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Conventional and novel cardiovascular risk factors and markers of vascular damage in rural and urban Indian men

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ABSTRACT

Background: India is undergoing rapid epidemiological and nutritional transition largely as a consequence of rapid urbanisation. We investigated conventional and novel cardiovascular risk factors in rural and urban Indian men and studied their association with markers of vascular damage.
Methods: We randomly selected and studied 149 rural, 142 urban slum residents and 150 urban middle class middle aged Indian men. We measured conventional (obesity, blood pressure, lipids, smoking habits) and novel (proinflammatory and prothrombotic factors) cardiovascular risk factors and markers of vascular damage (carotid intima media thickness (IMT), von Willebrand Factor (vWF), e-selectin).
Results: There was a progressive increase in most of the conventional cardiovascular (CV) risk factors from rural to slum to urban middle class men. Plasminogen activator inhibitor-1 (PAI-1), platelet count, total homocysteine and C-reactive protein showed similar patterns. Carotid IMT was similar in the three groups; vWF was highest in rural and e-selectin in slum men. Adjusting for location, age explained 17%, obesity 3% and conventional risk factors 1% of the variance in carotid IMT, whilst novel cardiovascular risk factors were without any significant impact.
Conclusions: Urbanisation increases obesity related as well as prothrombotic and proinflammatory CV risk factors in Indian men, but appears not to impact on IMT.

1. Introduction

There is a rapidly growing epidemic of non-communicable diseases (NCD) in India [1,2] which is projected to accelerate in the near future [3,4]. The epidemic is usually ascribed to rapid change ('transition') in nutritional and other lifestyle factors consequent upon urbanisation.

Indians are at higher risk of cardiovascular disease than other ethnic groups [5], and suffer at a younger age [6]. It has been suggested that in addition to the 'conventional' cardiovascular (CV) risk factors (obesity, glycemia, blood pressure, cholesterol and smoking) higher levels of 'novel' risk factors (total homocysteine (tHcy), prothrombotic and proinflammatory factors) might contribute [7]. There are few studies of both conventional and novel cardiovascular risk factors in rural and urban Indians [8–10].

In a preliminary study, we demonstrated that urban residents have higher circulating, pro-inflammatory markers compared to rural residents [11] and postulated that this contributed to increased risk of type 2 diabetes (T2D) and cardiovascular disease (CVD). We designed the CRISIS study (Coronary Risk of Insulin Sensitivity in Indian Subjects) to investigate the pattern of conventional and novel CV risk factors, as well as markers of vascular damage (carotid intima-media thickness (IMT), von Willebrand Factor (vWF), and e-selectin) in rural, urban slum and urban middle class men in and around Pune (Maharashtra, India). Having reported the association between adiposity, inflammation and glycemia [12], we now report the distribution of CV risk factors and markers of vascular damage.

2. Materials and methods

2.1. Subjects

We restricted the study to middle aged men in order to reduce the variability in CV risk factors related to age and gender. We randomly selected 2 villages (Karandi and Dhamari) approximately 50 km from Pune, and 2 slums and 2 middle class wards from Pune's 124 wards (55 slums). We made a register of men between the ages of 30 and 50 years, and measured their weight and height. Three of 354 rural men, 15/425 slum men and 21/443 middle class men were treated for diabetes, hypertension, or coronary heart disease (CHD) and were excluded from further sampling to

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obviate the effects of treatment. Eighty nine percent of the rural, 79% of the slum dwellers and 71% of urban middle class men agreed to participate in the study. From these, we randomly enrolled men until approximately 150 were studied from each location. The final study comprised 149 rural, 146 slum dwelling and 151 urban middle class men. There was no difference in the age and body mass index (BMI) of the participants and non-participants in each place of residence. The study was approved by the Ethical Committee of the King Edward Memorial Hospital and Research Centre. Individual consent was signed by all participants. The study took place between April 2000 and June 2001.

The subjects were admitted to the Research Unit the evening before, given a standard dinner, and a medical examination and X-ray chest were performed. Four subjects with intercurrent febrile illness were rescheduled. A morning fasting blood sample was drawn and a 75 g oral glucose tolerance test was done. Two blood pressure readings were taken 5 min apart in a supine position after 15 min rest, with a digital monitor (UA 767PC, A & D Instruments Ltd, Abingdon, UK). The second reading was used for the analysis. Lifestyle factors, education and occupation were recorded. Anthropometric measurements were made using a standardised protocol. Body fat was measured using a bioimpedance device (Multiscan 5000, Bodystat Ltd, Isle of Man, UK) using our own population-specific equation [13]. All subjects answered the Rose-WHO angina questionnaire [14] and a resting 12 lead electrocardiogram (ECG) was taken.

2.2. Laboratory methods

Appropriately anticoagulated blood samples were centrifuged at 4 °C and 3500 *g* for 15 min to obtain plasma. Aliquots were stored at −80 °C. Haematological measurements were performed on a Coulter A^C.T diff™ Analyser (Coulter Corporation, Miami, USA). Fibrinogen was measured by the clotting method of Clauss (Diagnostica Stago, Asnières-sur-Seine, France) and erythrocyte sedimentation rate (ESR) using a Westergren tube (Greiner Labortechnik GmbH, Kremsmunster, Austria). Biochemical measurements were made using standard enzymatic methods. Low density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula [15]. Randox International Quality Assessment Scheme (RIQAS) (Randox Laboratories, Crumlin, UK) results showed the intra- and inter-batch coefficient of variation (cv) for all these measurements were <4%.

Biochemical parameters were analysed on the same day whilst inflammatory and prothrombotic parameters were analysed within 6 months of the conclusion of study. Insulin was measured using in-house DELFIA methods. Insulin resistance was calculated from homeostasis model (HOMA-IR) [16]. Plasminogen activator inhibitor antigen (PAI-1) (Hypen Biomed, Andresy, France), E-selectin (R & D Systems Inc., Minneapolis, USA) and vWF (Diagnostica Stago, Asnières-Sur-Seine, France) were measured by ELISA method; the cvs were <14%, <9.0% and <11%, respectively. Plasma t-Hcy was measured using the IMx System (Abbott Laboratories, IL, USA), with a CV <10%. C-reactive protein (CRP) (United Biotech Inc. CA, USA), interleukin-6 (IL-6) (R & D Systems Inc. Minneapolis, USA) and Tumour necrosis factor-α (TNF-α) (R & D Systems Inc. Minneapolis, USA) were measured using ELISA kits, with cvs <11%, <13%, and <18% respectively.

Intima media thickness (IMT) of the common carotid artery (CCA) was measured by one ultrasonologist using ATL UM9 Colour Doppler Machine (Philips, Washington, USA). Freeze frame sagittal sections of the CCA were obtained from both sides, images printed and converted into bitmaps. Two observers independently processed these images, using in-house software which made five marks at 500 μm intervals from the beginning of the carotid bulb on the posterior wall. At each mark the IMT was measured as the distance between the interface between arterial lumen and intimal surface reflection and the interface between the intima-media complex and the adventitia. The number of pixels between the two cursors was directly added to the database. The observers were blinded to the identity of the subject and to their own measurements. All measurements were made in duplicate, and the mean of two observers' readings was used for analysis. The final mean thus represented an average of 19 (12 to 20) readings (called 'mean IMT'). We also used the highest reading for each individual to calculate 'maximum IMT' which was a mean of maximum readings by the two observers. We validated our CCA IMT method on 19 images provided by Prof Michiel Bots, Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, Netherlands. Video-prints of these images were processed in the same way. Our results were similar to the original measurements: (mean 670 (SD 120) μm, and 660 (150) μm; p = 0.24 for Wilcoxon's paired

Table 1
Conventional and novel cardiovascular risk factors in 3 places of residence.

	Rural	Urban slum	Urban middle class
n	149	142	150
Age (y)	38.2 (5.9)	37.6 (5.9)	40.7* (5.9)
Life style factors			
Smoking (current/past) (%)	23.5/13.4	38.7/14.1**	26.2/25.5*
Tobacco (current/past) (%)	62.4/2.7	60.6/0.7	28.9/4.0 ++
Alcohol (current/past) (%)	19.5/9.4	50.7/14.1**	42.3/15.4***, ++
Conventional cardiovascular risk factors			
BMI (kg/m^2)	20.1 (18.6–22.2)	21.1 (18.7–24.7)**	23.6 (21.0–25.9)**, ++
Total body fat (%)	22.4 (4.9)	23.7 (5.9)	28.1 (4.6)***, +++
Waist circumference (cm)	79.4 (9.1)	83.7 (14.1)**	90.4 (10.2)***, +++
Plasma glucose (mmol/L)			
Fasting	5.0 (4.7–5.4)	5.2 (4.7–5.5)*	5.3 (4.7–5.8)**
120 min	5.6 (4.7–5.4)	6.0 (5.2–7.0)***	6.8 (5.7–8.2)***, ++
Fasting Plasma insulin (pmol/L)	26.9 (19.4–37.9)	34.7 (20.9–50.6)**	49.5 (35.0–68.7)***, +++
HOMA-IR	0.58 (0.42–0.81)	0.76 (0.46–1.1)***	1.07 (0.79–1.46)***, +++
Plasma cholesterol (mmol/L)	3.72 (3.31–4.25)	3.89 (3.35–4.39)	4.13 (3.67–4.74)***, ++
High density lipoprotein- (HDL-) cholesterol (mmol/L)	0.93 (0.82–1.06)	0.92 (0.79–1.14)	0.89 (0.76–1.06)
Low density lipoprotein- (LDL-) cholesterol (mmol/L)	2.4 (0.6)	2.4 (0.7)	2.7 (0.7)***, ++
Plasma triglycerides (mmol/L)	0.92 (0.73–1.19)	1.0 (0.68–1.49)**	1.21 (0.84–1.72)***
Systolic blood pressure (mm Hg)	113 (9.6)	115 (11.3)	118 (14.4)***
Diastolic blood pressure (mm Hg)	66 (7.9)	70 (8.5)***	74 (9.9)***, ++
Novel cardiovascular risk factors			
Prothrombotic markers			
Plasminogen activator inhibitor-1 (ng/mL)	18.1 (10.7–30.6)	26.4 (12.4–50.7)***	43.3 (24.6–67.4)***, +++
Fibrinogen (mg %)	311.7 (147.4)	326.1 (186.6)	315.1 (157.6)
Platelet count 10^9/L	229.9 (58.1)	244.4 (61.4)**	249.8 (63.0)**
Total homocysteine (μmol/L)	14.6 (11.9–22.6)	14.2 (11.3–19.7)	23.7 (15.3–40.7)***, +++
Proinflammatory markers			
Total leucocyte count 10^{12}/L	0.0059 (0.0016)	0.0067 (0.0017)***	0.0063 (0.0014)+
Erythrocyte sedimentation rate (mm at 1 h)	5 (3–8)	6 (4–9)*	5 (4–10)
C-reactive protein (mg/L)	0.31 (0.17–0.80)	0.45 (0.26–1.29)	0.74 (0.38–1.50)***, +
Interleukin-6 (pg/mL)	1.65 (1.00–2.90)	2.30 (1.40–3.90)***	2.20 (1.40–3.10)**, +
Tumour necrosis factor-α (pg/mL)	1.61 (1.09–3.01)	1.87 (1.30–3.20)	1.46 (1.09–2.28)+

Values presented are mean (SD) otherwise median (25th–75th centiles) for skewed variables. Categorical data are shown using %.
*p<0.05, **p<0.01, ***p<0.001, different from rural and adjusted for age.
+p<0.05, ++p<0.01, +++p<0.001, different from urban slums and adjusted for age.
BMI: Body Mass Index; HOMA-IR: HOMA Insulin resistance.

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signed rank test). The limits of agreement by Bland Altman plot were (185 ± 40 μm), with no systematic bias ($p>0.05$).

The ECGs were coded normal, 'coronary possible' type (Minnesota codes 1.3, 4.1, 4.2, 4.3, 5.1, 5.2, 5.3) or 'coronary probable' abnormalities (codes 1.1, 1.2, 7.1) by a single trained observer.

2.3. Statistical methods

We excluded 5 subjects with clinical infective-inflammatory conditions (tuberculosis 3, leprosy 1, rheumatoid arthritis 1), and analysed data on 149 rural, 142 urban slum and 150 urban middle class men. Skewed variables were appropriately transformed to obtain normal distribution before statistical analysis. This included log transformation (BMI, fasting and 120 min glucose, HOMA-IR, plasma total and high density lipoprotein (HDL) cholesterol, plasma triglycerides, PAI-1, t-HCy, CRP, IL-6, TNF-α) and square root (fasting, 120 min insulin). The data in the 3 places of residence are presented as means and standard deviations, or as median and interquartile range when skewed. Categorical data are presented as percentages. Comparison between places of residence was made by analysis of variance for continuous variables using Bonferroni correction for multiple comparisons, and by chi squared test for categorical variables. An α level of 0.05 was regarded as statistically significant. The association between variables was studied by linear regression. Difference in the strength of association (slope) between 3 places of residence was judged from significance of the interaction term (place of residence × risk factor) in generalised linear models. The contribution of age, adiposity and other CV risk factors to the differences in levels of vascular damage markers between places of residence were tested by linear regression using indicator variables for places of residence.

Study numbers were calculated as sufficient to achieve an 80% power to detect a 5% difference in IMT between rural and urban men, and 39% difference in levels of HOMA-IR, a 49% difference in levels of IL-6 and a 30% difference in those of TNF-α all at the 5% level. The sample size provided adequate numbers to detect a significant correlation coefficient of 0.16 within group and a correlation coefficient of 0.10 in the whole population. Analysis was done using SPSS 16.0 (SPSS Corporation, Chicago, USA).

3. Results

3.1. Lifestyle, and conventional and novel cardiovascular risk factors (Table 1)

There was a small but significant difference in the age of the 3 groups, so that all analyses are age adjusted. More than 80% of rural and slum men, and >50% of urban middle class men either smoked or chewed tobacco. Alcohol drinking was more prevalent in the two urban groups than the rural. Family history of diabetes, hypertension and CHD was present in 1 rural, 1 slum and 12 urban middle class subjects.

BMI, % body fat and waist circumference increased from rural to slum to urban middle class men. Plasma glucose, insulin, HOMA-IR, total and LDL-cholesterol, triglycerides and blood pressure were highest in urban middle class men, whilst plasma HDL-cholesterol concentrations were similar in the 3 groups.

Levels of prothrombotic factors were in general higher in urban compared to rural men, except fibrinogen which was similar in the three groups. Plasma PAI-1 and blood platelet count were highest in urban middle class men. Levels of tHcy were substantially higher than those reported in European populations [17]. Inflammatory markers were in general higher in urban compared to rural men. Total leucocyte count (TLC), plasma IL-6 and TNF-α concentrations were highest in slum men whilst plasma CRP concentrations were highest in the middle class men.

All the conventional risk factors, and levels of PAI-1, CRP and IL-6, were related to measures of obesity ($r>0.1$ and $p<0.01$, for all). None was related to smoking or alcohol consumption ($p>0.05$).

3.2. Markers of vascular damage (Table 2)

Despite substantial differences in cardiovascular risk factors, carotid IMT was similar in rural, urban slum and urban middle class men. This was true for both mean and maximum IMT measurements. Coronary 'probable' ECG abnormalities were seen in only 4 men. Plasma vWF concentrations were highest in rural men whilst e-selectin concentrations were highest in the urban slum men. There were no significant correlations between the 3 markers of vascular damage.

3.3. Relationship between CV damage markers and CV risk factors (Table 3)

The strength of associations between CV damage markers and CV risk factors was similar in the 3 places of residence. We therefore investigated the associations between CV damage markers and CV risk factors by combining data from the 3 groups. Because these factors were strongly related to age, these analyses were adjusted for age and place of residence. Mean carotid IMT was positively related to obesity measures, plasma total and HDL-cholesterol, HOMA-IR, blood pressure, PAI-1 and CRP. Plasma vWF concentrations were related directly to% body fat, ESR and IL-6 but inversely to TNF-α. Plasma e-selectin concentrations were positively related to obesity measures, 2 h glucose, HDL-cholesterol, triglycerides, HOMA-IR, PAI-1 and leucocyte count. In these analyses age explained 17% of the variance in carotid IMT (Mean), measures of obesity an additional 3%, and conventional risk factors 1%, but novel cardiovascular risk factors were without any significant impact on IMT.

3.4. Risk factor adjusted difference in levels of CV damage markers in 3 places of residence (Supplementary data Table 4)

Despite higher levels of CV risk factors in the urban men, carotid mean IMT was similar in rural and urban men. Analysis showed that at any given level of adiposity (body fat percent) urban men had lower levels of carotid IMT compared to rural men. Further adjustment for cardiovascular risk factors (conventional or novel) did not alter the significance of these differences. The relationships for maximal IMT showed similar trends (data not shown). Adjustment for different CV risk factors did not influence the differences in circulating

Table 2
Markers of vascular damage in 3 places of residence.

	Rural	Urban slum	Urban middle class
n	149	142	150
Intima media thickness(μm)			
Mean	668 (94.7)	643 (89.9)	661 (95.8)
Maximum	754 (116.0)	760 (123.0)	772 (116.5)
Electrocardiogram			
Minnesota codes			
(Normal/Possible/Probable) (n)	139/7/2	129/9/2	136/11/0
von Willebrand Factor (%)	106.4 (38.4)	102.1 (38.2)	96.9 (38.0) *
E-selectin (ng/mL)	60.7 (42.1–80.8)	74.4 (56.2–104.1) ***	63.2 (47.4–87.5) ++

Values presented are mean (SD) otherwise median (25th–75th centiles) for skewed variables.
* $p<0.05$, ** $p<0.01$, *** $p<0.001$, different from rural and adjusted for age.
+ $p<0.05$, ++ $p<0.01$, +++ $p<0.001$, different from urban slums and adjusted for age.

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Table 3
Associations of cardiovascular damage markers with conventional and novel cardiovascular risk factors, on pooled data, adjusted for age and place of residence. Values are regression coefficients with 95% CI representing the change in IMT, von Willebrand Factor and e-selectin concentrations (as dependent variables) per 1 standard deviation increase in risk factors (as independent variables).

	Intima media thickness (μm)	von Willebrand Factor (%)	Logged e-selectin (ng/mL)
Age (y)	39.6 (31.5, 47.9)***	3. 9(0.3, 7.5) **	0.05 (−0.0001, 0.09)
Conventional cardiovascular risk factors			
BMI (kg/m^2)	30.5 (21.3, 39.7) ***	3.1 (−0.7, 6.9)	0.1 (0.04, 0.14) **
Waist circumference (cm)	29.9 (20.5, 39.2) ***	4.1 (−0.3, 8.0)	0.1 (0.04, 0.15) **
Body fat %	27.1 (17.1, 37.1) ***	4.4 (0.4, 8.5) ***	0.06 (0.01, 0.12) *
Fasting glucose (mmol/L)	9.3 (0.3, 18.3)	1.1 (−2.6, 4.7)	0.03 (−0.042, 0.08) +
2 h glucose (mmol/L)	12.3 (2.9, 21.5)	0.4 (−3.4, 4.2)	0.1 (0.03, 0.13) ***
HOMA-IR	16.4 (6.8, 25.9) **	1.7 (−2.2, 5.6)	0.1 (0.03, 0.14) +
Total cholesterol (mmol/L)	18.8 (9.8, 27.9) ***	2.2 (−1.5, 5.8)	0.04 (−0.001, 0.09)
High density lipoprotein- (HDL-) cholesterol (mmol/L)	5.4 (3.58, 14.3) *	−2.7 (−6.3, 0.8)	0.07 (0.02, 0.11) **
Low density lipoprotein- (LDL-) cholesterol (mmol/L)	15.6 (6.6, 24.6) **	2.9 (−0.8, 6.5)	−0.01 (−0.06, 0.04)
Triglycerides (mmol/L)	6.8 (−2.3, 5.9)	1.3 (−2.3, 5.0) +	0.1 (0.01, 0.1) **
Systolic BP (mmHg)	10.8 (1.6, 19.9) **	3.3 (−0.4, 6.9)	0.03 (−0.02, 0.1)
Novel cardiovascular risk factors			
Plasminogen activator inhibitor-1 (PAI-1) (ng/mL)	14.5 (4.9, 24.1) *	−0.1 (−3.9, 3.7)	0.1 (0.03, 0.13) **
Fibrinogen (mg %)	−6.6 (−15.9, 2.8)	−3.2 (−6.9, 0.5)	0.01 (−0.05, 0.05)
Platelet count (10^9/L)	1.9 (−7.3, 11.1)	−1.6 (−5.2, 2.6)	0.02 (−0.03, 0.07)
Total homocysteine (μmol/L)	4.1 (−5.1, 13.4)	1.2 (−2.6, 4.9)	−0.01 (−0.06, 0.04)
Total leucocyte count 10^{12}/L	0.8 (−8.3, 9.8)	1.5 (−2.1, 5.2)	0.1 (0.02, 0.12) ***
Erythrocyte sedimentation rate (mm at 1 h)	6.8 (−2.2, 15.8)	6.2 (2.6, 9.7)	0.05 (0.01, 0.1)
C-reactive protein (mg/L)	8.6 (−0.7, 17.9)	1.8 (−1.8, 5.5) +	0.02 (−0.02, 0.07)
Interleukin-6 (pg/mL)	6.7 (−2.3, 15.6)	4.7 (1.1, 8.3) **	0.03 (−0.02, 0.08)
Tumour necrosis factor-α (pg/mL)	−0.5 (−9.3, 8.4)	−4.6 (−8.2, −1.1) **	−0.02 (−0.07, 0.03)

* $p<0.05$, ** $p<0.01$, *** $p<0.001$ for regression coefficients.
+ indicates significant interaction between risk factor and place of residence. This suggests that the slope was significantly different in 3 places of residence.
Columns IMT, von Willebrand Factor and e-selectin are dependent variables. Rows (Cardiovascular risk factors are) independent variables. Each cardiovascular risk factors has been included as independent variable. The values represent regression coefficients with 95% CI representing the change in the dependent variable for each standard deviation change in the independent variable.
BMI: Body Mass Index, HOMA-IR: HOMA Insulin Resistance.

vWF or e-selectin concentrations between geographical groups (data not shown).

4. Discussion

CRISIS is the first systematic comparison of a comprehensive range of conventional and novel cardiovascular risk factors, and markers of vascular damage, in rural and urban Indian men. Risk factors related to obesity were highest in the urban middle class men, whilst most of the pro-inflammatory factors were highest in the slum men. Our findings of higher levels of risk factors in urban compared to rural individuals are similar to other studies [8–10], On the other hand, the distribution of vascular damage markers was different from that of CV risk factors. IMT was similar in the three groups, vWF was highest in rural subjects and e-selectin highest in slum dwellers.

Our study has many strengths and some limitations. We carefully sampled representative subjects from the population and measurements of IMT have been validated by comparison with those of a reputed vascular laboratory in Europe. Physical and laboratory measurements were quality assured. However we have studied a relatively small number of subjects, using power calculations for differences between groups in IMT, HOMA-IR and inflammatory markers. The choice of age range resulted in very low rates of exclusion for prevalent disease (<3%). Given the cross-sectional design we cannot be certain of causality.

The rural–urban differences highlight the consequences of rapid transition. Nutritional factors, lack of physical activity, psychosocial stress and atmospheric pollution may all contribute to increasing levels of risk factors in cities. Slum dwellers live in unhygienic crowded environments, contributing to high levels of prothrombotic and proinflammatory risk factors. The urban middle class are more adipose, and in consequence have the highest levels of conventional as well as novel (prothrombotic and CRP) risk factors. Despite this, however, urban middle class men did not have the highest levels of vascular damage markers. The similarity of IMT in the three groups suggests that this may not be a good marker of atherosclerosis in Indians, or that the increased risk of CV disease in urban Indians relates more to prothrombotic and inflammatory mechanisms, perhaps mediated through nutritional or other differences. The possibility that CV risk factors may have a differential impact on vascular damage in rural and urban men is not supported by tests of homogeneity.

There are few reports of novel risk factors and vascular damage markers in rural and urban Indians. The SHARE study in Canada showed that migrant Indians had higher risk of CV disease, and had higher levels of conventional and novel risk factors but lower measures of carotid IMT compared to Europeans and Chinese, again possibly suggesting that IMT could be a poor predictor of CV disease in Indians [18]. On the other hand, an Indo-Australian comparison reported higher carotid IMT in rural south Indian subjects compared to predominantly Europid Australians [19]. The reasons for the differences between these studies are not clear.

The largest study of cardiovascular risk factors in India comes from the Indian arm of the INTERHEART Study [6], a case–control study of subjects with myocardial infarction, which suggested that ~85% of the variance of risk could be explained, statistically, by 8 conventional risk factors. However subjects were sampled after suffering an acute event. Moreover, the contribution of central obesity to risk, with WHR 'explaining' 36% of the variance, opens a range of possible pathophysiological mechanisms whereby central fat may increase cardiovascular risk, including through the conventional and novel risk factors which were not measured [20–22]. A recent study of the evolution of CV risk factors in urban migrant Indians [10] found a rapid increase in body fat and waist circumference in the first 10 years with other CV risk factors generally increasing in parallel, supporting the notion that deposition of body fat and its distribution are amongst the important mediators of increased CV risk on urbanisation.

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Other studies have explored CV risk factors in urban Indians [23,24] but have not compared slum-dwellers with middle class subjects, and have not explored newer risk factors. There are only a few reports of novel cardiovascular risk factors and carotid IMT in Indians, and no rural–urban comparisons. Gokulakrishnan et al. reported carotid IMT measurements on a large number of subjects, and found that it was strongly related to glucose intolerance, to circulating CRP and TNF-α concentrations [25].

Our results suggest a greater degree of endothelial dysfunction in rural and urban slum men than in urban middle class men. This finding is unlikely to be explained by inflammation and smoking because adjustment for these did not significantly change the difference. The role of environmental pollution needs to be investigated [26]. Another interesting possibility is the influence of early life (intrauterine and postnatal) nutritional deprivation which is a known risk factor for CV disease [27].

Ethnic-geographic patterns of CVD have been described [28]. Our findings support the existence of an Indian phenotype of hypertriglyceridemic waist [29], high prothrombotic and proinflammatory risk factors without a proportionate increase in carotid IMT. These findings suggest that thrombosis and inflammation might play a contributing role in the reported excess of CV disease in migrant Indians compared to local populations, and in urban compared to rural Indians. Such a hypothesis will require further study.

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