

Ketonuria and Ketonemia in type 2 Diabetes mellitus patients attending an Indian endocrine clinic

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ABSTRACT

Introduction: The occurrence of ketonuria in type 2 diabetes been reported by various authors studying separate ethnic groups. There has been an explosion of type 2 diabetes in the Indian subcontinent, and this has been accompanied by an increase in the research done in this field. However, not much emphasis has been laid on finding the incidence of ketosis- prone type 2 diabetes in the South Asian population.

Objectives: This study aims to assess the frequency of ketonuria and ketonemia amongst type 2 diabetic patients attending an endocrine OPD in northern India.

Material and Methods: Two hundred patients of type 2 diabetes mellitus, at risk of developing ketosis, were tested for urine ketones. Any person with diabetes, mellitus not known to be a case of type 1 diabetes mellitus, with any of these inclusion criteria: fasting blood glucose >200 mg%, post prandial or casual blood glucose >300 mg%, abdominal symptoms, any acute illness including altered sensorium, an 'atypical' presentation, pregnancy and alcohol intake, was included in the study.

Results: The most frequent indications for ketone testing were post prandial or casual blood glucose >300 mg%, fasting blood glucose >200 mg% and first presentation to the hospital. The highest yields, of ketonuria were in patients of high blood glucose and acute illness if seen in absolute terms, or as a percentage of total ketonuric patients. Three patients had positive ketonemia, including one with acute pancreatitis. Percentage – wise, ketonuria was more often seen in patients with abdominal symptoms, pregnancy, alcohol intake and acute illness like balanoposthitis, gastroenteritis and tuberculosis. Moderate or high ketonuria was observed more often in pregnancy and abdominal symptoms. Ketonuria was frequently encountered (17%) in "type 2" diabetic individuals with specific signs, symptoms or presentations. Ketonuria is frequent, while ketonemia is infrequent (but not absent) in type 2 diabetic patients in India.

Conclusion: The study reveals that urine ketone testing should be done in so called type 2 diabetes patients with specified symptoms or presentations. This economical investigation plays an important role in deciding the appropriate treatment for the patient, and prevents potentially fatal delays in instituting insulin therapy. [IJEM 2007;(3&4):7-9]

Keywords: Ketonuria, Ketonemia, type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus was earlier classified as IDDM (insulin dependent diabetes mellitus) and NIDDM (non insulin dependent diabetes mellitus). The latter entity was thought to be non insulin requiring and ketoacidosis was thought to be a complication limited to IDDM.

Gradually, with advances in understanding the pathophysiology of the disease, many variants of the illness were noted. Type 2 diabetes mellitus (earlier named NIDDM) was seen to present with ketonuria, and later get controlled with oral hypoglycemics, in American-Africans(1,2,3). This entity

was named Type 1.5 diabetes or 'Flatbush' diabetes(4).

The occurrence of ketonuria in type 2 diabetes been reported by various authors studying separate ethnic groups(5,6,7). This entity is thought to be less common amongst Asians than Africans.

There has been an explosion of type 2 diabetes in the Indian subcontinent, and this has been accompanied by an increase in the research done in this field. However, not much emphasis has been laid on finding the incidence of ketosis- prone type 2 diabetes in the South Asian population.

This study aims to assess the frequency of ketonuria and ketonemia amongst type 2 diabetic patients attending an endocrine OPD in northern India. It also aims to assess the cost-effectiveness of advising blood and urinary ketone estimation in different subgroups of patients with diabetes mellitus.

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MATERIAL & METHODS

Two hundred patients of type 2 diabetes mellitus fulfilling the inclusion criteria, presenting to our endocrine OPD located in northern India were tested for urine ketones by dipstick method (Keto – Diastix from Bayer Diagnostics). Some patients were also assessed for ketonemia using Optium blood ketone sticks (Abbott England). Blood ketone testing was not possible in many patients because of intermittent availability of sticks during the study period, and because of paucity of funds in the resource – challenged centre.

The inclusion criteria were all of the following:

- 1) Any person with diabetes mellitus not known to be a case of type 1 diabetes mellitus.
- 2) Any person with diabetes mellitus not on chronic insulin therapy for more than 3 months.
- 3) Any person presenting with one or more of the following symptoms, signs or presentations:
 - a) fasting blood glucose >200 mg%, b) post prandial or casual blood glucose >300 mg%, c) abdominal symptoms: nausea, vomiting, abdominal pain, d) any acute illness including altered sensorium, e) first presentation to the hospital, f) an 'atypical' presentation, as assessed by the multipurpose diabetes worker, g) pregnancy and h) alcohol intake in the preceding 24 hours.

Each patient fulfilling inclusion criterion 1, 2 and 3 was tested for urinary ketones by dipstick (Keto Diastix from Bayer Diagnostics, Germany). The 48 patients had a blood ketone estimation done (Optium Ketone sticks from Abbott Laboratories, England).

Results were analyzed to assess the correlation of different variables with ketonuria and ketonemia.

RESULTS

All 200 patients were included in the study, 48 of whom had a blood ketone determination done.

The characteristics of ketonuria positive and ketonuria negative patients are presented in Table 1.

Table 1: Patient characteristics in both groups

	Ketonuria positive (n=34)	Ketonuria negative (n=166)
Age (mean ± S.D) yrs	36.21 ± 6.04	41.23 ± 5.32
Gender (M/F)	20/14	97/69
BMI (mean ± S.D) kg/m ²	27.28 ± 2.23	26.26 ± 2.12
Duration of diabetes (mean ± S.D) yrs	3.42 ± 1.92	6.51 ± 2.91
H/o prior insulin use (%)	3/34(8.82%)	27/166(16.26%)
Newly diagnosed diabetes (%)	9/34(26.47%)	22/166(13.25%)

Ketonuria positive patients were younger, had diabetes of shorter duration, and were more likely to have newly

diagnosed diabetes than patients without ketonuria. There was no significant difference with regard to gender distribution and body mass index (BMI). The symptoms, signs or presentations which the patients had are detailed in Table 2.

Table 2: Indications and results of urine ketone testing

Indication	All patients (n=200)	Ketonuria negative (n=166)	Ketonuria positive (n=34)
Fasting blood glucose >200 mg%	69 (34.5%)	54(32.53%)	15(44.11%)
Post prandial or casual blood glucose >300 mg%	92(46.0%)	77(46.38%)	15(44.11%)
Abdominal symptoms: nausea, vomiting, abdominal pain.	11(5.5%)	6(3.61%)	5(14.70%) *
Any acute illness including altered sensorium	30(15%)	21(12.6%)	9(26.47%) *
First presentation to the hospital	58(29%)	56(33.73%)	2(5.8%)
An 'atypical' presentation, as assessed by multipurpose diabetes worker	17(8.5%)	14(8.43%)	3(8.82%)
Pregnancy	4(2%)	1(0.6%)	3(8.82%) *
Alcohol intake in the preceding 24 hours.	4(2%)	2(1.2%)	2(5.8%) *

* = $p < 0.05$

The most frequent indications for ketone testing were post prandial or casual blood glucose >300 mg%, fasting blood glucose >200 mg% and first presentation to the hospital. The highest yields, of ketonuria were high blood glucose and acute illness if seen in absolute terms, or as a percentage of total ketonuric patients.

The same figures, when calculated as percentage total subjects for a particular indication, are shown in Table 3. The highest percentage of positivity was seen in pregnancy, alcohol intake, abdominal symptoms and acute illness. Moderate or high ketonuria was observed most often in pregnancy and abdominal symptoms. The lowest yield of ketonuria was in patients with post prandial or casual blood glucose >300 mg% and first presentation to the hospital.

The 48 patients who had blood ketone tested are detailed in Table 4. The patients with positive ketonemia included a total of three patients. All had abdominal symptoms and two of them had high fasting blood glucose values in the setting of acute illness. One of the ketonemia positive patients (5.6 mmol/l) was a 24 year old male with abdominal symptoms, who was later diagnosed as having acute pancreatitis. The other two were lean women aged 50 - 60 years old with gastroenteritis, dehydration and altered sensorium. Both responded to intravenous fluids and insulin.

The details of the ketonuria – positive 'acute illness'

which were an indication for testing ketones are: gastroenteritis (2/9), tuberculosis (2/9) and balanoposthitis (5/9). The 'atypical' presentations with ketonuria which prompted a multipurpose diabetes worker to ask for ketone test were profuse sweating (1/3), and obese adolescent (2/3).

Table 3: Ketonuria positivity in different indications

Indication	Total	No (%) of ketone positivity	Ketones trace/small no.	Ketones moderate/large
Fasting blood glucose >200 mg%	69	15(21.73%)	10(14.49%)	5(7.2%)
Post prandial or casual blood glucose >300 mg%	92	15(16.30%)	10(10.86%)	5(5.43%)
Abdominal symptoms: nausea, vomiting, abdominal pain	11	5(45.45%)	1(9.09%)	4(36.36%)
Any acute illness including altered sensorium	30	9(30%)	3(10%)	6(20%)
First presentation to the hospital	38	2(5.26%)	1(2.63%)	1(2.63%)
An 'atypical' presentation, as assessed by multipurpose diabetes worker	17	3(17.64%)	1(5.88%)	2(11.76%)
Pregnancy	4	3(75%)	1(25%)	2(50%)
Alcohol intake in the preceding 24 hours	4	2(50%)	0	1(25%)

Table 4: Ketonemia positivity in different indications

Indication	All patients (n=48)	Ketonemia positive (>5.6 mmol/l) (n=3)	Ketonemia equivocal (2.6-5.6 mmol/l) (n=0)	Ketonemia negative (<2.6 mmol/l) (n=45)
Fasting blood glucose >200 mg%	19(39.58%)	2(66.66%)	0	17
Post prandial or casual blood glucose >300 mg%	23(47.91%)	0	0	23
Abdominal symptoms: nausea, vomiting, abdominal pain.	7(14.58%)	3(100%)	0	4
Any acute illness including altered sensorium.	7(14.58%)	2(66.66%)	0	5
First presentation to the hospital	0	0	0	0
An 'atypical' presentation, as assessed by multipurpose diabetes worker	3(6.25%)	0	0	3
Pregnancy	0	0	0	0
Alcohol intake in the preceding 24 hours.	2(4.16%)	0	0	2

DISCUSSION

In this study ketonuria was frequently encountered (17%) in "type 2" diabetic individuals with specific signs, symptoms or presentations. Ketonemia, however, was much less frequently seen(1.5%). Similar observations regarding ketonuria have been made by researchers from various parts of the world(4, 5, 6). Not much work, however, has been done regarding ketonemia in "type 2" diabetes. This study has shown that the ketonuria is frequent, while ketonemia is infrequent (but not absent) in type 2 diabetic patients in India.

The maximum number of ketonuric patients had fasting blood glucose >200 mg% or postprandial blood glucose >300 mg%. Percentage – wise, ketonuria was more often seen in patients with abdominal symptoms, pregnancy, alcohol intake and acute illness like balano–posthitis, gastroenteritis and tuberculosis. Abdominal symptoms, acute illness and pregnancy were associated with higher incidence of moderate or large ketouria.

These findings have major diagnostic and therapeutic implications. Urine ketone testing should be done in so called type 2 diabetes patients with specified symptoms or presentations. It is a simple and cost effective investigation which has bearing on further management of the patient.

Physicians, nurses, laboratory technologists and other diabetes care providers should be sensitized to the existence of this subset of patients with diabetes. They usually respond to short term insulin therapy and remain well controlled on diet, exercise and oral drugs once the acute illness is resolved. The difficulty in classifying these patients should not mean that they shouldn't be treated appropriately(8).

The diagnosis may be missed, and proper therapy delayed, if urinary ketone estimation is not performed, multi purpose diabetes workers can be trained to recognize 'atypical' presentation, and order urinary ketones for a pre selected list of indications in certain ethnic groups. This will help in early institution of appropriate therapy.

The study suffers from some limitations. Blood ketones were not estimated in all subjects, due to paucity of resources. A bias is evident towards ordering blood ketones in 'more sick' patients. The under privileged character of the

area where this study was performed has meant that islet cell antibodies, GAD antibodies or other auto immune markers, and glycated haemoglobin could not be estimated in the subject population.

In spite of these limitations, however, this work will help in redefining investigative and therapeutic strategies in Indian type 2 diabetes patients with acute illness and hyperglycemia.

CONCLUSION

The study reveals that urine ketone testing should be

done in so called type 2 diabetes patients with specified symptoms or presentations. This economical investigation plays an important role in deciding the appropriate treatment for the patient, and prevents potentially fatal delays in instituting insulin therapy.

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