Dipstick urinalysis for diabetes screening in TB patients

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Introduction: Diabetes knowledge among TB patients can contribute to improved TB treatment outcomes, but lack of diabetes diagnosis awareness is a limitation in developing countries. Given its low cost, the sensitivity of urine glucose dipsticks for diabetes screening in TB patients was assessed.

Methods: Glycosuria was assessed in 90 newly diagnosed TB patients (38 with diabetes) in south Texas, USA (n = 20) and northeast Mexico (n = 70) during January 2009–December 2010.

Results: Glycosuria was detected in 65% of the diabetic patients with chronic hyperglycemia (positive predictive value 91%, negative predictive value 84%).

Conclusion: We propose that TB clinics with limited budgets where portable glucometers may not be available conduct universal screening for diabetes with urine dipsticks. This could be followed by blood glucose or HbA_{1c} testing in the subset of patients requiring confirmation or higher sensitivity assessment, to improve the comanagement of TB and diabetes.

Keywords: Tuberculosis, Diabetes, Urine glucose, Urine dipstick, Glycosuria

Introduction

TB accounted for 1.4 million deaths and 8.8 million new cases worldwide in 2010.¹ Type 2 diabetes is a chronic metabolic disease that is on the rise: there are an estimated 285 million cases worldwide with a projected increase to 438 million by 2030.² This pandemic is mostly growing in developing countries where TB is also endemic. There is growing recognition of the re-emerging importance of diabetes in TB control.³ It is estimated that 13–25% of new TB cases are attributable to diabetes.^{4,5} Diabetes knowledge at the time of TB diagnosis can affect TB patient management since patients with the comorbidity appear to be more likely to have a delayed response to TB treatment, fail to respond to treatment or die.⁶ A group of experts reviewed the available data on the association between TB and diabetes to make policy recommendations.³ A reported need was to identify cost-efficient approaches to screening for diabetes at TB clinics given that countries with the highest burden of TB have limited resources. Urine dipsticks are the lowest cost option for diabetes screening (<US\$0.50 per test). A study in Indonesia showed that glycosuria (and diabetes) was threefold higher among TB patients than in controls without TB, but the usefulness of this assay for diabetes screening was not evaluated.⁷ We conducted a case–control study to assess for the first time the potential of urine glucose dipsticks for diabetes

screening in TB clinics given their low cost, temperature stability, long shelf-life and non-invasiveness.

Methods

Newly diagnosed TB patients ≥ 18 years old were sequentially identified and enrolled in south Texas, USA (n = 20) and northeast Mexico (n = 70) between January 2009 and December 2010. Participant enrollment and their characteristics were described previously.⁴ All patients signed an informed consent prior to enrollment in the study.

A spot urine sample was collected at enrollment and urine glucose, ketones and proteins were recorded (Multistix 10 SG strips; Bayer-Siemens, Deerfield, IL, USA). Urine glucose was compared with hyperglycemia (AccuCheck Advantage, Roche, Indianapolis, IN, USA), chronic hyperglycemia (HbA_{1c} $\geq 6.5\%$; Helena Laboratories, Beaumont, TX, USA), or the American Diabetes Association definition for diabetes diagnosis: self-reported diabetes or hyperglycemia or chronic hyperglycemia.⁸

Results and Discussion

Diabetes was diagnosed in 38 of the 90 TB patients (42%): 24 (63%) had hyperglycemia, 31 (82%) chronic hyperglycemia and

Table 1. Association between urine dipstick results and TB patient characteristics

	n	Glucose ≥ 100 mg/dL		Ketone ≥ 0 mg/dL		Protein ≥ 100 mg/dL	
		n (%) ^a	OR (95% CI)	n (%) ^a	OR (95% CI)	n (%) ^a	OR (95% CI)
Sociodemographic characteristics							
Age (years) [mean $\pm$ SD]							
18–35	38	7 $\pm$ 18	1	11 $\pm$ 29	1	1 $\pm$ 3	1
36–50	25	6 $\pm$ 24	1.4 (0.41–4.79)	9 $\pm$ 36	1.3 (0.47–4.05)	1 $\pm$ 4	1.5 (0.09–25.80)
>50	27	9 $\pm$ 33	2.2 (0.70–6.96)	10 $\pm$ 37	1.4 (0.50–4.12)	4 $\pm$ 15	6.4 (0.67–61.20)
Gender							
Male	56	14 (25)	1.1 (0.40–2.94)	20 (36)	1.3 (0.53–3.34)	6 (11)	
Female	34	8 (24)	1	10 (29)	1	0	
Body mass index							
Under or normal weight	69	16 (23)	1	25 (36)	1	4 (6)	1
Overweight or obese	21	6 (29)	1.33 (0.44–4.00)	5 (24)	0.6 (0.18–1.68)	2 (10)	1.7 (0.29–10.10)
Smoking	30	5 (17)	0.5 (0.17–1.54)	10 (33)	1.0 (0.40–2.53)	1 (3)	0.4 (0.04–3.40)
Drug abuse	11	0		2 (19)	0.4 (0.08–2.00)	1 (9)	1.5 (0.16–14.00)
Alcohol abuse	10	3 (30)	1.4 (0.32–5.85)	2 (20)	0.5 (0.09–2.30)	0	
HIV	3	0		0		0	
Self-reported signs and symptoms associated with diabetes and family history							
Tingling/numbness in hands/feet	14	7 (50)	4.1 (1.24–13.37)	4 (29)	0.8 (0.22–2.69)	4 (29)	14.8 (2.40–91.50)
Polyuria	14	7 (50)	4.1 (1.24–13.37)	3 (21)	0.5 (0.13–1.93)	3 (21)	6.6 (1.29–37.13)
Excessive thirst	11	5 (45)	3.1 (0.83–11.18)	3 (28)	0.7 (0.18–2.95)	2 (18)	4.2 (0.67–26.05)
Kidney failure	4	1 (25)	0.9 (0.1–9.2)	2 (50)	2.0 (0.28–15.5)	1 (25)	5.4 (0.47–61.75)
Diabetes family history	46	17 (37)	4.6 (1.51–13.83)	20 (43)	2.6 (1.05–6.53)	4 (9)	2.0 (0.35–11.50)
Diabetes diagnosis and defining laboratory findings							
Diabetes ^b							
Yes	38	20 (53)	27.2 (5.77–128.34)	14 (37)	1.4 (0.57–3.41)	6 (16)	
No	52	2 (4)	1	15 (29)	1	0	
Hyperglycemia ^c							
Yes	24	15 (63)	14.1 (4.50–43.86)	12 (50)	2.7 (1.05–7.01)	5 (21)	17.1 (1.88–155.39)
No	66	7 (11)	1	18 (27)	1	1 (2)	1
Chronic hyperglycemia							
HbA _{1c} $\geq 6.5\%$	31	20 (65)	50.9 (10.37–249.84)	12 (39)	1.5 (0.61–3.81)	6 (19)	
HbA _{1c} $< 6.5\%$	59	2 (3)	1	18 (31)	1	0	

^a Percentage is based on the total number of cases with available information for each variable.

^b Diabetes based on the American Diabetes Association 2010 definition.⁸

^c Hyperglycemia based on fasting glucose ≥ 126 mg/dL or random glucose ≥ 200 mg/dL.

32 (84%) self-reported diabetes (Table 1). Urine glucose (≥ 100 mg/dL; Table 1) was detected in 20 (53%) of the diabetes patients (positive predictive value [PPV] 91%, negative predictive value [NPV] 74%) and 20 (65%) of those with high HbA_{1c} (PPV 91%, NPV 84%). Two of six TB patients who were not previously aware of their diabetes status had glycosuria. Urine glucose was not associated with participant sociodemographics, but there was a trend for a higher frequency of positives with older age. In contrast, glycosuria was significantly associated with diabetes features (such as self-reported tingling or numbness in hands or feet), polyuria and family history of diabetes (Table 1). The semi-quantitative values of glucose in urine (0–2000 mg/dL) were correlated with hyperglycemia ($p = 0.48$; $p < 0.001$) and HbA_{1c} ($p = 0.51$; $p < 0.001$) (Table 1).

Urine ketone and protein levels were also associated with diabetes or hyperglycemia. When diabetes patients have a shortage of insulin, the body burns triglycerides for energy instead of glucose resulting in the accumulation of ketone bodies that can lead to diabetic ketoacidosis. Ketones in urine were nearly threefold more likely in individuals with hyperglycemia ($p = 0.03$). However, a high proportion of individuals with euglycemia ($n = 18$; 27%) or no diabetes ($n = 15$; 29%) also had detectable ketones. Diabetes patients are also more prone to kidney disease and microalbuminuria can be an early sign of defective renal glomerulus filtration.⁹ The presence of ≥ 100 mg/dL of protein in urine was detected in 6 (16%) of the diabetes patients, but none without diabetes. Microalbuminuria was 17-fold more frequent in chronic hyperglycemia.

Our findings in TB patients are coherent with the requirement for high blood glucose (generally ≥ 180 mg/dL) for urine glucose detection, and hence, the higher association between urine glucose with hyperglycemia rather than a diabetes diagnosis. Alternatively, the glycosuria in 2 of 52 non-diabetic individuals (4% false positives; Table 1) is consistent with variations between individuals in their renal glucose threshold.¹⁰ So, should urine dipsticks be ruled out to screen for diabetes at TB clinics? Not necessarily as this will depend on the resources at each setting. HbA_{1c} would provide the highest sensitivity (82% in our study population), but point-of-care devices for this assay cost approximately US\$20.00 each (e.g. A1cNow from Bayer). The second choice is a portable glucometer (63% sensitivity in our diabetes patients) with an approximate cost of US\$28 per unit and US\$0.90 for each lancet and test strip. In contrast, the cost of a urine strip for glucose and protein is approximately US\$0.20, and a ketone strip is US\$0.09. Even though urine glucose was detected in 65% of the individuals with hyperglycemia, this sensitivity could be potentially improved by testing the first morning urine; collecting urine about 2 h after a high carbohydrate meal; or testing a population where diabetes awareness is low. This was not the case in our study population, where 84% of the diabetes patients were previously cognizant of their diagnosis. However, our findings encourage the conduct of similar studies to assess the contribution of glycosuria to diabetes screening in TB clinics with limited resources and where diabetes diagnosis awareness is low.

In summary, in TB clinics with limited resources the urine dipstick could be afforded to screen all adults with TB. This would identify an estimated 65% of individuals with chronic hyperglycemia: those who would benefit most from becoming aware of their diabetes status. Depending on availability of funds, further testing (blood glucose or HbA_{1c}) could then be limited to a subset of patients for either diabetes confirmation, or to improve the sensitivity in individuals who tested negative but are at high risk for diabetes. Our findings suggest that adults reporting signs and symptoms compatible with diabetes, or who have a diabetic family member should be prioritized. However, as diabetes becomes more prevalent worldwide, every community should establish the profile that is most likely to identify diabetic TB patients to improve their comanagement.

Authors' contributions: BIR designed the study, analysed and interpreted the data and wrote the article; PAP, IZ and FM-G collected, processed and interpreted the data and critically revised the article. All authors read and approved the final manuscript. BIR is guarantor of the paper.

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