Original Article

Noncommunicable disease in rural India: Are we seriously underestimating the risk? The Nallampatti noncommunicable disease study

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ABSTRACT

Aim: To assess the prevalence of noncommunicable diseases in a true rural farming population in South India and compare the data with the landmark contemporary Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study. **Methods:** Local Ethics Committee approval and informed consent was obtained from all participants. Inclusion criteria were participants, aged ≥20 and ≤85 years, from Nallampatti, a classical farming village from Tamil Nadu state, India. All participants were administered a detailed questionnaire, had anthropometric measurements including height, weight, and waist circumference. Bloods were drawn for random blood glucose, glycated hemoglobin (HbA1c), nonfasting lipid profile, Cystatin C, uric acid, and hemoglobin. All participants had carotid intima-media thickness (CIMT) done by high-resolution B-mode carotid ultrasound. **Results:** More than 50% of the population had either diabetes or prediabetes based on HbA1c. Nearly, 40% of the population had hypertension with suboptimal control in those with known hypertension. Nearly, a third of the population had dyslipidemia, elevated cystatin C levels, and abnormal CIMT. The burden was higher than the comparable ICMR-INDIAB study in rural Tamil Nadu. **Conclusion:** One-third to one-half of this rural farming population is at risk of cardiovascular disease, with poor control of preexisting cardiovascular risk factors. Current Indian data may underestimate the risk in different ethnic populations and regions of India. Long-term follow-up of this cohort for the incident cardiovascular disease will shed light on the true cardiovascular risk in a typical South Indian rural farming population.

Key words: Cystatin C, Nallampatti noncommunicable disease, noncommunicable disease, prediabetes

Introduction

For many decades, the focus in India was on communicable diseases. Targeted efforts have led to a significant reduction in morbidity and mortality from communicable diseases. Unfortunately, the burden of noncommunicable diseases (NCD) in South Asia as a region is rising at a rate that exceeds global increases in such conditions.[1] For example, a recent study shows that six in ten adults in large South Asian cities such as Chennai, Delhi, and Karachi have either diabetes or prediabetes.[2] A higher prevalence of diabetes, dyslipidemia, and hypertension was observed in educated and more affluent groups in urban areas.[3] Such studies reinforce the notion that urbanization, westernization, and affluence have a significant role in the huge explosion of NCDs in countries like India. Intuitively, one would expect a lower prevalence of NCD in a rural

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population who traditionally lead a more active lifestyle compared to their urban counterparts. This hypothesis is backed up by a Global Physical Activity Questionnaire study done in India showing significantly more inactivity in urban areas of India compared to rural areas.[4] However, physical activity may be only one cog in the wheel underpinning the explosion of metabolic and cardiovascular diseases in India. We had reason to speculate that NCD's were as much an issue in rural India as in urban areas.[5,6] We, therefore, set out to explore the prevalence of NCDs in a completely rural South Indian farming village and compare the results with the rural Tamil Nadu arm of the landmark Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study to look for similarities and differences.

Methods

Nallampatti is a classical farming village in Erode district, Tamil Nadu state, India [Figure 1] with a population of approximately 3000. This village was chosen for several reasons including a true farming rural population, ease of access, logistics, and local contacts with the village heads. Advertisements were given through leaflets (door to door) and word of mouth, the week preceding the visit. Local Ethics Committee approval was obtained. Inclusion criteria included all those native to the village, ≥20 and ≤85 years of age. Excluded were people <20 years of age, pregnant mothers and those not native to Nallampatti. Informed consent was obtained from all participants. The study was conducted over a 4-week period from March 15, 2015.

A detailed questionnaire was administered exploring the educational status, employment, alcohol intake, smoking status, pesticide exposure, family history, and past medical history. Anthropometric measurements were obtained in all participants. Blood investigations included a random glucose (hexokinase/glucose oxidase-peroxidase/endpoint method), glycated hemoglobin (HbA1c) (automated high performance liquid chromatography method), serum creatinine (Jaffe-kinetic method), cystatin C (Nephlometric method-BN Prospec), nonfasting lipid profile, uric acid (Uricase Endpoint method), and hemoglobin (sodium lauryl sulphate method). Fasting and post meal glucose were not considered due to logistical issues in a farming village. Blood investigations were analyzed at National Accreditation Board for Testing and Calibration Laboratories. All participants had carotid intima-media thickness (CIMT) done using high-resolution B-mode ultrasound.

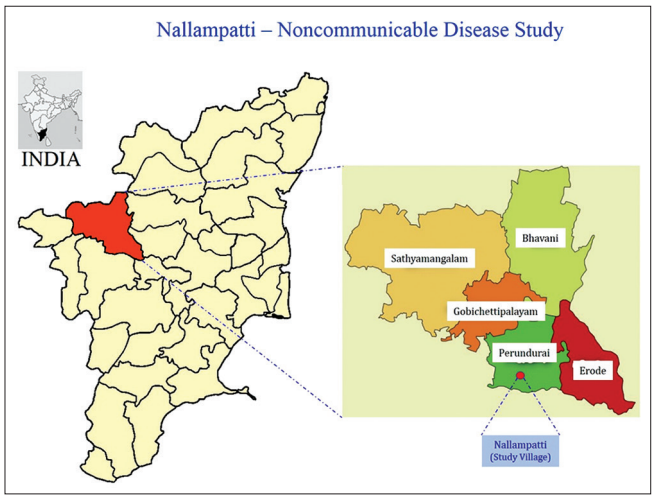

Figure 1: Geographical location of Nallampatti village

Generalized obesity (GO) was defined as a body mass index (BMI) ≥25. Diabetes was defined as either having a history of diabetes on medications or HbA1c of ≥6.5% in those without a history of diabetes. Prediabetes was defined as HbA1c between 5.7% and 6.4% (American Diabetes Association [ADA]) in those without a history of diabetes. Hypertension was defined as either having a history of hypertension on medications or a systolic blood pressure (SBP) of ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg on two occasions taken 15 min apart. Dyslipidemia was defined as a low-density lipoprotein cholesterol (LDL-C) ≥130 mg/dl, high-density lipoprotein cholesterol (HDL-C) <40 mg/dl in males and <50 mg/dl in females. Triglycerides were non fasting samples due to logistical issues related to fasting samples. Elevated cystatin C was defined as a level >1 mg/l. An abnormal CIMT was defined as a value ≥0.1 cm.

Results were tabulated on Microsoft Excel and transposed to SPSS for statistical analysis (SPSS). Data were analyzed using IBM SPSS version 15. Results are expressed as mean and standard deviation.

Results

The baseline characteristics of the study population are depicted in Table 1. A total of 865 participants responded to this study, of which 48% (n = 415) were males and 52% females (n = 450). The age distribution of the study population is as follows: 47% of the study population were between 40 and 60 years of age, 33% were between 20 and 40 years, and 20% were more than 60 years.

The mean BMI was 23.2. The prevalence of GO as defined by a BMI cutoff of ≥25 was 31.6% in this rural farming population. The baseline characteristics of the population based on glucose status is depicted in Table 2. Not surprisingly, diabetes patients were older, had a higher BMI, higher waist circumference, and a stronger family

Table 1: Baseline characteristics of the study population

Parameter	Mean±SD
Age (years)	48.2±13.7
Sex	
Male: female	415:450
BMI	23.2±4.1
SBP (mm Hg)	130.7±20.9
DBP (mm Hg)	82.1±11.7
Waist circumference (cm)	91.3±8.9
Random blood glucose (mg/dl)	106.5±50.2
Creatinine (mg/dl)	0.67±0.13
Uric acid (mg/dl)	4.75±1.3
HbA1c (%)	5.9±1.1
Total cholesterol (mg/dl)	185.6±38.8
LDL-C (mg/dl)	109.7±31.4
HDL-C (mg/dl)	44.1±9.6
Cystatin C (mg/dl)	0.94±0.29
CIMT (cm)	
Right	0.065±0.01
Left	0.066±0.01
Hemoglobin (g/dl)	
Males	13.9±1.9
Females	11.7±1.6

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HbA1c: Glycated hemoglobin, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, CIMT: Carotid intima-media thickness, SD: Standard deviation

Table 2: Baseline characteristics of the study population based on glucose status

	Diabetes	Prediabetes	No diabetes
Age (years)	57.3±0.9	52.3±0.9	44.8±0.6
Male (%)	59.6	37.6	48.6
Diabetes family history (%)	17.7	10.2	12.3
Alcohol intake (%)	34.7	17.8	22.6
Smokers (%)	34.0	22.9	30.0
Tobacco usage (%)	22.7	24.8	22.2
Height (cm)	158.5±0.7	156.5±0.8	159.5±0.4
Weight (kg)	60.6±1.0	59.1±1.0	58.4±0.6
Waist circumference (cm)	92.4±0.8	91.3±0.8	88.6±0.4
Uneducated (%)	34.6	39.5	30.0
Farmers (%)	61.7	75.1	59.0

history. The prevalence of diabetes as defined by a HbA1c of ≥6.5% was 16.2%, prediabetes was 42% based on ADA criteria (HbA1c 5.7%–6.4%) and 18% based International Expert Consensus criteria (IEC, HbA1c 6.0%–6.4%). Of the 141 participants with diabetes, 79 had known history of diabetes (56%), and 62 had new diagnosis of diabetes due to screening (44%). Within those with a self-reported diagnosis of diabetes, the mean HbA1c was 7.59% with an average duration of diabetes of 59 months. Approximately, 30% of those with diabetes (both new and preexisting) had an HbA1c of >9%.

The prevalence of hypertension in this population was 37.8% (13% with preexisting hypertension and 26% with a new diagnosis of hypertension). Of those with known hypertension, 66% had an SBP ≥140 mm Hg and 47% had a DBP of ≥90 mm Hg, indicating suboptimal treatment for a vast majority of participants.

Total cholesterol was ≥200 mg/dl in 33% (289/865), LDL-C was ≥130 mg/dl in 24.4% (209/865), and low HDL-C was found in 58% of the population. Around 52% of males had an HDL-C <40 mg/dl and 63.5% of females had an HDL-C <50 mg/dl. A total cholesterol to HDL-C ratio ≥4.5 was found in 40% of the study population.

The differences between our Nallampatti noncommunicable disease results and the ICMR-INDIAB study are tabulated in Table 3. The prevalence of GO, diabetes, hypertension, and dyslipidemia with the exception of low HDL-C was much higher in our study compared to the ICMR-INDIAB results. Two parameters, cystatin C and CIMT not included in the ICMR-INDIAB study has been added to our study [Table 3]. Cystatin C, not only a renal but also atherosclerotic cardiovascular risk marker, was elevated (>1 mg/l) in 28.4% of the population. CIMT was ≥0.1 cm in 10.3% of the study population. When the cutoff was lowered to 0.07 mm, the numbers increased to 33.8%.

Discussion

Our study highlights the worrying burden of NCDs in rural India, a population where the triple burden of lack of awareness, costs, and poor health-care facilities add to the woes of complications and delayed treatment. We also demonstrate a significantly increased prevalence of NCDs, especially diabetes and prediabetes compared to the ICMR-INDIAB study completed in rural Tamil Nadu 5 years ago.

The prevalence of diabetes in our study cohort was 16.2%. This was nearly twice the results reported in rural Tamil Nadu arm of the ICMR-INDIAB Study.[7] The prevalence of prediabetes was staggeringly high (fivefold higher) in our study compared to the ICMR-INDIAB cohorts.[7] Significant methodological reasons may be one reason for this discrepancy as the definitions of diabetes and prediabetes in both these studies were different. We used a HbA1c based definition whereas the ICMR-INDIAB study used capillary glucose to define diabetes and prediabetes. While technically a very robust methodology, one significant limitation of the ICMR-INDIAB study was the use of fasting and 2 h postglucose capillary glucose rather than venous plasma glucose estimations. While the authors have shown a very good correlation between capillary and venous plasma glucose for the 2 h post load samples, the correlation in fasting samples were much lower.[8] In addition, though most glucometers are accurate,

Table 3: Comparison between Indian Council of Medical Research-India Diabetes study and Nallampatti noncommunicable disease study

Factors	ICMR-INDIAB study		NNCD study	
	Definitions	Tamil Nadu (Rural)	Definitions	Tamil Nadu (Rural-Nallampatti)
n		2480		865
KD (%)	IFG + IGT	4.1	HbA1c ≥6.5	9.1
NDD (%)		3.8		7.1
Ratio of KD: NDD		1:0.9		1:0.78
Total diabetes (%)		7.8		16.2
Prediabetes (%)	IFG or IGT or both	7.1	HbA1c 5.7-6.4 (ADA)*	42
Hypertension (%)	SBP ≥140 and/or DBP ≥90	26.2	SBP ≥140 and/or DBP ≥90	37.8
Hypercholesterolemia (%)	≥200 mg/dl (≥5.2 mmol/L)	16	≥200 mg/dl (≥5.2 mmol/L)	33.4
Hypertriglyceridemia (%)	≥150 mg/dl (1.7 mmol/L)	29.6	≥150 mg/dl (1.7 mmol/L)	43.5
L-HDL (%)	<40 for men (1.04 mmol/L)/<50 for women (1.3 mmol/L)	67.6	<40 for men (1.04 mmol/L)/<50 for women (1.3 mmol/L)	58.2
H-LDL (%)	≥130 mg/dl (≥3.4 mmol/L)	13.2	≥130 mg/dl (≥3.4 mmol/L)	24.1
Generalized obesity (%)	BMI ≥25 kg/m^2	22.1	BMI ≥25 kg/m^2	31.6
Cystatin C (%)	NA	NA	≥1 mg/L	28.4
CIMT (%)				
Right	NA	NA	≥1.0 mm	7.5
Left	NA	NA	≥1.0 mm	7.9

*American Diabetes Association. KD: Known diabetes, NDD: Newly detected diabetes, IFG: Impaired fasting glucose, IGT: Impaired glucose tolerance, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, H-LDL: High low-density lipoprotein cholesterol, L-HDL: Low high-density lipoprotein cholesterol, BMI: Body mass index, NA: Not available, CIMT: Carotid intima-media thickness, ICMR-INDIAB: Indian Council of Medical Research-India Diabetes, HbA1c: Glycated hemoglobin, NNCD: Nallampatti noncommunicable disease

the best of the meters have inaccuracies in the order of 5%–7.7%.[9] There are other potential sources of error with point of care glucometers that may have relevance in large epidemiological studies including strip factors, physical factors like temperature, patient factors especially with contaminants if hands are not washed properly and interfering medications.[9] Finally, there are studies showing that point of care glucometers significantly underestimate the true blood glucose at levels used for diagnosis of diabetes.[10]

Various Expert Committees have presented compelling arguments on practical grounds for the use of HbA1c as a diagnostic test.[11,12] Arguments for the use of this test include prediction of complications, superior technical attributes, clinical convenience, and less biologic variability. However, there is always a question of normative distribution of HbA1c in Asian Indian population and whether the cut-offs used in Expert Committees predominantly reflecting western populations are applicable to an Asian Indian population. A population-based study from the landmark Chennai Urban Rural Epidemiology study suggests that a HbA1c of ≥6.0 may be optimal for diagnosing diabetes with a high level of accuracy in south Indian population.[13] Since we have defined diabetes as a HbA1c of ≥6.5% in those without known diabetes, we are certain that our results are reflective of the true prevalence of diabetes, though it would have been ideal to have a fasting/2 h venous glucose to corroborate our results. In terms of prediabetes, applying the ADA criteria results in a very high prevalence of around 42%; this reduces to 18% when the IEC criteria are applied. It is well recognized that relatively more dysglycemia is identified by HbA1c than impaired fasting glucose/impaired glucose tolerance criteria in South Asians.[14] It is unclear at this point whether the greater prevalence of HbA1c defined prediabetes in Asian Indian population translates into cardiovascular risk with some studies from the United Kingdom suggesting that prediabetes defined by HbA1c in South Asian population showed significantly weaker associations with cardiovascular risks compared to western counterparts.[15,16]

Our results are consistent with a recent systematic review showing a significantly increasing trend of hypertension in India over time.[17] The prevalence of hypertension in our study was much higher than the ICMR-INDIAB study of rural Tamil Nadu population (37.8% vs. 26.2%) using the same definition for hypertension. We have shown a similar high prevalence of hypertension in other rural areas of Tamil Nadu as well.[5] While age, male gender, salt intake, physical activity, diabetes, and alcohol consumption were significantly associated with hypertension,[18] we believe that there are novel pathophysiological mechanisms that may aggravate hypertension in a rural population of India. Indian agricultural workers are exposed to toxic effects of pesticides due to unsafe work practices, especially not wearing personal protective equipment like safety masks or gloves.[19] Pesticides have been implicated in concentric left ventricular remodeling and hypertension.[20] It is pure speculation at this point to state that individuals with a

genetic predisposition to hypertension in rural areas of India may be more susceptible due to cardiac and vascular effects of pesticides in the long term. Further studies are needed to explore this hypothesis.

Lipid patterns in our study reflected the general observations in the ICMR-INDIAB study.[21] There was a high prevalence of lipid abnormalities in this rural population with a nearly two-fold increase in high LDL-C compared to the ICMR-INDIAB study but a lower prevalence of low HDL-C. These results are consistent with the Asian Indian phenotype of increased waist circumference, excess visceral fat, and low adiponectin levels.

Several studies have shown that cystatin C has a stronger cardiovascular association than serum creatinine.[22,23] There have been very few Indian studies evaluating the association between cystatin C and cardiovascular disease. Higher cystatin C levels in Indian patients seem to be significantly and independently associated with the presence of coronary artery disease even in those with normal renal function.[24] In addition, Indian subjects with higher cystatin C are shown to have more severe disease, especially triple vessel disease.[25] Ours is the largest Indian study to date in terms of cystatin C levels in an Indian population. Nearly, a third of our study population had elevated cystatin C levels. Long-term follow-up of this cohort stratified by cystatin C levels will be helpful in augmenting the utility of this test as a renal and atherosclerotic risk marker.

There are certain limitations to our study that may have relevance to the results. It is possible that there may be a selection bias which could have exaggerated the outcome of the study. The total population of Nallampatti village is around 3000 of which we managed to screen 865 subjects. We did extensive door to door canvassing and apart from the exclusion criteria outlined in the methodology section, there were no limitations for the study population to participate in the screening. According to the latest available census, around 8% of the Nallampatti population is under 6 years of age, and we guestimate that around 20% of the population to be under 20 years (our exclusion criteria for the study was age <20 years or >85 years). If one includes pregnant women, the very elderly, those not native to Nallampatti and subjects not in the village during study visit, it is possible that this would have therefore excluded approximately 1000 subjects. It is likely that the nonresponders in the remaining population are more likely to be in the younger age group (ranging from 20 to 30 years) and therefore to some extent, it is possible that the prevalence of disease may be exaggerated.

Conclusion

We show a very high prevalence of NCD in a rural South Indian population, much higher than the current estimates based on the landmark ICMR-INDIAB study. This calls for urgent strategies from both governmental and private health-care organizations to step up and reduce the risk factors for cardiovascular disease in rural India.

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Conflicts of interest

There are no conflicts of interest.

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