sugar. Admission with hypoglycaemia has been an increasing burden in diabetes mellitus in the previous two decades which was not parallel the glycated haemoglobin level,[15] in the current study, nearly all the participants experienced hypoglycaemia during the last year (some had nineteen attacks). The frequent attacks of hypoglycaemia can be simply explained by insulin and sulphonylureas use. However, the current findings of using three sites of insulin injection and inappropriate rotation of these sites (84.7 per cent) may lead to different absorption, fluctuating glucose levels, and hypoglycaemia. Another explanation could be lipohypertrophy.[16,17] Fear of hypoglycaemia, especially after an attack, may lead to poor glycaemic control and ketoacidosis, furthermore, hypoglycaemia is associated with arrhythmia, car accidents, and dementia.[18] Urgent preventive intervention is highly needed including using one site of insulin injection site and rotating injection within this site for a month, education regarding meals and exercise to insulin, continuous glucose monitoring to increase time in range and avoiding the dangerous glucose fluctuation are highly needed. Besides, the use of novel medications with cardiorenal protection and lower rates of hypoglycaemia like sodium-glucose co-transporter inhibitors (not used in the current sample) may solve the issue.

Conclusion

The current study showed an alarming situation regarding patients on insulin injection in Tabuk City. The patients were not storing their insulin in a proper site in domestic refrigerators and were rotating insulin injection sites

inappropriately which push them towards high admission with both hypoglycaemia and ketoacidosis. Urgent educational and management plans are highly needed to prevent the deleterious consequences of acute diabetes complications. Further multi-centre studies focusing on the measurement of domestic refrigerators temperature and lipohypertrophy are recommended.

Study limitations

The limitations of the current study were: The study was conducted at a single tertiary centre, so generalization cannot be insured, the information reported by the participants may be prone to subjectivity, and we did not measure the temperature of the domestic refrigerator.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

Ethical approval was obtained from the ethical committee of the Medical College, University of Tabuk, Saudi Arabia

Table 1: The study group characters (range, Mean± SD)

Character	Range, Mean±SD
Age	
Range	12-67
Mean±SD	33.91±11.08
Insulin dose	
Range	3-75 units/day
Mean±SD	42.89±13.97
Duration of insulin use/years	6.64±6.12
Number of pens	
Range	1-3
mean±SD	1.35±0.51
Duration of pen use	
Range	2-8
Mean±SD	5.28±1.22
Number of hypoglycemic episode/year	
Range	0-19
Mean±SD	10.71±14.37

Table 2: Basic characters of patients with diabetes mellitus

Character	No %
Type of diabetes	
Type 1	28 (8%)
Type 2	321 (92%)
Sex (total=308)	
Males	165 (53.6%)
Females	143 (46.4%)
Types of insulin	
Short-acting	31 (8.9%)
Long-acting	256 (73.4%)
Both	26 (17.8%)
Therapy other than insulin	
Lifestyle only	46 (13.2%)
Metformin	244 (69.9%)
Sulphonylureas	36 (10.3%)
DPP-4inhibitors	23 (6.6%)
Storing insulin in fridge	323 (92.6%)
Site of storage in the fridge	
Upper shelf (butter)	64 (18.3%)
Middle shelf	247 (70.8%)
Lower shelf	38 (10.9%)
How many sites are you using for injection	
One site	10 (2.9%)
Two sites	116 (33.2%)

Three sites	223 (63.9%)
Whether rotating insulin injection sites	
Yes	305 (87.4%)
No	44 (12.6%)
If regular assessing the glycated hemoglobin according to guidelines	
Yes	288 (82.5%)
No	61 (17.5%)
Admission for ketoacidosis during the last year	
Once	27 (7.7%)
Twice	10 (2.9%)
Three times	1 (0.3%)
Four times	1 (0.3%)
Experienced hypoglycemic episodes during the last year	
Yes	343(98.3%)
No	6 (1.7%)

***Table 3. The effects of the site of insulin storage and ketoacidosis and hypoglycaemia**

Character	**Insulin storage (middle shelf)**	**Insulin storage (butter place and lower shelf)**	**P-value**
Ketoacidosis	0.11±0.39	0.26±0.65	<0.001
hypoglycemia	7.07±9.54	19.51±19.46	0.007

*Independent-Sample T-Test