Special Article

Type 2 diabetes in rural India — new paradigms in its epidemiology and evolution

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"Though his face is covered with fat and his waist bulges with flesh, he will inhabit ruined towns where no one lives and his house crumbles to rubble.........."

........Job 15: 27-28. This is a verse extracted from the Old Testament of the Bible and is also found in Islamic and Jewish scriptures. A close scrutiny of the text gives us a glimpse of the metabolic syndrome in yesteryears, also emphasising that it may be associated with poverty.

Diabetes has been cited to be a growing epidemic over the last decade and a half in India, particularly in urban areas. Several epidemiological surveys have shown us over the years that glycaemic disorders have become more common, progressively. The NUDS (National Urban Diabetes Survey)[1] has quoted a prevalence of diabetes mellitus in the population of less than 40 years of age of 13% with a prevalence of impaired glucose tolerance of 4%. The study which was performed in 7 cities across the country, had expressed the tendency for the disease to be urban dominated. More recently, the prevalence in urban areas has increased even further, with figures of 17% and 19% being cited from Tamil Nadu and Kerala, respectively.

These studies suggest an ever increasing urban-rural divide being established over the years, suggesting that either diabetes or prediabetes may hardly be of any importance in many rural parts of India.

A study[2] from Gandhigram in Tamil Nadu has suggested a prevalence rate of 13% impaired fasting glycaemia/ impaired glucose tolerance (IFG/IGT) and a 5.1% prevalence of diabetes mellitus (DM). The inverted ratio of a greater percentage of more IFG/IGT than DM is a phenomenon that is equated with a gradual increase in prediabetes which subsequently progresses to diabetes over the years.

For example in the NUDS study the prevalence of IFG/ IGT is lower than that of diabetes; this is because in urban areas, the increase in DM to some extent replaces the IFG/ IGT prevalence.

Therefore, the high IFG/IGT prevalence may be a predictor of more ominous things to come and possibly a higher prevalence of diabetes in less than a decade in the same geographical region, when epidemiological studies are subsequently repeated.

Raghupathy *et al*[3] have demonstrated that in Gudiyattam Taluk in the rural part of Vellore district that the prevalence of glycaemic disorders was high in those below the age of 30 years. They reported an 18% prevalence of IGT in the urban region with 14% prevalence in the rural area, indicating that rural areas are showing a rapid progression of prediabetes which may be comparable to that of urban areas.

In contrast, the PODIS study[4] that was conducted in rural Karnataka in 2005 cited a prevalence rate of 3.7% for diabetes above the age of 25 years and 2.8% for IGT, one of the lowest prevalence being cited in recent times.

One of the most astounding figures that have been published more recently is the epidemiological work in the Godavari region of Andhra Pradesh[5], a relatively fertile part of South India where agrarian practices are prevalent. Over here, they cited a prevalence of diabetes amounts to 13% diabetes–approximately half of which were newly diagnosed. There was also an additional burden of 14% of IFG.

However, one should be cautious in interpreting data which may show superabundance in the prevalence of diabetes and prediabetes in a so called rural or urban region. Indeed we should always pause to ask the question, was the survey done in a genuinely rural part of the country?

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The other fallacies that come into the picture include epidemiological quirks like lead time bias where first time screening may include a cumulative number of subjects who were in fact cases of diabetes belonging to a previous decade. Length time bias is a form of selection bias where in a statistical distortion of results occurs leading to an incorrect conclusion about the data. Length time bias can occur when the lengths of intervals analysed by selecting intervals that occupy randomly chosen points in time or space. This process favours longer intervals, thus skewing the data[6]. Thus there is an over representation of IFG and IGT in screening surveys which does not necessarily indicate subsequent progression of disease. The newer cut-off of 100mg/dl for IFG leads to earlier detection of the disease and enhancing the long term prognostic outcome of prediabetes falsely causing another bias in the form of "lead time bias".

Nevertheless, the abundance of data from the Southern part of India, which makes the epidemiologist wonder as to whether there are ethnic factors that predispose subjects from the Southern part of India for a greater propensity to develop diabetes. Is there a genetic Dravidian propensity to develop the disease the merges its effect with the very obvious lifestyle changes that occur?

The North East part of India is comprised of several ethnically variable groups of subjects who are Mongoloid in origin[7]. Hypothetically speaking, one would probably have expected a slightly lower trend with regards to the prevalence of diabetes in this part of the country when compared to the Dravidian dominated Southern population. Moreover, the socio-economic indices and the degree of urbanisation in the North East part of India may not be as profound and one might expect that the impact of lifestyle changes may be significantly less.

With this in mind, we conducted a survey in the North-Eastern state of Tripura in a rural area[8], through a project sponsored by the World Diabetes Foundation which was initially meant to train 100 hospitals across rural India to improve diabetes infrastructure in rural areas from 2004 to 2009.

There were several salient features that stood out. Firstly, the prevalence of diabetes was relatively high in this largely rural set up- 9%. One could argue that since it was the first survey of its sort in that part of the country, there may be an element of length time bias – wherein the could be an accumulation of cases over a period of time leading to a falsely increased number of diabetes at the time of the first survey. Nevertheless, the trend is significant, whatever the case may be. Secondly, the population that was assessed was a blend of the local tribal population and a Bengali speaking population in a ratio of 3 : 2. There was no statistically significant difference seen between the two ethnic groups, implying that ethnicity per se and the mongoloid race itself did not seem to confer a protective effect on the population against developing diabetes. So also the economic status did not have an influence on the prevalence of diabetes.

Thirdly, a physical activity questionnaire was administered to the subjects during the course of the survey. The result of which was that there was a reduced propensity for diabetes to occur in those subjects with a higher physical activity score: This achieved statistical significance on assessment.

Some of the baseline demographic figures of the study[8] bear interesting similarities to that seen in the NUDS and PODIS studies (Table 1).

Table 1 — *Comparative Data between Three Indian Studies*

Characteristics	North East Study	NUDS	PODIS
Total number	200	11216	18363
Sex distribution	M:F= 46:54	M:F= 46:54	M:F= 46:51
Mean age	44.5 + 15	44.4	44
Ethnicity	Indian Tribal 61% Immigrant 39%	Indian 6 major cities	Indian Urban 40 Rural 33

M-Male; F-Female

At the end of the day, this study is an important blip on the radar screen indicating that the increase in the prevalence of diabetes may be a ubiquitous feature right across the country, transcending all socio-economic and ethnic groups and that rapid lifestyle changes are inducing the development of disease in both urban and rural parts of the population in many corners of the country.

But why has this explosion become more ubiquitous, why has the epidemic spread to such an extent? What are the reasons- is it merely that "coco-cola colonisation" has started to permeate the traditionally rustic rural areas of our country or is it more than just that?

Drewnowski and Specter[9] had shown that in subjects who were in the lower socio-economic group, there was tendency to take more carbohydrate and fat rich food in greater abundance since it was cheaper than that of the food which was lower in calories and contained a larger quantum of free radicals and vitamins. Hence the socio-economically deprived, may in fact have a greater propensity to develop weight gain through the food which they eat, rather than those who are well off. In other words certainly cheaper oils are abundantly and are not expensive compared to fresh fruits and vegetables. This lends further credence to the statement: "An apple a day keeps the doctor away".

Looking at the Indian population in rural areas, nutrition is still less than satisfactory, hence, mothers who are pregnant are substantially underfed in terms of protein intake, leading to small, low birth weight babies[10]. These babies, according to Barker *et al*[11] who first proposed this hypothesis in 1990, are more prone to diabetes and the metabolic syndrome, when they grow up; in fact the quantum of fat in their bodies exceeds that of the normal birth weight (NBW) subjects. The prevalence of low birth weight (LBW) in India is pandemic– 26% of the babies born in rural India[12], even in the region surrounding Vellore; the prevalence is as high as 17%.

In general South Asians have a lower birth weight and are more insulin resistant than their European counterparts. When comparing babies born in the United Kingdom with Indian babies– Indian babies are approximately - 800 g lighter, 30 mm shorter, 0.3 kg/m3 thinner, have less muscle but a much higher content of adiposity[13]. The natural tendency of a mother is to over feed a low birth weight baby when she sees that it is small and to try and deliberately increase the size of the infant. She would not realise that overfeeding in itself would substantially increase the risk of diabetes for these infants later on in life.

Why are these infants more prone for such a problem?

A collaborative venture at Vellore is unravelling some of the factors in assessing the pathogenesis of low birth weight induced diabetes. A population based cohort of 60 LBW subjects and 60 NBW subjects born at term was taken from a rural part in the of North Arcot district where Vellore town is located. The subjects were 18 to 22 years old at the time of recruitment.

Several indices have been used in epidemiological studies to measure and insulin resistance were assessed, including a hyperinsulinaemic euglycaemic clamp study (using an M value). Assessment of total energy expenditure was performed using an Actiheart device and resting energy expenditure using an indirect calorimeter.

Amongst 100 subjects, the mean BMI was 19.12 kg/m^2 and waist circumference 69.65 cm which is strikingly low, but one should bear in mind that these were healthy young males who were not malnourished. The M value had a mean of 11.28, HOMA-IR was 0.975, QUICKI 0.416, and McCauley's index was 11.47. Truncal fat and total body fat as estimated by DEXA (dual energy x-ray absorptiometry) was 13.03% and 14.53% respectively. Strong statistically significant correlations were obtained between the BMI and the waist circumference (r=0.85), truncal fat (r=0.778) and fasting insulin (r=0.39). One should remember that these correlations have occurred at a relatively low BMI indicating a slope in the insulin resistance patterns occurring at a relatively low BMI. Truncal fat correlated strongly with the fasting insulin (r=0.532), triglycerides (r=0.434) and LDL cholesterol (r=0.422). Insulin sensitivity (M-value) correlated with a fasting insulin (r= -0.478), HOMA (r= -0.406), QUICKI (r= 0.39), McCauley's Index (r= 0.365) and also with body composition: Truncal fat (r= -0.453), total fat (r = -0.419) and waist circumference (meaning $p<=0.0001$).

Regardless of the low BMI of these subjects, the M value as a measure of insulin sensitivity correlates negatively with total body and truncal fat content indicating a threshold for reduction in insulin sensitivity at BMIs below 20 kg/m^2. This suggests that rural subjects may be prone for insulin resistance at a relatively low BMI which could explain the increased propensity for diabetes in relatively thin individuals later on in life.

Analysis of the data on energy expenditure obtained from the Actiheart indicates that there is an inverse correlation between birth weight and the energy spent by the body (r=0.512, p=0.005). A similar finding was obtained on resting energy expenditure assessment being assessed by indirect calorimetry (r= 0.235, p=0.032).

Therefore, energy expenditure is reduced in those born low birth weight which could account for an increase account for storage of energy in the form of fat thereby enhancing insulin resistance.

Taking into account the impact of the disease on rural areas and the sweeping effect it is likely to have on the community over the years[14], is there any possibility for the medical community to halt its progression?

The Gandhigram study was interesting, in that with in a short period of time, through lifestyle intervention measures and education, there was an 11% reduction in prediabetes in adults, a 17% reduction in the youth and a reduction of the prevalence of diabetes by 25% in a period of just 7 months. This interventional study holds great promise for the future.

In conclusion, the prevalence of type 2 diabetes and related glycaemic disorders appears to be increasing significantly in various parts of the country transcending the borders of ethnicity. Besides changes in lifestyle, the quality of food and the epigenetic effect of low birth weight have a significant impact in augmenting the progression of the disease.

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