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Cigarette Smoking Affects Urinary Liver-Type Fatty Acid–Binding Protein Concentration in Patients With Early Diabetic Nephropathy

Cigarette smoking causes a decrease in the glomerular filtration rate in diabetic patients with normal renal function, independent of confounding factors including severe proteinuria (1). It increases the risk of microalbuminuria and accelerates the progression from microalbuminuria to overt proteinuria as well as the progression of renal failure in patients with type 2 diabetes (2). It is widely accepted that the rate of functional decline correlates with the degree of renal tubulointerstitial fibrosis. Previous studies have shown that renal function in patients with type 2 diabetes correlates better with tubular changes than with glomerular pathology (3). Further studies on tubulointerstitial injury in patients with diabetic nephropathy may provide additional insight into the pathogenesis of diabetic nephropathy and lead to the identification of therapeutic targets. Liver-type fatty acid–binding protein (L-FABP) is expressed in the proximal tubules, where it plays a key role in fatty acid metabolism. We and other investigators reported that urinary L-FABP may be a useful clinical marker for type 2 diabetic nephropathy (4–6). However, little is known about the effect of cigarette smoking on the urinary L-FABP level.

Fifty type 2 diabetic patients with microalbuminuria (28 men and 22 women, mean age 50.0 years), including 30 smokers (18 men and 12 women) and 20 nonsmokers (10 men and 10 women), were enrolled in the present study. No patient had a serum creatinine (Cr) level >1.2 mg/dl. Urinary L-FABP levels were measured by an enzyme-linked immunoassay kit as described previously (4–6). The urinary L-FABP level was significantly higher in smokers (20.5 ± 10.5 μg/g Cr) than in nonsmokers (10.5 ± 5.5 μg/g Cr) ($P < 0.05$). The smokers were divided into two groups: those who stopped smoking ($n = 10$, group A) and those who continued smoking ($n = 20$, group B). The angiotensin receptor blocker, ACE inhibitor, statin, antidiabetic drugs, and antiplatelet drugs used in the two groups were similar. After 24 months, the urinary L-FABP level in group A decreased significantly from 21.5 ± 10.0 to 13.5 ± 8.0 μg/g Cr ($P < 0.05$); however, that in group B increased significantly from 20.0 ± 11.0 to 27.5 ± 15.5 μg/g Cr ($P < 0.05$). These data suggest that cigarette smoking may be associated with tubulointerstitial injury in patients with early diabetic nephropathy.

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The Prevalence and Management of Diabetes in Rural India

Very high levels of diabetes have been reported in urban areas of India (1), but few data are available for rural regions where >70% of the population lives. Data from a new large-scale survey done in 2005 suggest rural India may soon experience the same epidemic of diabetes. A total of 4,535 individuals aged ≥30 years (response rate 81%, mean age 46.8 years) were sampled at random age and sex strata from 20 villages representative of Godavari, a developing rural area of Andhra Pradesh. Data were collected using a structured questionnaire and a brief physical examination with fasting finger-prick blood glucose measured in all participants using B-Braun USV meters (Melsungen, Germany). Fasting venous samples were also done in a random subsample of 1,070 individuals. Estimates of diabetes prevalence for the 20 villages were calculated by applying sampling weights derived from a census done in 2004 with diabetes defined by disease history and/or fasting glucose of 7.0 mmol or over.

On the basis of the finger-prick measurements, the prevalence of diabetes was 13.2% (95% CI 12.1–14.3), of which 6.4% (5.6–7.2) were known and 6.8% (5.9–7.6) were previously undiagnosed. A further 15.5% (14.2–16.8) had impaired fasting glucose (Table 1). Overall estimated mean fasting glucose levels from USV meters was 5.8 mmol/l (5.7–5.9). In the subsample, venous blood measurements gave a lower estimated mean glucose of 5.6 mmol/l (5.4–5.7). The systematically lower levels for the venous samples likely reflect the delay in assay, consequent upon transport of the samples to the local laboratory, and the higher finger-prick estimates are probably a more accurate reflection of the true prevalence of diabetes in this community.

Of those with known diabetes, 67% (61–73) were taking oral hypoglycemic therapy, 3% (1–5) were using insulin, and 46% (40–53) were taking blood pressure–lowering agents. These relatively high levels of treatment suggest that even in fairly poor rural settings, proven preventive therapies are accessible to many and that strategies to improve detection

Table 1—*Prevalence of known diabetes, undiagnosed diabetes, and impaired fasting glucose in rural Andhra Pradesh, India, 2005 by age and sex groups*

	Overall	By age-group			
		30–39	40–49	50–59	60+
All					
Known	6.4 (5.6–7.2)	2.4 (1.3–3.5)	5.6 (4.1–7.2)	9.1 (7.1–11.1)	11.5 (9.5–13.6)
Undiagnosed	6.8 (5.9–7.6)	2.8 (1.7–3.9)	7.9 (6.0–9.8)	10.0 (7.9–12.2)	9.0 (7.3–10.7)
IFG	15.5 (16.8–14.0)	14.0 (11.6–16.3)	17.3 (14.6–19.9)	17.1 (14.3–19.8)	14.5 (12.4–16.6)
Male					
Known	6.8 (5.6–7.9)	2.6 (4.3–6.3)	6.3 (4.0–8.6)	10.1 (7.1–13.0)	11.5 (8.8–14.3)
Undiagnosed	7.5 (6.3–8.8)	3.1 (4.9–8.0)	8.0 (5.3–10.8)	11.5 (8.3–14.8)	10.7 (8.2–13.2)
IFG	16.6 (14.7–18.5)	16.4 (12.6–20.2)	18.1 (14.2–22.0)	18.7 (14.5–22.8)	13.4 (10.6–16.2)
Female					
Known	6.0 (5.0–7.1)	2.2 (0.8–3.5)	4.8 (2.9–6.9)	8.1 (5.5–10.7)	11.6 (8.6–14.5)
Undiagnosed	6.0 (4.9–7.0)	2.5 (1.2–3.9)	7.7 (5.1–10.2)	8.5 (5.7–11.3)	7.5 (5.2–9.7)
IFG	14.3 (12.7–15.9)	11.6 (8.8–14.4)	16.3 (12.7–19.8)	15.4 (11.8–19.0)	15.5 (12.3–18.6)

Data are percent (95% CI). IFG, impaired fasting glucose.

and treatment rates could produce substantial health benefits.

While these data are by no means representative of rural India as a whole, they do provide a reasonably precise and reliable estimate of diabetes and its treatment in the study area. Since much of rural India is likely to develop to a similar or greater extent as the Godavari region of Andhra Pradesh (2), the data provide an early indication of the likely huge burden of diabetes that will occur in rural India in the coming few decades. The generation of new evidence about detection and management strategies suited to resource poor setting is an urgent public health priority for India.

Additional data from this study can be viewed at: http://thegeorgeinstitute.org/

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COMMENTS AND RESPONSES

Validity of Glycemic Index Estimates in the Insulin Resistance Atherosclerosis Study

Response to Liese et al.

The article by Liese et al. (1) investigated the association of glycemic index, glycemic load, and total carbohydrate and fiber intake with direct measures of insulin sensitivity, insulin secretion, and adiposity in a cohort of 979 adults with normal and impaired glucose tolerance. The authors concluded that there were no significant associations of glycemic index, glycemic load, and carbohydrate intake with any measure of insulin sensitivity or secretion.

In their study, usual dietary intake was assessed via a 114-item food frequency questionnaire (FFQ) that had been previously "validated" in a subsample of the Insulin Resistance Atherosclerosis Study (IRAS) population. Unfortunately, the validation study showed that the FFQ did not confidently predict total carbohydrate intake as assessed by repeated 24-h recall of food intake. The Pearson correlation coefficient between the two methods was only 0.37 after adjustment for energy. Furthermore, the correlation coefficients for starch and sucrose were similarly low at $r = 0.33$ and 0.46, respectively (2).

Is a correlation coefficient between 0.3 and 0.4 adequate for the purposes of validation? Brunner et al. (3) have suggested that a value "of about 0.5 for most nutrients and 0.8 for alcohol between methods is good evidence that the FFQ has the ability to rank individuals . . . according to nutrient intake." Indeed, correlation coefficients in the order of 0.6–0.7 are more typical for energy-adjusted nutrients in FFQs (4). In the Nurses Health Study (5) and Health Professionals Follow-up Study (6), the correlation coefficient for energy-adjusted total carbohydrate was $r = 0.69$ (7).

Like most current FFQs, the IRAS questionnaire was not originally constructed for the purpose of measuring glycemic index, and glycemic index was not