Research Article

Managing patients with Diabetes Mellitus after a cholera attack: A retrospective analysis in a tertiary center and specialty clinic in Sana'a Yemen

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Abstract

Objective: We aimed to investigate patients with diabetes mellitus who presented for management of their diabetes after developing cholera during the cholera epidemic in Yemen.

Patients and methods: This is a retrospective chart review of all patients with the diagnosis of Diabetes Mellitus (DM) who presented after an attack of cholera from June 2018-June 2019 in 2 clinics (endocrinology and nephrology) in the University of Science and Technology hospital in Sana'a Yemen and a private endocrinology clinic. Also, 120 charts were reviewed as a control group on patients with diabetes mellitus with no history of cholera.

Result: A total of148 charts were reviewed, 28 patients with diabetes mellitus who presented within 2 months of developing cholera and 120 patients with diabetes mellitus but no history of cholera who served as the control group. The mean age of the patients with a history of cholera was 54.8 (SD 14.7) and in the control group was 52.4 (SD 17.4). In the 21 patients with cholera that were on oral hypoglycemic agents (OHA) or no medications before the attack, 66.7% (N=14) required insulin after developing cholera. In comparison to the control group, 54.2% (N=65) patients were on OHA or no medications at presentation and none of these patients were started on insulin at the initial visit (p-value <0.001).

In those patients who had been switched to insulin in the cholera group 78.5% (N=11) of them still required insulin months after developing cholera and only 21.5% (N=3) were able to switch back to OHA. Among the 7 patients on insulin before the attack, 85% (N=6) of them required an increase in the dose of insulin.

Conclusion: The majority of patients who presented to us after developing cholera required insulin and those already on insulin required an increase in their dose. Physicians caring for cholera patients should be aware of this and if not able to manage while the patient is being rehydrated should advise the patient to seek medical attention for management of their diabetes after rehydration if having hyperglycemia.

Introduction

The cholera epidemic in Yemen started in October 2016. It started approximately one year after the brutal war started in Yemen. A second more severe wave of cholera started in April 2017 and in January 2019 the number of cases reported by the WHO was approximately 1.4 million cases with ~2900 related deaths [1]. This cholera epidemic in Yemen is considered the worst in the world in recent times [1-4]. The majority of these patients were treated in cholera treatment centers and oral rehydration points around the country and only a small number were treated in hospitals [3].

On reviewing the literature no studies could be found on managing patients with diabetes mellitus after an attack of cholera. We noticed that patients presenting to our clinic after a cholera attack had uncontrolled diabetes mellitus even 1-2 months after their recovery and a large number of them required insulin. This is a retrospective study on 28 patients who presented to an endocrinology clinic and nephrology clinic in the University of Science and Technology hospital(USTH) after developing cholera also a third of the patients were seen in a private endocrinology clinic outside the hospital.

Methods

A total of 28 charts were reviewed (20 females and 8 males) in patients that presented to the outpatient endocrinology or nephrology clinic in the USTH and a private endocrinology clinic from June 2018-June 2019 because of uncontrolled diabetes following a cholera attack. Unfortunately, we were not able to revise the charts of patients seen in other internal medicine clinics in the hospital because of a problem with the computer system in the hospital which led to loss of all the data on patients in the USTH during a 2-year period. The control group consisted of 120 patients (59 females and 61 males) with DM who presented to the endocrinology clinic during the same period without a history of cholera. The patients that had recovered from cholera presented within 2 months after the attack. The HBA1c and Creatinine levels were recorded from the chart. Medications were categorized into OHA, insulin, OHA, and insulin or no medications, these were also recorded for the control group. Any adjustment in the patients' medications was noted from the chart. Patients admitted to the USTH during the cholera attack had their charts reviewed and the highest creatinine level was recorded, also any diabetes medication change at discharge was noted. For patients that were admitted elsewhere for the treatment of their cholera no data was available.

The study was approved by the ethical committee at the University of Science and Technology hospital.

Statistical Analysis

Qualitative variables were expressed as frequencies and percentages. Quantitative variables were expressed as means and standard deviation (SD). In this study, significance was identified as a p-value <0.05. The data was analyzed using SPSS version 23.

Results

A total of 148 patients with diabetes mellitus were seen in outpatient clinics. The group of patients that came following a cholera attack (8 males and 20 females) was seen in the endocrinology clinic or nephrology clinic in the USTH or a specialized private endocrinology clinic seen by the same endocrinologist. The control group consisted of 120 patients with diabetes that were randomly chosen and seen during the same period without a history of cholera. The mean age of the patients was 54.8 years (SD 14.7) and in the control group was 52.4 (SD 17.4) this can be seen in Table 1.

Variable		Case (n=28)				Control (n=120)				*p*-value	OR	95% CI of OR	
		Mean	SD	N	%	Mean	SD	N	%			Lower	Upper
Age (year)		54.8	14.7			52.4	17.4						
	≤ 45			6	21.4			35	29.2	0.41	0.66	0.25	1.77
	> 45			22	78.6			85	70.8				
	Female			20	71.4			59	49.2	0.033	2.59	1.06	6.32
	Male			8	28.6			61	50.8				
	Type 1 DM			2	7.1			11	9.2	1	0.76	0.16	3.62
	Type 2 DM			26	92.9			109	90.8				

Table 1: Characteristics of the patients with cholera (n=28) and the control group (n=120).

The majority of the patients had type 2 diabetes mellitus (N=26) in the cholera group and (N=109) in the control group. Only 2 patients had type 1 diabetes and cholera and 11 patients had type 1 diabetes in the control group. The renal function tests from the hospital admissions for treatment of the cholera attack were available in 14 patients who were admitted to the USTH for treatment this can be seen in Table 2.

Variable		Range	Mean	SD	N	%
Required dialysis						
	Temporarily				1	7.1
	No dialysis				13	92.9
Creatinine level during cholera attack (mg/dl)		0.82 – 8.91 (mg/dl)	4.4	2.1		
Creatinine level at presentation (mg/dl)		0.52 – 2.56 (mg/dl)	1	0.4		

Table 2: Data of renal function of DM patients with cholera during the hospital admission (N=14).

The other patients were admitted to cholera treatment centers or oral rehydration centers elsewhere or were treated as outpatients and no information was available on the renal functions during the attack. Only one patient required temporary dialysis for acute renal failure, none of the patients developed chronic renal failure, and by the time they came to the outpatient clinic all of them had a normal or near-normal creatinine (mean creatinine at presentation 1 mg/dl). One of the patients was diagnosed to have type 2 DM during the

cholera attack. Only one of the patients had insulin glargine added to previous medications on discharge the other 13 patients no management changes were made regarding diabetes medications on discharge from the hospital.

The patients' medications before the cholera attack were categorized into the following groups; oral hypoglycemic agents (OHA) (N=16) 57.1%, insulin (N=5) 17.9%, OHA, and insulin (N=2) 7.1% and no medications (N=5)17.9%. In the control group all of the patients were on treatment at presentation, 54.2% were on OHA (N=65) at presentation, 25.8% (N=31), and 20% (N=24) were on OHA and insulin.

The HBA1c was ordered on all patients at the clinic visit, it was documented in the charts of 24 of the patients, the mean HBA1c was 8.8% (SD 1.8) and in the control group, it was 9.5% (SD 9.5) with no significant difference between both groups.

In the patients that were on OHA or no medications before having a cholera attack (N=21) a total of 14 patients (66.7%) required insulin and out of these 11 patients (78.5 %) continued to require insulin months after the attack and 3 (21.5%) were able to switch back to oral agents. Among the control group, none of the patients were started on insulin at their first visit to the clinic (p-value <0.001). Among the patients on insulin before developing cholera (N=7) 85% of them required an increase in the dose of insulin and only one patient didn't require any change in the insulin dose.

Discussion

Studies have shown an increase in hyperglycemia and new-onset diabetes after critical illnesses and acute renal failure [5-9]. There is an increased risk of hyperglycemia during infections which are known to precipitate diabetic ketoacidosis and hyperosmolar hyperglycemic state [10]. Infections are known to cause an increase in the counter-regulatory hormones as catecholamines which enhance glycogenolysis in the liver, also growth hormone and cortisol stimulate gluconeogenesis. In addition, there is an increase in insulin resistance. These factors all lead to stress-induced hyperglycemia [8,11,12]. There is also increased insulin resistance due to endoplasmic reticulum stress, which may eventually lead to β-cell death [12]. The insulin resistance and β-cell failure may explain why many of our patients were unable to continue on oral agents even after a period of recovery from cholera.

This is the first study to discuss the management of diabetes after a cholera attack. Little was done for the patients regarding the management of diabetes during their admission to the hospital and rehydration centers for the treatment of cholera even among the patients that developed acute renal failure during the hospital admission. All of the patients with the exception of one were continued on the same oral medications they were on before developing cholera on discharge from the hospital. More recently

in patients with COVID-19 infection, there has been much attention on the management of diabetes in these patients due to the increased morbidity and mortality among patients with DM [13,14]. It has been advised that medications such as metformin and Sodium-glucose co-transporter-2 inhibitors should be discontinued during the acute phase of COVID-19 infection [15]. Patients that had cholera and were on metformin before admission to the hospital were restarted on it on discharge. Metformin was not discontinued or replaced with another medication in any of our patients on discharge from the hospital. During the hospital admission, patients were kept on a sliding scale of regular insulin which was discontinued on discharge.

In the rehydration centers, a glucometer was used to check the blood sugar if the patient had a history of diabetes and it was checked again on discharge, for those with high sugars the patient was advised to seek medical attention after discharge. Electrolytes and renal function tests were done only in patients in critical condition or with decreased urine output and not done routinely, (As reported by a physician working in one of the rehydration centers, and this may not apply to all centers as they were supported by different organizations). These rehydration centers were overwhelmed with patients during the epidemic [2]. The resources available were limited with the inability to treat pre-existing conditions in those presenting to them. Patients treated in these centers did not have any documentation of their blood glucose levels and creatinine during the attacks when they presented to us. Patients with critical illnesses often develop hyperglycemia and require insulin during the acute episode. This has been known for a long time [8,10,16]. We noticed that only one of the patients with cholera had insulin added to his medications on discharge from the hospital. The majority of the patients coming to us had uncontrolled diabetes with severe hyperglycemia that required insulin treatment or an increase in the dose for those already on insulin. Physicians should be aware of the possibility of hyperglycemia in patients with diabetes developing cholera and manage them as any critically ill patient to prevent the morbidity associated with delaying the appropriate treatment.

Conclusion

This is a study on the management of patients with diabetes after a cholera attack. Limitations of this study are the small number of patients and the results may be biased since patients who did not have high glucose levels probably did not seek any medical help for their diabetes after developing cholera. Another limitation is that patients in rural areas may not have access to hospitals nearby and may not seek medical help for hyperglycemia due to poverty and difficulty in traveling during the war. Physicians should be aware of the risk of hyperglycemia after cholera and patients with DM should be advised after treatment of cholera to check their glucose levels and if high to seek medical attention for adjustment of their medications.

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