

Hyperglycemic emergencies in Indian patients with diabetes mellitus on pilgrimage to Amarnathji yatra

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) represent two distinct metabolic derangements manifested by insulin deficiency and severe hyperglycemia, with estimated mortality rates of 2.5–9%. In patients with type 2 diabetes mellitus (DM) controlled by diet or oral agents, DKA does not occur unless there is significant severe stress such as severe sepsis, major surgery, trauma, etc. We observed many such emergencies occurring in pilgrims. **Objective:** We analyzed the data of 13 patients with DM admitted in our endocrine department with hyperglycemic emergencies during 2 years of the annual pilgrimage (yatra) to Amarnathji. **Materials and Methods:** We reviewed and analyzed the case records of 13 yatis with DM who were referred and admitted in our hospital with hyperglycemic emergencies during the yatra season (July–August) of 2006 and 2007. **Results:** Eleven of 13 had DKA and 1 each had HHS and hypoglycemia. After initial clinical assessment and blood sampling for blood counts, electrolytes, blood gases, urinalysis, chest radiography, and electrocardiography, these cases were managed with standard protocol published by American Diabetes Association (ADA) for the management of DKA and HHS. Average blood glucose was 466 mg/dl and nine subjects had moderate to severe ketonuria. All the cases, except one, were in stable condition at the time of discharge. **Conclusion:** High altitude, strenuous exertion of going uphill, withdrawal of insulin or oral hypoglycemic drugs, starvation, sepsis, and alcohol intake were recorded as predisposing factors. Therefore, there is an immense need for institution of a special health education program to all the yatis before taking the endeavor.

Key words: Amarnath shrine, diabetic ketoacidosis, high altitude climbing, starvation, type 2 diabetes mellitus

INTRODUCTION

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) represent two distinct metabolic derangements manifested by insulin deficiency and severe hyperglycemia. DKA is defined as the presence of all three of the following: (1) hyperglycemia (blood glucose > 250 mg/dl), (2) ketosis, and (3) acidemia (pH < 7.3).^[1] Hyperglycemic emergencies such as DKA and HHS are very rare in the West (2). Annual incidence as reported by the largest epidemiological study is 4.6/100,000 of diabetic

population and 0.14 cases/100,000 in general population.^[2] Earlier, we had recorded 36 cases of DKA (20 males and 16 females) out of 1249 juvenile onset diabetics admitted at our institute, giving a relatively higher incidence [13.77 DKA episodes per 100 of type 1 diabetes mellitus (DM)].^[3] Mortality rates have been reported to range from 2.5 to 9% in recent western studies,^[4] but the emergencies still take heavy tolls in the developing countries as mortality rate in our series was 33.3%. Analyzing mortality trends in type 1 DM, we also noticed DKA (6.69%) as an important contributor even though more common causes were infections (33.83%), chronic renal failure (30.85%), coronary artery disease (16.36%), cerebrovascular disease (13.75%), and hypoglycemia (7.81%).^[5] In patients with type 2 DM controlled by diet or oral agents, DKA does not occur unless there is significant severe stress such as severe sepsis, major surgery, trauma, etc.^[4] More than half of African-American persons with new diagnoses of DKA have clinical, metabolic, and immunologic features of type 2 DM.^[6] Infection remains the most common

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precipitating cause, accounting for 20–40% of all the cases of DKA and HHS, respiratory tract infection (RTI) and urinary tract infection (UTI) being the commonest.^[2] The other factors incriminated in the precipitation of DKA are factors such as insulin omission, alcohol, surgery, trauma, first presentation of type 2 DM, drugs (steroids, thiazides, sympathomimetics, interferon, ribavirin, protease inhibitors, recreational drugs, and antipsychotics like risperidone, clozapine, and olanzapine).^[4] Infection was found to be the commonest cause (77.7%) in our series.^[3] Ordinarily, strenuous exertion is not rated as the precipitating factor, especially in type 2 DM.

Amarnathji shrine is located in the mountain of Karakorum ranges in Kashmir at 3888 m and is 363 km from Jammu [Figure 1a and b]. Annual yatra begins in the month of June and ends on full moon night (*purnima*) in the month of August. Annually, approximately, more than 100,000 people from all over India visit this shrine. The annual pilgrimage to Amarnathji is a very stressful endeavor and requires strenuous physical effort, especially for the diabetics, the elderly, and persons with other chronic illnesses. Although the data about total number of diabetics visiting every year are not available, we present a series of 13 cases with DM who were admitted in our department with hyperglycemic emergencies during the 2-year yatra seasons.

MATERIALS AND METHODS

The data are from the Department of Endocrinology of

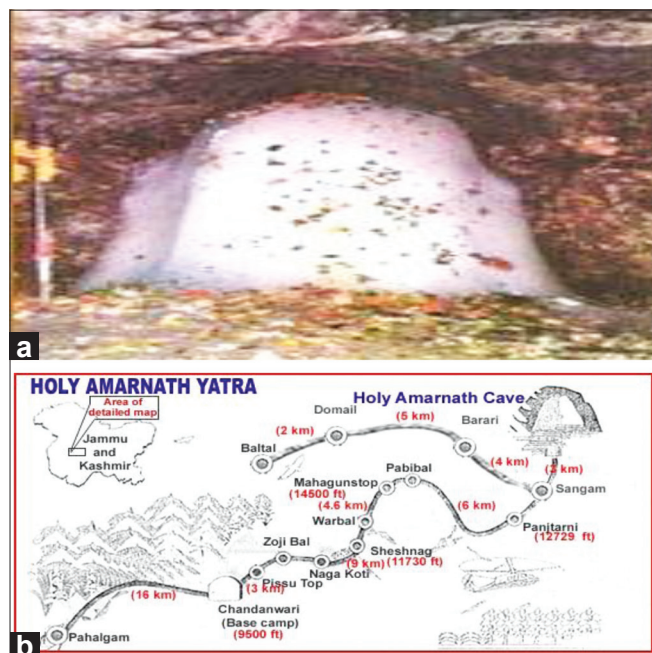


Figure 1: (a) The holy cave of Amarnathji at Phalagam India; (b) the road map to be taken by yatrīs to the holy cave of Amarnathji

Sheri-Kashmir Institute of Medical Sciences, Srinagar, Kashmir (India), a tertiary care center in the northern part of the country where the holy shrine is located. This is a 650-bedded hospital located in the center of Kashmir valley, which is the only referral center for the valley of Kashmir.

We reviewed and analyzed the case records of 13 DM patients among the yatrīs, who were referred and admitted in our hospital during the yatra season (July–August) of 2006 and 2007. Out of 13 subjects, 11 were diagnosed as DKA and 1 each had HHS and hypoglycemia. These patients were referred from the base camp organized by state government health agency, The Health Services of Kashmir at Baltal, which is supposed to provide first aid service to all the pilgrims. The base camp is located at Baltal which is 11 km from the holy cave and 90 km from Phalgam. This high-altitude transit may be crucial in the absence of resuscitation. The first aid camp is about 2 hours drive from our institute.

These cases were received by emergency department of our hospital and were shifted as early as possible to endocrine floor after initial clinical assessment and taking blood samples for blood counts, electrolytes, blood gases, urinalysis, chest radiography, and electrocardiography. After shifting to our ward, these cases underwent detail clinical assessment and relevant investigations and were managed accordingly. Most of these subjects reached after a significant delay to the emergency department. All the patients were managed with standard protocol as published by ADA for the management of DKA and HHS.^[7] Institutional ethics committee that looks into the ethical aspects of human experimentation approved the study.

RESULTS

The clinical profile indicated an average age of 41.9 ± 7.3 years, with a sex distribution of male:female of 8:5. The state-wise distribution of cases was as follows: three from Gujarat, two each from Delhi, Mumbai, and Rajasthan, and one each from Madhya Pradesh, Chhattisgarh, Calcutta, and Indore [Table 1]. The diagnosis of type 2 DM was clear in six patients and type 1 diagnosis was clear in four patients, and three were first time detected and diagnosis was unclear. In epidemiological studies, it was observed that 20% of patients admitted with DKA had previously undiagnosed diabetes. Average duration of DM was 8.62 ± 1.2 years (5–14 years) and six cases were on insulin and four on various oral hypoglycemic agents. DKA was diagnosed in 11 cases and HHS and hypoglycemia were diagnosed in one each. The biochemical characteristics revealed severe

Table 1: Clinical profile of the pilgrims who presented with hyperglycemic emergencies

Case #	Age yrs	sex	Residence	Diagnosis at presentation	Duration	Type of DM	Severity	Hospital stay (days)	Complication If +
1	25	F	Gujarat	DKA	6	Type 1	Severe	3 days	None
2	45	M	Indore	DKA	11	Type 1	Severe	4	Azotemia
3	48	F	Chatisgarh	DKA	14	Type 2	Moderate	4	None
4	43	F	Calcutta	DKA	First		Severe	8	None
5	26	F	Rajasthan	DKA	8	Type 2	Moderate	5	None
6	28	F	Rajasthan	DKA	10	Type 2	Moderate	2	None
7	45	M	Mumbai	HONK	12	Type 2 Tripathy	HONK	5	azotemia
8	45	M	MP	DKA	5	Type 2	Moderate	3	None
9	73	M	Gujarat	Hypoglycemia	2	Type 2	Severe	4	None
10	31	M	New Delhi	DKA	First p		Severe	3	None
11	28	M	Delhi	DKA	2 M	Type 1	Severe	7	None
12	26	M	Mumbai	HONK	First p		Severe	1	None
13	32	M	Gujarat	DKA	5	Type 1	Severe	4	None

DKA ($\text{HCO}_3^- < 12$ mmol/l) in nine and hyperosmolar state in one subject. Average pH in DKA patients was 7.11 (6.9–7.25) with average serum bicarbonate levels found to be 7.04 (2.5–11.1) mmol/l. Average blood glucose was 466 mg/dl and nine subjects had moderate to severe ketonuria. In our series, five patients were documented to have infections: culture-negative UTIs in two, upper RTIs in another two, and acute gastroenteritis in only one patient. Azotemia with serum creatinine of more than 1.5 mg/dl was present in 6/13 and altered sensorium at presentation was evident in 8/13 cases. Only two patients were having hypotension, defined as systolic BP of less than 90 mm Hg. Most of the cases urged for very early discharge and average hospital stay of patients was 4.7 ± 1.6 days. Also, almost all these subjects were without any medical records of illness, investigations, or any medications. Understandably, most subjects were carried by the medial aid team and some fellow yatri, and had little financial and family support. All the cases, except one patient who died, were in stable condition at the time of discharge. This patient was actually managed for 24 hours in another hospital, and hence there was a significant delay in the management. None of the patients has followed our department till the writing of this case series, and hence their long-term follow-up remains unavailable. They were, however, in telephonic contact till they reached their respective physicians. We also propose some guidelines for the yatri with DM (type 1 or 2) who wish to undertake this holy pilgrimage.

DISCUSSION

Though insulin omission remains a common cause of DKA in adolescent population,^[4] in our series of 13 adult patients, not all of them were on insulin (6 out of 13 patients were on insulin) and not all of them omitted insulin. Another established cause of DKA precipitation is infection.^[2] Here, five patients were documented to have infections:

culture-negative UTI in two, upper RTI in another two, and acute gastroenteritis in one patient, but none of the infections was so severe to alone account for precipitation of DKA/HHS. Almost all of our patients complained of extreme exertional fatigue and attributed their illness to it and 4 of 13 patients had starved themselves for more than 1 day. Only two patients were forthcoming with history of taking alcohol, but we were not able to estimate the alcohol content in their blood or in the blood of other patients in whom we suspected alcohol consumption as a precipitating factor. Treacherous uphill trek leading to Amarnathji cave at high altitude where there is risk of associated hypoxia can be considered as one of the important combination of factors in the causation of hyperglycemic crises, as the literature has shown that the severe stress impinging on neuroendocrine axis may worsen glycemic control and lead to precipitation of hyperglycemic emergencies.^[7,8] Although data and the prevalence of diabetics attending the holy yatra are not available, we recorded the series of 13 patients admitted with hyperglycemic crises: 11 were having DKA and 1 each had HHS and hypoglycemia in two seasons (i.e. 2006–2007). There are also not much data on the diabetics developing acute complications while on pilgrimages or such endeavors where some specific factors can be considered as precipitants in addition to the usual ones. In Medline, there are, however, some reports on diabetic pilgrims on Hajj. In a prospective study in four hospitals in two different locations, a cohort of 76 patients from Arafat hospitals and 84 patients from Mina hospitals were included (total 160 patients) during Hajj. Pre-existing co-morbid medical conditions included bronchial asthma and chronic obstructive pulmonary disease (COPD; 22.5%), hypertension (17.5%), and DM (15%).^[9,10] We also published recently that duration of diabetes, older age, and presence of complications are risk factors for infection in diabetics.^[11]

Average age of yatriis admitted with us was 42 years, and cases were eight men and five women. Some studies earlier have reported female predominance,^[6] but in our series, the male preponderance could be due to significant dominance of males opting for the yatra. Most of these cases were type 2 DM and it is unlikely that withdrawal of insulin/oral hypoglycemic agent caused DKA as would the minor infections. In epidemiological studies, it has been observed that 20% of patients admitted with DKA had previously undiagnosed diabetes and average age of presentation was 40–50 years.^[6] In a study to assess the needs of the Omani diabetics during 1996 Hajj (DOH), out of 10,800, only 169 Hajjes were with DM (prevalence rate 16/1000). It included 4% insulin-dependent DM (IDDM), 7% on dietary control, and 89% on oral hypoglycemic agents. All Hajjes (pilgrims) with IDDM and 96% on oral hypoglycemic agents had brought their medicines with them. During the Hajj period, 2.4% of DOH had random blood sugar (RBS) <75 mg/dl, 14% had 75–110 mg/dl, and 49% were hyperglycemic (RBS > 200 mg/dl). About half of the DOH (48%) knew the clinical presentation of hyperglycemia and a fourth (24%) knew about the symptoms of hypoglycemia. Only 9.5% were trained to test themselves for blood sugar. The median age of DOH was 54 years (inter-quartile range 50–62). Some 7.5% females and 4.9% of males were obese (body mass index > 30 kg/m²). All DOH, except one, were not wearing protective shoes, and 70% did not have identification wrist bands that show their diabetic status and regimen for treatment.^[10] None of the subjects had any medical records of previous therapy nor had they any medications. In our subjects, the history about pre-yatra medical examination, education about sick day guidelines, wearing of wrist bands, and protective shoes was lacking. Average duration of DM in our series was 8.62 years (range 5–14 years); six were on insulin and two cases were taking oral anti-diabetic agents. In four patients, diabetes was complicated by chronic diabetes specific complications like distal sensory motor neuropathy (all four), proteinuric nephropathy (two), tripathy (one), and only one patient was having Wegner's grade II foot ulcer. Mortality among patients with DKA has been related to age and other clinical features at presentation; besides this, there appears to be an increased risk of microvascular complication of diabetes with long-term follow-up of survivors of DKA.^[2] We have recently published that longer duration of diabetes, older age, and presence of diabetic complications predispose them to various infections which can be a major cause of mortality.^[11]

We conclude that hyperglycemic emergencies are not uncommon in diabetics during the yatra. The trek being uphill, long, non-motorable, and in hypoxic zones, the

milieu seems to be conducive for the precipitation of hyperglycemic emergencies. Since we did not have baseline data of total unknown diabetics in the yatra, we cannot find the incidence of these emergencies, which can be considered a limitation of the study. Therefore, there is an immense need for a special health education program and for special services for the diabetics during yatra. Yatriis should undergo pre-pilgrimage health clearance, carry their medical records, should learn about symptoms and signs of hypoglycemia, importance of hydration, need of caloric intake, compliance with medications or insulin, and importance of periodic glucose monitoring, in addition to wearing protective shoes and identifying wrist bands. Specialized services for the diabetics would alleviate a lot of the stress during yatra among the diabetics.

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