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Hypertriglyceridaemia either in isolation or in combination with abdominal obesity is strongly associated with atherogenic dyslipidaemia in Asian Indians

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ABSTRACT

Aim: To assess the prevalence of isolated hypertriglyceridaemia (iHTG) and hypertriglyceridaemic waist phenotype (HTWP) in urban adult Asian Indian population and to study their associations with atherogenic dyslipidaemia.

Methods: Data of an epidemiological survey ($n = 2117$, M:F 1007:1110) was used. Prevalences of iHTG (fasting triglycerides (TG) $\geq$ 1.7 mmol/l) and HTWP (waist circumference male $\geq$ 90 cm and female $\geq$ 80 cm and TG $\geq$ 1.7 mmol/l), were assessed. Their prevalences in relation to glucose intolerance were also studied. Associations of iHTG and HTWP with the occurrence of atherogenic dyslipidaemia indicated by elevated LDL-C/HDL-C ratio of $\geq$ 2.5 were assessed using multiple logistic regression analyses.

Results: iHTG, and HTWP were present in 13.4% and 17.8% respectively. Prevalence of HTWP was significantly higher among women. Prevalence of HTWP progressively increased with glucose intolerance. Nearly 60% of the subjects with iHTG or HTWP had atherogenic dyslipidaemia and prevalence was similar in both groups.

Conclusions: Hypertriglyceridaemia, present either as iHTG or HTWP was strongly associated with atherogenic dyslipidaemia. Dyslipidaemia occurred more frequently in glucose intolerance since the prevalence of both forms of hypertriglyceridaemia increased with glucose intolerance.

1. Introduction

Asian Indians have several characteristic features which promote development of diabetes and atherogenesis. These include presence of insulin resistance despite having comparatively lean body mass index (BMI), high percentage of body fat, a predominance of visceral adiposity and prevalence of atherogenic lipid profiles [1–10]. They have high prevalence of hypertriglyceridaemia (HTG) which is a surrogate marker of insulin resistance [11].

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Abbreviations: 2hPG, 2 h plasma glucose; Apo B, Apo lipoprotein-B; BP, blood pressure; BMI, body mass index; CHD, coronary heart diseases; CVD, cardio vascular diseases; DM, diabetes mellitus; FPG, fasting plasma glucose; HDL-C, high density lipoprotein cholesterol; HTN, hypertension; HTG, hypertriglyceridaemia; HTWP, hypertriglyceridaemic waist phenotype; iWC, isolated waist circumference; iTG, isolated triglycerides; IGT, impaired glucose tolerance; iHTG, isolated hypertriglyceridaemia; IFG, impaired fasting glucose; LDL-C, low density lipoprotein cholesterol; NGT, normoglycaemia; NCEP, National Cholesterol Education Programme; NHANES III, National Health and Nutritional Examination Survey; OR, odds ratio; OGTT, oral glucose tolerance test; WC, waist circumference; TG, triglycerides.

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A combination of increased waist circumference (WC) and elevated fasting triglyceride (TG) concentrations, which is termed as hypertriglyceridaemic waist phenotype (HTWP) has been used to identify subjects with metabolic syndrome, fasting hyperinsulinaemia, elevated apo lipoprotein-B (Apo B) and higher amounts of small low density lipoprotein cholesterol (LDL-C) particles, all of which promote atherogenesis [12]. It is suggested that elevated TG levels could be used as a marker of ‘‘dysfunctional adipose tissue’’ in people with increased waist line [12–15]. It is generally agreed upon that the combination of WC and HTG could be useful as an inexpensive screening tool to identify people with increased risk of cardiovascular diseases (CVD) and type 2 diabetes [13–16].

The National Cholesterol Education Programme (NCEP) guidelines recommend specific target levels of low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C), for determining CVD risk and evaluating effectiveness of lipid-lowering therapies [17]. Measurement of LDL-C and HDL-C is common, and LDL-C/HDL-C ratio is shown to be an excellent predictor of CVD risk and also helps to monitor the effectiveness of lipid-lowering therapies [17,18]. The Framingham study [18] showed that LDL-C/HDL-C ratios are stronger predictors of CVD than their individual levels.

In view of the high prevalence of diabetes, CVD and HTG among the Asian Indian population especially in the urban areas [2,7–10], this analysis was done with the following objectives.

1. To find out the prevalence of isolated hypertriglyceridaemia (iHTG) and HTWP in the urban adult population in Chennai, Tamilnadu, India.
2. To assess the differences in their prevalence among normoglycaemic (NGT), prediabetic (impaired glucose tolerance (IGT)) and diabetic subjects.
3. To find out whether the association of iHTG and HTWP with atherogenic dyslipidemia, (indicated by raised LDL-C/HDL-C ratio) differed.

The epidemiological data collected in a survey conducted in 2006 in Chennai, Tamilnadu, India was used for this analysis. The details of the methodology are published [2]. Previously, the data had been analysed with different objectives and the overall prevalence of diabetes and cardiovascular risk factors in relation to urbanization had been published [2]. This analysis was done with the objectives mentioned above.

2. Subjects, materials and methods

The data was collected by a survey done in subjects aged ≥20 years, in three locations namely Chennai city, in Kancheepuram town and in Panruti an urbanizing rural area in Tamilnadu, India. In all areas a multistage random sample selection was done in the census wards and the samples were representative of the general population. Participants gave informed consent and the study protocol was approved by the Institutional Ethics Committee. Details on demography, anthropometry, medical history, education, socio-economic status, occupation, physical activity and diet habits were collected using standard procedures. For known diabetic cases fasting plasma glucose (FPG) and 2 h postprandial were measured. Others underwent the standard oral glucose tolerance test (OGTT) [19]. Diabetes was diagnosed if FPG value was ≥7.0 mmol/l and/or 2-h postglucose (2hPG) was ≥11.1 mmol/l, impaired fasting glucose (IFG) if FPG was between 6.1 and 6.9 mmol/l, and IGT if the 2-h values were ≥7.8 mmol/l and <11.1 mmol/l with fasting values <6.1 mmol/l. Fasting serum lipid profile was estimated by standard enzymatic procedures (Roche Diagnostics). HDL-C was estimated by the direct assay method.

This analysis was done only in the Chennai urban sample. All details for the analyses were available in 2117 of the 2192 subjects surveyed. BMI of ≥25 kg/m^2 was considered to indicate obesity. Cutoff values for normal WC for men and women ≥90 and ≥80 cm, respectively. Study subjects were grouped as having iHTG if they had only elevated TG levels and as having HTWP if this levels of WC and TG were elevated. Cutoff values for lipid parameters were as follows: LDL-C ≥ 2.6 mmol/l, TG ≥ 1.7 mmol/l, and HDL-C < 1.04 mmol/l for men and <1.23 for women. LDL-C/HDL-C ratio was calculated. Values ≥ 2.5 were considered abnormal.

Table 1 – Characteristics of the study subjects in relation to glucose tolerance (*n* = 2117) demography, anthropometry and biochemical variables.

Variables	Normoglycaemia	Impaired glucose tolerance	Diabetes
M:F	685:777 (4.7:5.3)	122:133 (4.8:5.2)	200:200 (5:5)
	Mean ± SD		
Age (years)*	35.2 ± 11.4	40.5 ± 11.7	49.5 ± 11.5
BMI (kg/m^2)*	23.7 ± 4.7	25.5 ± 4.9	25.9 ± 3.9
Waist circumference (cm)*	82.0 ± 10.9	86.4 ± 11.2	89.0 ± 9.6
Plasma glucose (mmol/l)			
Fasting*	5.1 ± 0.5	5.8 ± 0.7	8.9 ± 3.6
120 min*	5.6 ± 0.9	8.0 ± 1.6	13.6 ± 5.8
Lipids profile (mmol/l)			
Triglycerides**	106	136	154.5
Low density lipoprotein–cholesterol*	2.7 ± 0.8	2.9 ± 0.9	2.9 ± 1.1
High density lipoprotein–cholesterol*	1.2 ± 0.3	1.1 ± 0.3	1.1 ± 0.2
LDL-C/HDL-C*	2.4 ± 0.8	2.6 ± 0.9*	2.6 ± 1.0

*One-way ANOVA, $p < 0.0001$, **median value, $p < 0.0001$ by Kruskal–Wallis Test.

Table 2 – Prevalence of hypertriglyceridaemia, elevated waist circumference and HTWP in relation to glucose intolerance.

Abnormalities	Total†		Glucose tolerance: Normoglycaemia†		Impaired glucose tolerance†		Diabetes†	
Men:women	n = 2117 1007:1110		n = 1462 685:777		n = 255 122:133		n = 400 200:200	
	n	%	n	%	n	%	n	%
Isolated hypertriglyceridaemia (iHTG)								
Men*	215	21.4	131	19.1	31	25.4	53	26.5
Women	68	6.1	44	5.7	11	8.3	13	6.5
Isolated elevated waist circumference (iWC)								
Men	145	14.3	90	13.1	18	14.8	37	18.5
Women**	486	43.8	344	44.3	64	48.1	78	39.0
Hypertriglyceridaemia and increased waist circumference (HTWP)								
Men#	129	12.8	51	7.2	23	18.9	55	27.5
Women#	248	22.3	120	15.4	39	29.3	89	44.5

Under glucose tolerance – trend χ^2 *$p = 0.041$ in men, **$p = 0.006$ in women, #$p < 0.0001$ in men and women.
† Differences between men and women were highly significant ($p < 0.001$) in all categories.

2.1. Statistical analysis

Mean ± SD are reported for normally distributed variables and median values are reported for skewed variables. Student's *t* test or oneway ANOVA was used as relevant for group comparisons and chi square test was used to test categorical variables. For comparing the median values, Kruscal–Wallis test was used. Multiple logistic regression analyses (enter method) were done to identify the variables significantly associated with dyslipidaemia indicated as LDL-C/HDL-C ratio of ≥ 2.5. In the analysis age, sex, BMI, WC, FPG, 2hPG and iHTG vs normal TG and WC were included as the independent variables, and in another model HTWP Vs normal TG and WC was included. A *p* value of <0.05 was considered as significant. SPSS for windows (version 10.0; SPSS, Chicago, IL) was used.

3. Results

Table 1 shows the characteristics of the study subjects in the categories of glucose tolerance. Mean values of age, WC and TG increased with increasing glucose intolerance. BMI, LDL-C, LDL-C/HDL-C were significantly higher and HDL-C was lower in IGT and diabetes when compared with NGT. The values were similar in IGT and diabetes.

Among the study subjects ($n = 2117$), fasting hypertriglyceridaemia (HTG) was present in 660 subjects (31.2%), among them 283 (13.4%) had iHTG and 377 (17.8%) had HTWP.

Table 2 shows sex-specific prevalences of iHTG, iWC and HTWP in categories of glucose tolerance. Prevalence of iHTG was higher in glucose intolerant men (IGT + diabetes) ($p = 0.041$). Women had significantly lower prevalence of iHTG than men. Women had higher prevalences of iWC and HTWP than men, in all categories of glucose tolerance. Prevalences of iWC and HTWP progressively increased with increasing glucose intolerance, in both sexes ($p < 0.0001$ for both).

Prevalence of obesity was higher among men and women with HTWP than with iHTG ($p < 0.0001$ for both sexes) (Table 3). Rate of obesity was similar among men and women with HTWP while women with iHTG had lower rates of obesity than men ($p = 0.02$). Prevalence of atherogenic dyslipidaemia was similar in both sexes with either iHTG or HTWP.

Logistic regression analysis showed that iHTG or HTWP had independent and significant associations with dyslipidaemia (elevated LDL-C/HDL-C ratio) (Table 4). Age and BMI also had independent associations with the abnormal ratios while plasma glucose did not show an association.

4. Discussion

The study showed that urban Asian Indians had a high prevalence of HTG (31.2%) and 57% among them had HTWP. The prevalence of iHTG was similar in all categories of glucose tolerance. However a concomitant increase in TG and WC resulting in HTWP occurred in persons with glucose intolerance; the highest percentage was seen in diabetes.

Table 3 – Association of obesity and dyslipidaemia with isolated hypertriglyceridaemia (iHTG) and hypertriglyceridaemia and increased waist circumference (HTWP).

Men:women	Isolated hypertriglyceridaemia (n = 283) 215:68		Hypertriglyceridaemia and increased waist circumference (n = 377) 129:248	
	n	%	*n*	%
Associated abnormalities				
Obesity (≥25 kg/m^2)				
Men	52	24.2	98$^{\#}$	76.0
Women	7	10.3*	183$^{\#}$	73.8
LDL-C/HDL-C (≥2.5)				
Men	126	58.6	80	62.0
Women	39	7.4	161	64.9

Chi-square test, $^{*}p$ = 0.02 vs men, $^{\#}$men and women, $p < 0.0001$ vs iHTG.

Table 4 – Results of multiple logistic regression analyses – association of isolated hypertriglyceridaemia and HTWP with LDL-C/HDL-C ratio.

Independent variables	β-Coefficient	Odds ratio (OR)	95% Confidence interval	p Value
Panel-1[a]	Dependent variable LDL-C/HDL-C			
Age	0.016	1.016	1.006–1.027	0.002
Body mass index	0.071	1.074	1.018–1.133	0.009
Isolated hypertriglyceridaemia vs normal [b]	0.732	2.079	1.544–2.799	0.000
Panel-2[a]				
Age	0.011	1.011	1.001–1.022	0.025
Body mass index	0.058	1.060	1.010–1.112	0.019
HTWP vs normal[b]	0.529	1.696	1.099–2.619	0.017

[a] FPG and 2 h PG were not significantly associated.
[b] Normal triglycerides and waist circumference.

In this study, higher prevalence of elevated waist levels were seen in women than in men; women had higher percentages of iWC and HTWP. In the third National Health and Nutritional Examination Survey (NHANES III) in the USA, HTWP was prevalent in about 25%, irrespective of the sex [15]. The prevalence of the phenotype was 19% in adult men, both in the Quebec Health Survey [20] and in the Tehran Lipid and Glucose Study [21] though different cutoffs were used for WC and TG levels. All the studies showed that the prevalence increased with age.

Higher percentage of obesity among persons with HTWP was expected, as increased WC would be generally associated with higher BMI. Measurement of HTWP is a good index of dyslipidaemia and obesity especially of upper body adiposity. Our study showed that iHTG and HTWP had equally strong association with atherogenic dyslipidaemia.

Mixed or atherogenic hyperlipidaemia includes hypertriglyceridaemia and associated elevation of LDL-C which is often accompanied by reduced levels of HDL-C. This form of dyslipidaemia favours increasing number of circulating remnant particles. In our study this form of dyslipidaemia was present in nearly 60% of persons with HTG. In the Scandinavian Simvastatin Survival Study [22] cardiovascular event rates were nearly 2-fold higher in the placebo treated patients having this triad of dyslipidaemia compared with the placebo-treated patients with isolated elevations in LDL-C. A similar relationship was observed between the coronary heart diseases (CHD) events and the lipid triad in the Helsinki Heart Study [23], which was a randomized coronary primary prevention trial in middle-aged men who had dyslipidaemia. We noted that HTG was strongly related to insulin resistance in our population [11]. In the Framingham Study [18] HTG was shown to be associated with low HDL-C. Low HDL-C is strongly associated with insulin resistance as well.

Studies by several groups [12,13,15,24] had shown that HTWP can be used to identify viscerally obese individuals at risk for CVD and HTWP was a better predictor of CV risk than the metabolic syndrome. An abnormal LDL-C/HDL-C ratio which has been shown to be accurate predictor of CV risk is found in association with hypertriglyceridaemia, either as iHTG or as HTWP, in Asian Indian population.

With the development of glucose intolerance the occurrence of HTWP increases, and the atherogenic risk increases concomitantly. Increasing age, BMI and WC increase the risk of HTWP, and also enhance the risk of diabetes and CVD. The higher risk of atherogenesis in diabetes is probably mediated through the higher rates of HTWP. A strong link been HTWP and abnormal ratios of cholesterol/HDL-C has been demonstrated in several studies [13,15,20,24]. Type 2 diabetic patients with HTWP have been shown to be a subset with greater degrees of visceral adiposity and subclinical atherosclerosis that may be related to pro atherogenic lipoprotein changes [24].

In summary the study highlights the high prevalence of HTG in the Asian Indian population. The prevalence of HTWP increases with development of glucose intolerance or diabetes. The presence of iHTG itself is strongly associated with abnormal LDL-C/HDL-C ratio, the propensity of which increases with development of glucose intolerance. These findings underscore the need to identify the presence of HTG in Asian Indians and to institute appropriate therapeutic interventions as a primary prevention strategy for CVD.

From a clinical stand point, elevated TG poses considerable health risk which has been well documented by several prospective studies such as the Framingham Study [18], the 4S study [22] and the Helsinki Heart Study [23] and the PROCAM Study [25]. Asian Indians tend to have high atherogenic lipid profile despite having lower levels of obesity and serum cholesterol levels than the white population, probably due to higher prevalences of HTG and HTWP. Among Asian Indians the presence of iHTG itself could be a surrogate marker of atherogenic dyslipidaemia.

Author contributions

Chamukuttan Snehalatha designed the study, researched, analysed, discussed and prepared manuscript.

Nanditha Arun contributed to discussion, reviewed manuscript.

Ananth Samith Shetty contributed to discussion, reviewed manuscript.

Ambady Ramachandran designed the study, researched, analysed, discussed and edited manuscript.

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Conflict of interest

There are no conflicts of interest.

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