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Challenges in Type-1 Diabetes Management during the Conflict in Syria

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Abstract

Background In Syria, a country at war for one decade, medical care has been severely affected by shortages in medications, resources, food, and physicians.

Objectives This study reviews the quality of care for patients with type-1 diabetes (T1D) receiving treatment in a private endocrinology service in Raqqa City, Syria.

Patients and Method A cross-sectional medical record review for patients with T1D followed-up at a private clinic run by a certified endocrinologist in Raqqa, Syria. All medical records were evaluated for patients' characteristics and multiple diabetes care indicators.

Results One hundred and ninety-seven patients with T1D were evaluated; 109 (55.3%) patients were females. The median age of participants was 16 (1.7–42) years, median duration of diabetes was 4 (0–27) years, and mean hemoglobin was A1C, 9.1% (8.7–9.5%). One hundred and twenty-five (63.5%) patients used premixed insulin. Eighty-one (42.4%) patients performed regular self-monitoring of blood glucose (SMBG) at least twice daily. Episodes of hypoglycemia and diabetic ketoacidosis (DKA) were reported in 62.4 and 54.4% of patients, respectively. There were significant correlations between the incidence of DKA and female gender and premixed insulin regimens.

Conclusion In this private endocrine practice in Raqqa City, Syria, the majority of patients are treated with premixed insulin. Only a minority have their glycosylated A1c monitored regularly. Our unprivileged population is poorly controlled with increased risk of hypoglycemia and admissions with diabetic ketoacidosis.

Keywords
- Syria
- type-1 diabetes
- diabetes care indicators
- A1C
- hypoglycemia
- insulin treatment
- diabetic ketoacidosis
- self-monitoring of blood glucose

Introduction

The prevalence of diabetes in Syria was estimated to be 12.6 to 14.8% in 2011, with type-1 diabetes (T1D) involving 5 to 7% of all patients with diabetes.[1,2] Syrians typically access medical care in the private sector or facilities run by the ministry of health and universities' hospitals.

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According to United Nations' official reports, as of early 2021, a total of 5.6 million Syrian people were displaced to neighboring countries, and an additional 6.7 million were internally displaced because of the war.[3] Based on prevalence of T1D, we estimated that more than 120,000 patients with T1D had to change their locations, providers, and perhaps treatments at least once within the past few years.

The recent novel coronavirus disease 2019 (COVID-19) pandemic, fuel shortages, and currency depreciation added to the burden and intensified the medical demand in the country. Recent UN sources confirm that 13 million Syrians need humanitarian assistance, including shelter, clean water, food, and medications.[3]

Al Raqqa, the sixth largest city in Syria, is located on the northeast bank of the Euphrates River, approximately 160 km east of Aleppo.[4] According to the ministry of health documents, the city is the provincial capital of the Raqqa Governorate. According to the ministry of health documents, six certified endocrinologists serve approximately 1 million residents. During the war, people with T1D were confronted with many survival challenges, including inadequate access to insulin and food, limited testing supplies, restricted access to basic laboratory assessment, and shortages of expert providers. Many patients faced serious interruption of insulin supplies with consequent life-threatening hyperglycemia and increased risk of diabetic ketoacidosis (DKA). On the other hand, health care providers faced enormous challenges in constantly modifying treatment, giving proper diabetes education, and managing life-threatening complications in suboptimal situations.

Although there are few reports on the prevalence of diabetes and the medical situation for Syrian refugees with diabetes in neighboring countries,[5–10] there is no report on the challenges in managing patients with T1D who remained in the country during the past decade. In this article, we review the management of patients with T1D followed in a private clinic in the city of Raqqa, Syria, and highlight the challenges that preclude patients' optimal care.

Patients and Methods

Study Population

A cross-sectional medical record review for patients with T1D followed-up at a private clinic run by a certified endocrinologist in Raqqa, Syria, from October 2018 to November 2021. All patients or guardians gave verbal agreement to share medical information. One hundred and ninety-seven medical records were evaluated for patients' characteristics and several diabetes indicators. Due to a significant shortage of pediatric endocrinologists, this service was managing both pediatric and adult endocrine patients.

Insulin regimens included the twice-daily premixed biosynthetic human insulin Mixtard 30 (ratio: 30% rapid and 70% intermediate Neutral Protamine Hagedorn [NPH] insulin), or the basal bolus regimen with glargine or NPH insulins once daily used as basal insulins, and regular or humalog insulins used before meals as bolus insulins.

Definitions

Self-monitoring blood glucose (SMBG) was achieved by monitoring of blood glucose utilizing capillary blood samples at least twice daily and whenever symptomatic. Hypoglycemia was defined as any episode by a plasma glucose concentration below 70 mg/dL, with or without signs and symptoms, diabetic ketoacidosis (DKA) was diagnosed when serum glucose level was greater than 250 mg/dL, a pH less than 7.3, a serum bicarbonate level less than 18 mEq per L, an elevated serum ketone level; ketone assessment was based on semiquantitative methods using nitroprusside reaction, and results more than 2+ were considered as positive.

Statistical Analysis

Data were analyzed by IBM SPSS Statistics software (version 23, Chicago, Illinois, United States). Categorical variables were analyzed by Pearson's Chi-square and Fisher's exact tests. Comparing means was performed using an independent sample *t*-test and comparing nonparametric variables as possible using the Mann–Whitney *U*-test. A *p*-value of <0.05 was considered statistically significant.

Results

One hundred ninety-seven patients with T1D were evaluated; 109 (55.3%) patients were females. The median age of participants was 16 (1.7–42) years, participants were distributed as follows: children less than 12 years ($n=54$), adolescents aged 12 to 17 years ($n=62$), and adults aged 18 years or older ($n=81$). Median duration of diabetes was 4 (0–27) years, and mean hemoglobin A1C 9.1% ± 1.7 (95% confidence interval [CI]: 8.7–9.5; ►**Table 1**). Premixed insulins formulations constituted the bases of treatment for 125 (63.5%) patients. During the 3-year observation period, 26 (13.4%) patients had to change their insulin regimen at least once.

While all patients had a microfilament evaluation whenever indicated, however, hemoglobin A1C, retinal examination, and urine albumin to creatinine ratio (UACR) evaluation were performed for 60, 69, and 82.5% of the participants, respectively. Furthermore, 110 (57.6%) patients, did not have the means to practice self-monitoring of blood glucose SMBG (►**Table 2**).

Further review of medical records revealed that 121/194 (62.4%) patients had at least one episode of hypoglycemia, and 105/193 (54.4%) had one or more episodes of diabetic

Table 1 Patients characteristics

Variables	Median (range)
Sex (males/females)	88 (44.7%)/109 (55.3%)
Age (y)	16 (1.7–42)
Duration of diabetes (y)	4 (0–27)
HbA1c (%)	9.12 (8.74–9.5)[a]

[a]HbA1c was normally distributed so this value is interpreted as mean and 95% confidence Interval.

Table 2 Patients' treatment, indicators of metabolic control and monitoring for diabetic kidney and eye disease

Indicator (number of valid data from 197)			*n* (%)
Treatment	Premixed Insulin		125 (63.2)
	MDI		72 (36.5)
Hypoglycemia	No		73 (37.6)
	Yes		121 (62.4)
	Unknown[a]		3
DKA	No		88 (45.6)
	Yes		105 (54.4)
	Unknown[a]		4
HbA1c testing	Not done		119 (60.4)
	Done once		50 (25.4)
	Many times		28 (14.2)
SMBG	Not done		110 (57.6)
	Regular		81 (42.4)
	Unknown[a]		6
Eye examination	Indicated	Not done	79 (68.7)[b]
		Done once	22 (19.1)
		Regularly	14 (12.2)
	Not indicated[c]		82
UACR testing	Indicated	Not done	94 (82.5)[b]
		Done once	16 (14)
		Regularly	4 (3.5)
	Not indicated[c]		83

Abbreviation: DKA, diabetic ketoacidosis; MDI, multiple-dose injections; SMBG, self-monitoring of blood glucose; UACR, urine albumin to creatinine ratio.
[a]Unknown cases were excluded from analysis.
[b]Percentages were calculated based on number of cases in indicated testing.
[c]Screening for complications in type-1 diabetes starts after 5 years of diagnosis.

ketoacidosis during the observed 3 years. While there was no statistically significant correlation between hypoglycemia and gender or type of insulin, hypoglycemia incidence was more common among patients older than 18 years compared with younger patients, 76 versus 55%, respectively, $p = 0.004$. Additionally, there was a significant association between the incidence of DKA and female gender, $p = 0.002$, and the use of premixed insulin regimens, $p = 0.004$ (►**Table 3**).

Discussion

All international diabetes authorities recommend optimal glycemic control for patients with T1D. Management of hyperglycemia and prevention of DKA requires individualized insulin therapy complemented by proper nutritional advice, diabetes education consultation, and glucose monitoring to achieve this task, while avoiding hypoglycemia at the same time.[11] Patients should ideally be treated with intensive insulin regimens using multiple daily injections or insulin pumps. While they are considered as cheaper alternatives to insulin analogs, premixed insulin formulations are not considered as the optimal choice for patients with T1D because of the increased risk of hypoglycemia and difficulty in dose adjustment.[11–13]

The list of supplies for a patient with T1D is financially overwhelming to many families. These include insulin vials, syringes, blood glucose meters, lancets, and strips. Additionally, many expensive assessments might be indicated in the evaluation including hemoglobin A1C, lipid testing, and screening for urine microalbumin among many others.[11]

Many Syrians with T1D had to relocate more than once, looking for safety during the past decade. Many patients had temporarily no access to insulin, especially those who moved into new geographical locations. Lack of appropriate preservation and refrigeration compromised the integrity of insulin for many. Moreover, and since synthetic insulins were not affordable, many patients were started or switched to 70/30 premixed types of insulins.[14]

Due to shortages of specialized medical personnel, pediatric and adult patients with T1D were frequently followed by nonskilled health care providers where primary nutritional and diabetes education could not be addressed. The vast majority of patients reported having not been educated on diabetes self-management and glucose monitoring

Table 3 The incidence of hypoglycemia and diabetic ketoacidosis by sex and type of insulin treatment regimen

Variables		Incidence		*p*-Value[a]
		No	Yes	
Hypoglycemia ($n = 194$):				
Sex	Female	41	66	0.80
	Male	32	55	
Treatment	Premixed	41	82	0.10
	MDI	32	39	
Age group	Younger than 18 years	57	70	0.004
	Older than 18 years	16	51	
Diabetic ketoacidosis ($n = 193$):				
Sex	Female	38	69	0.002
	Male	50	36	
Treatment	Premixed	46	76	0.004
	MDI	42	29	
Age group	Less than 18 years	61	66	0.346
	Older than 18 years	27	39	

Abbreviation: MDI, multiple-dose injections.
[a]Chi-square test.

before. Assessing food and water security, housing situation, psychosocial issues, smoking status, family stresses, and social adjustment to the illness and life changes were too luxurious and could not be achieved in the vast majority of patients.

The financial burden would most certainly lead to noncompliance with regular follow-ups, glucose monitoring, and regular evaluations. Furthermore, the only way for disadvantaged families to maintain their children's limited and precious insulin supplies is by cutting down on insulin doses.

More than 60% of our patients in the study were treated with premixed insulin. Glycosylated hemoglobin, the standard of care in monitoring treatment and management decisions, was evaluated only in 39.6% of the participants. Retinal examination and urine albumin to creatinine ratio were not checked even when indicated in 69 and 82.5% of participants, respectively. Of note, none of the participants in this study has received the COVID-19 vaccine when writing this review.

As expected, the consequences were substantial. The incidence of DKA in our unprivileged population was alarming at 54.4% during the 3-year observation period, compared with about two episodes per 100 patient-years of T1D in the developed countries.[15]

Causes of increased rate of DKA incidence must have included many factors: the remoteness of the area, the socioeconomic disadvantage of this unprivileged population, poor education and knowledge levels, poor diabetes education on the management of insulin on sick-days, poor glycemic control, poor awareness of DKA and consequences, poor compliance with treatment plan, poor access to glucose monitoring devices, no access ketone-testing supplies, poor access to insulin and medical care, insulin unaffordability, insufficient insulin administration, and incorrect insulin dosing.

The rate of hypoglycemia was 62.4% and significantly increased with the use of premixed insulin, also its incidence was more common in older patients.

Conclusion

In this private endocrine practice in Raqqa City, Syria, the majority of patients are treated with premixed insulin. Only a minority have their glycosylated A1c monitored regularly. Our unprivileged population is poorly controlled with increased risk of hypoglycemia and admissions with diabetic ketoacidosis.

Author's Contributions

I.A. has full access to all the data presented and takes responsibility for the integrity and accuracy of the content. All patient's data are available upon request as SPSS sheet. Both authors contributed to the conception and writing of the manuscript, literature search, revision, and approval of the final version.

Compliance with Ethical Principles

The study was undertaken as a quality assurance exercise, and it was approved by health local authorities.

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None.

Conflict of Interest

None declared.

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