Original article:

Study the close relations with clinical profile of impaired glucose tolerance (IGT) in newly diagnosed hypertensive patients

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Abstract

A close relations ship exists between hypertension and diabetes it is necessary to diagnose diabetes or risk of diabetes as early as possible avoid complication. The present study was conducted in 100 newly diagnosed patients of hypertension. These patients were meticulously studied for risk factors for hypertension, clinical presentation, ECG and biochemical investigation. These patients were subjected to OGTT and were accordingly grouped. 34 subjects had impaired glucose tolerance for OGTT and 66 subjects were normal for OGTT. We found the prevalence of abnormal glucose tolerance test was high in hypertensive subjects, especially those who have moderate to severe hypertension, elderly population, females, higher cholesterol level, abnormal WHR, have history of habitual addiction, non vegetarian dietary habits, have urban life style are indulged in sedentary jobs, have a family history of diabetes and have ECG abnormalities (left ventricular hypertrophy). So testing for impaired glucose tolerance should be carried out frequently in these individuals.

Keywords: Hypertension, Impaired glucose tolerance, Diabetes

Introduction

Hypertension often affects people with type-2 diabetes. It is unknown why there is such a significant correlation between the two diseases, but it is widely assumed that obesity, a high-fat, high-sodium diet, and inactivity have led to a rise in both conditions [1-3]. Hypertension is known as a silent killer because it has no obvious symptoms and many people are unaware that they have it. Diabetes mellitus (DM) is a syndrome characterized chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency of insulin secretion and/or insulin action [4].

Hypertension or diabetes is an iceberg disease according to recent estimate the prevalence of in adults was around 4% worldwide. The population in India has an increased susceptibility to DM [5]. The prevalence of disease in adult was found to be 2.4% in rural and 4 to 11.6% in urban population. Diabetes accounts for more than 200,000 deaths, 82,000 amputations and 44,400 new cases of end-stage renal disease and up to 24,000 new cases of blindness each year in the developing county [6]. A serious gap exists between established recommendations and the actual care that patients receive, especially with associated conditions such as hypertension, which further contribute to morbidity and mortality in these patients [1–3].

Most adverse diabetes outcomes are a result of vascular complications, both at a macrovascular level (coronary artery disease, cerebrovascular disease or

peripheral vascular disease) and a microvascular level (retinopathy, nephropathy or neuropathy). The importance of preventing the macrovascular complications of type-2 diabetes has started to receive greater attention. Numerous trials have examined the benefit of management of the highly prevalent risk factors, such as hypertension. Hypertension affects up to 60% of patients with type-2 DM, and there are a growing number of pharmacologic treatment options [4-6].

Impaired glucose tolerance (IGT) is categories that permit classification of individuals whose glucose tolerance is above conventional normal range but lower than the level considered diagnostic for DM [7]. IGTcannot be defined on the basis of fasting glucose concentration; an oral glucose tolerance test (OGTT) is needed to categorize such individual. In most subjects IGT represent a transient stage during development type-2 diabetes [8].

Although diabetes and hypertension are two distinct entities with their own independent complication yet they appear to be closely related. DM is responsible for the genesis and acceleration of hypertensive process. Hypertension is known to accelerate the macroangiopathic and microangiopathic complications of diabetes the effect of blood pressure on risk of fatal coronary heart disease are 2 to 5 times greater than known diabetic people. The risks of nephropathy & end stage renal disease are also increased 2 to 3 times by hypertension [7-9].

As a close relations ship exist between hypertension and diabetes it is necessary to diagnose diabetes or risk of diabetes as early as possible avoid complication. The goals of this study to early detection of IGT in newly diagnosed hypertensive patients and prevent or delay the development of overt diabetes by mode of changes in life style, dietary habits and exercise.

Material and Methodology

The study included 100 subjects; studied sample were taken from wards & OPD. The study included subjects who are first time diagnosed as a hypertensive admitted in wards or attended out patients department. Those persons selected for the study were asked about the symptoms pertaining to the DM. A complete general and systemic examination was carried out including relevant anthropometric measurements such as height, weight, body mass index, waist hip ratio; height and weight were measured with participants standing without shoes and heavy outer garments. Body mass index was calculated by weight in kg divided by height in meter square, waist and hip circumference were measured with participants standing without heavy outer garments and with empty pockets. Waist was measured at the level midway between lower rib margin and iliac crest with the participant breathing out gently. Hip was recorded as the maximum circumference over the buttocks. Both measurements were rounded to the nearest centimeter. After the above mentioned complete procedures the all persons were subjected to OGTT.

Results

The prevalence of IGT was found in 34% subjects & NGT was found in 66% subjects. Those subjects belonging to age group 25-44 yrs 20% subject had IGT, while those belonging to age group 45-59 yrs 35.6% had IGT. The incidence of IGT was 43.3% in subjects with 60-75 yrs of age group. It was concluded that prevalence of IGT increases with increment of age. Prevalence of IGT was 32.1% in male subjects & 36.2% in female and was statistically

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insignificant in both groups. Higher prevalence of IGT among urban resident was observed.

Most common symptoms among IGT subjects were weakness giddiness & headache(Table 1).Tobacco smoking (48.3%) was a significant risk factor for IGT in hypertension. Alcohol alone does not showed significant risk for IGT in hypertension. Most of the subjects of IGT group had a non-vegetarian dietary habit (59.4%). While vegetarian dietary habit was found in 22.1% subject with IGT. (Table 1)

The family history of hypertension among subjects was not a significant risk factor for impaired glucose tolerance in hypertension subjects. The family history of DM was found in 13% subjects, out of which 61.5% had IGT and 38.5% had NGT and results showed that family history of diabetes is a significant risk factor for IGT. No association of BMI was observed with presence of IGT. Among the males, the waist hip ratio was normal in 69.8% subjects while it was abnormal in 30.2% subjects. Out of those with normal WHR, 29.7% had IGT, while those with abnormal WHR 37.5% had IGT. The results showed statistically insignificant. Among the female was having normal WHR were 12.8% of which no subject had IGT while those with abnormal WHR 41.5% had IGT, the result showed statistically significant. The central pattern of obesity was significantly more prevalent in IGT females than males. The BMI was comparably insignificant between both groups; this reveals that not obesity but it is the distribution of body fat that possesses risk factor of IGT in hypertension. In relation to the degree of hypertension, the prevalence of IGT in mild hypertension was 15.8% with moderate hypertension 31% and with severe hypertension it was found to be 46.2%, the result was statistically significant. It revealed that as the severity of hypertension increases the chance of IGT also increases. Of the 100 subjects 64% subject had high cholesterol level out of which IGT was found in 42.2% subject. Out of 36% subjects with low cholesterol level 19.4% subject had IGT, the results were statistically significant. Electrocardiographically, the prevalence of LVH (66.7%) was high in IGT patients as compared to ischemia (30%) and conduction disturbance (23.8%).

Table 1: Demographic and Clinical Characteristics of patients with IGT and NGT

		IGT		NGT		Pvalue
		No.	%	No.	%	
Age Wise Distribution of Cases						
25-44 Years		5	20.0	20	80.0	<0.05
45-59Years		16	35.6	29	64.5	
60-75Years		13	43.3	17	56.7	
Prevalence of IGT In Relation To Sex						
Male		17	32.1	36	67.9	>0.05
Female		17	36.2	30	63.8	
Relationship of IGT In Relation To Their Habitat						
Rural		9	19.6	37	80.4	<0.05
Urban		25	46.3	29	53.7	
Relationship Between Symptoms And IGT Among Subjects						
Chest pain		9	24.3	28	75.6	<0.05
Palpitation		5	29.4	12	70.5	<0.05
Sweating		1	25.0	3	75.0	<0.05
Nausea/vomiting		3	30.0	7	70.0	<0.05
Headache		9	47.3	10	52.6	<0.05
Weakness		16	48.4	17	51.5	<0.05
Giddiness		10	33.3	20	66.6	<0.05
Blurred vision		2	25.0	6	75.0	<0.05
Epistaxis		2	50.0	2	50.0	<0.05
Breathlessness		5	29.4	12	70.5	<0.05
Relationship Between Symptoms And IGT with Addictions						
Non- Addictions		16	26.2	45	73.8	<0.05
Addictions		18	46.2	21	53.8	<0.05
Tobacco (Smoking)		14	48.3	15	51.7	<0.05
Alcohol Only		3	42.9	4	57.1	>0.05
Tobacco+Alcohol		1	33.3	2	66.7	<0.05
Relationship Between Symptoms And IGT with Dietary Habits						
Non-Vegetarian		19	59.4	13	40.6	<0.001
Vegetarian		15	22.1	57	77.9	
Distribution According to BMI (kg/m^2)						
<18.5 (Underweight)		2	28.6	5	71.4	>0.05
18.5-24.9 (Normal)		21	29.2	51	70.8	
25-29.9(overweight)		9	50.0	9	50.0	
>30(Obese)		2	66.6	1	33.3	
Distribution According To WHR						
Male 17	≤1.0(normal)	11	29.7	26	70.3	>0.05
	≤1.0(normal)	11	29.7	26	70.3	
Female 17	≤0.9(normal)	0	0.0	6	100	<0.05
	>0.9(Abnormal)	17	41.5	24	58.5	
Relation of IGT with degree of hypertension						
Stage-1 hypertension		03	15.8	16	84.2	<0.05
Stage-2 hypertension		13	31.0	29	69.0	
Stage-3 hypertension		18	46.2	21	53.8	
Distribution According To Their Serum Cholesterol Level						
≤200		7	19.4	29	80.6	<0.05
>200		27	42.2	37	57.8	
Relation of IGT with ECG changes						
Ischemia		3	30	7	70	>0.05
Conduction disturbance		5	23.8	16	76.2	>0.05
Left ventricular hypertrophy		20	66.7	10	33.33	<0.001

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Discussion

In this study, out of 100 subjects; 34 subjects found to have abnormal glucose tolerance. Jain et al[10] in their study showed that out of 150 subjects who participated in the study 64 (42.6%) had abnormal glucose tolerance (30.6%) IGT and 12% had newly detected diabetes. Studies conducted in western countries have also shown high prevalence of abnormal glucose tolerance of 52.3% (36.1% IGT and 16.2%) type II diabetes) in patients of young ischemic heart disease. In study of Japanese population (2001) with IHD, the prevalence of disturbance of glucose metabolism was very high 67.7% (IGT 32.3% and type II diabetes 35.4%) [10].

In CURES-17, the overall crude prevalence of diabetes using WHO criteria in CURES was 15.5% (age standardized 14.3%), while that of IGT was 10.6% (age-standardized 10.2%). There was a shift in the age at diagnosis of diabetes to a younger age in CURES compared with NUDS. Compared with earlier studies, the prevalence of diabetes in Chennai, representing urban India, has increased while that of IGT has decreased [11].

Zagar et al,in Kashmir valley reported that 1.89% of the general population have known diabetes, 4.25% have undiagnosed diabetes and 8.09% have impaired glucose tolerance test; making the total load of abnormal glucose tolerance 14.23% in Kashmir valley [12]. Ramachandran et al, in their study, including 475 subjects (age 20- 75 yrs), from a population data base were studies for the MetS using ATP III criteria, but with a modified waist circumference (WC) appropriate for Indians showed MetS was present in 41.1%. WC was increased in 31.4%, TG in 45.6%, Low HDL-C in 65.5%, hypertension in 55.4% and raised FPG 26.7%. METS was present in 27.9% of subjects with FPG <6/mmol/L and its prevalence increased to > 70% with higher FPG values [13].

In contrast to our study Williams et al reported that the distribution of impaired glucose metabolism differs by sex. For men and women the prevalence of diabetes (22.0 Vs 21.8% respectively) and the prevalence of coexisting IGT (3.2 vs 2.9%) were similar. However, men were twice as likely as women to have isolated IFG (5.1%) (4.2-6.0) vs 2.9% (2.3-3.5), despite being younger, thinner and with low plasma insulin but higher lipids. Conversely, the prevalence of isolated IGT was lower in men [9.0% (7.9-10.2) vs 13.9% (12.6-15.1)]. Among non diabetic individual, fasting glucose was higher in men than women, whereas 2h glucose was higher in women [14]. In England, estimated prevalence of total diabetes for all people was 4.41% in 2001 diabetes prevalence was estimated to be higher in women (5.17%) than in men (3.61%) [15].

In present study the prevalence of IGT was noted to be higher in urban population as compared rural population. However Ramachandran et al in their study showed that prevalence of IGT was similar in both populations [16].Demographic transition due to improved living conditions in rural India was associated with a three-fold increase in the prevalence of diabetes. Increased upper body adiposity and physical inactivity showed significant association with this phenomenon [17].Similar to our study Jain et al, in their study showed statistically significant ($p < 0.001$) number of subjects were positive for IGT belonging to urban area (61.1%) highlighting the fact that higher incidence is a consequence of urban life culture, awareness, and easy availability of diagnostic approaches for detection of glucose intolerance .Physical inactivity is associated with the components of metabolic

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syndrome and coronary artery disease in urban south Indian population in Chennai [10]. Sedentary habits are mostly associated with a higher risk of developing impaired glucose tolerance. Increasing physical activity can reduce the risk of type-2 diabetes. The protective effect of physical activity was observed in subjects with an excessive BMI and elevated glucose levels. Physical activity and weight control are critical factors in diabetes prevention in subjects with both normal and impaired blood glucose regulation [18].

Ourresults shows that patients with smoking had significant relationship with hypertension in IGT.Cigarette smoking may be an independent, modifiable risk factor for non-insulin dependent DM. Moderate alcohol consumption among healthy people may be associated with increased insulin sensitivity and a reduced risk of diabetes [19].Eliasson et al reported that the risk of diabetes for snususers was not significantly increased. Smoking was associated with prevalent and incident cases of diabetes. Ex-tobacco users tended towards more pathological glucose intolerance [20].Persson et al reported that heavy users of cigarettes or moist snuff have an increased risk of type 2 diabetes. The result could suggest that tobacco use is associated with a low insulin response [21].

In CARDIA (Coronary artery risk development in young adults) prospective cohort study it was found that during follow-up, 16.7% of participants developed glucose intolerance. A graded association existed between smoking exposure and development of glucose intolerance. The 15 year incidence of glucose intolerance was highest among smoker (21.8%), followed by never smoker with passive smoke exposure (17.2%) and then previous smokers (14.4%); it was lowest for never smokers with no passive smoke exposure (11.5%). These findings support a role of both active and passive smoking in the development of glucose intolerance in young adulthood [22].

The higher prevalence of IGT in the non-vegetarian group is noted to be statistically highly significant ($p < 0.001$).In Botnia Dietary study, it was concluded that a high intake of dietary fiber is associated with enhanced insulin sensitivity and therefore may have a role in the prevention of type 2 diabetes [23].Singh et al reported the prevalence of CAD and coronary risk factors was higher in urban Indian with low and high saturated fat intake than those with lower saturated fat intake. These findings suggest that the saturated fat intake should be < 7% energy / day for prevention of CAD in Indians [24].Fukagawa et al reported that the intake of fat, especially that of saturated fatty acids, is associated with the development of IGT and diabetes.. Studies showed that, diet very high in fat and very low in carbohydrates, results in decreased insulin sensitivity [25].

The prevalence of IGT was found to be higher in those subjects who gave a positive family history of DM when compared to those in whom the family history was negative (61.5% vs 29.9%). This finding was statistically significant. In the present study, family history of hypertension was present in 12 subjects, 88 subjects had no family history of hypertension. 5 subject (41.7%) with positive family history and 29 subjects (33.0%) with negative family history had IGT. No significant difference in the prevalence of IGT was obtained between the two groups.

A genetic predisposition to type-2 diabetes is evident from the high familial aggregation of the disease. Asian Indians have strong familial aggregation of diabetes with high prevalence of diabetes among first

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degree relatives and vertical transmission through two or more generations. It was found that 45% of the Indian compared to 38% of the Europeans have positive family history of diabetes. An analysis of family history of diabetes patients attending the Diabetes Research Centre, Madras, India showed that 54% of the probands had a parent with known diabetes. The prevalence of diabetes increased with increasing family history of diabetes. It was noted that the prevalence of diabetes among offspring when one diabetic parent was 36% which increased to 54% with positive family history of diabetes on the non-diabetic parental side also. The prevalence rate (62%) and risk (73%) increased further when both parents had diabetes [26].

In present study, the association of IGT with body mass index was not found to be statistically significant. However, the prevalence of IGT is noted to be more among the overweight subjects (50%) when compared to thin built (28.6%) and normal subjects (29.2%).The prevalence of IGT among the male with abnormal waist hip ratio was 37.5% and prevalence of NGT in the same group was 62.5%.This observation was statistically significant. The prevalence of IGT and NGT in female with abnormal waist hip ratio was 41.5% and 58.5% respectively. This observation was statistically significant.

In the Quebec family study, a cross-sectional study which included 313 men and 382 women, it was found that a large waist circumference in men and women (adjusted for age, BMI and hip circumference) was associated significantly with low HDL-cholesterol concentration ($p< 0.05$) and high fasting triglyceride, insulin and glucose concentration ($p < 0.01$). In women alone, a large waist circumference was also associated with high LDL-cholesterol concentration and blood pressure. A narrow hip circumference (adjusted for age, BMI, and waist circumference) was associated with low HDL-cholesterol and high glucose concentration in men ($p < 0.001$) and high triglyceride and insulin concentrations in men and women ($p < 0.05$). Waist and hip girths showed different relations to body fat, fat-free mass and visceral fat accumulation [27].From Hoorn study, it was concluded that large hip and thigh circumference are association with a lower risk of type 2 diabetes, independently of BMI, age, and waist circumference, whereas a larger waist circumference is associated with higher risk [28].

In the present study, the subjects were grouped into three based on the severity of hypertension. Among 19 subjects with mild hypertension, 3(15.8%) subjects had IGT. 13(31.0%) subjects out of 42 subjects with moderate hypertension had IGT and in 39 subjects with severe hypertension, 18(46.2%) subjects had IGT. The study revealed that as the severity of hypertension increases, the prevalence of IGT increases. Chen et al reported that non dipper hypertensive patients are more glucose intolerant than are dipper patients. The abnormalities of glucose metabolism in non-dippers could be explained by insulin resistance and beta-cell dysfunction. The results of spectral analysis of heart rate variability suggest that abnormal autonomic outflow may represent a possible link between hypertension and associated metabolic dysfunction [29].Falkner et al reported that early attention in glucose metabolism affects an upward shift in BP. The higher BP in IGT and DM may be due to vascular endothelial cell resistance to insulin action [30].High blood pressure is prevalent in obesity and in diabetes, both candidates with insulin resistance. Ferrannini et al reported that this insulin resistance involves glucose

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but not lipid or potassium metabolism, is located in peripheral tissues but not the liver, is limited to non-oxidative pathways of intracellular glucose disposal, and is directly correlated with the severity of hypertension [31].Essential hypertension in elderly is associated with impairment in complex cognitive function [32].The trial of antihypertensive Interventions and management study examined the effect of weight loss, alone or in combination with medication, and diastolic blood pressure in patient with stage I hypertension. The results showed that a weight loss of 4.5 kg or more (> 5% of baseline weight) lowered diastolic blood pressure to the same extent as a single dose of anti-hypertensive medications [33].Individuals with above-optimal BP, including stage I hypertension, can make multi-lifestyle changes that lower BP and reduce their cardiovascular disease risk [34].

In the present study, the prevalence of IGT is found to be more in those hypertensive subjects with higher cholesterol level (42.2%) when compared to those with normal cholesterol level (19.4%) and this observation is statistically significant. Hypertriglyceridemia is common in subjects with NIDDM and IGT and is often associated with low HDL cholesterol, high total cholesterol, hyperinsulinemia, and elevated serum uric acid concentration [35].Davidson et al reported that insulin resistance defined as a high ratio of triglyceride to high-density lipoprotein, is associated with blunted diurnal blood pressure variation before the development of abnormal levels of fasting blood glucose [36].Castelli in Framingham study has shown that men and women having high triglycerides levels and low HDL cholesterol levels are at high or risk of coronary heart disease. 4% of the normotensive subjects had high (>2.4 mmol/L) TG levels together with an increased total cholesterol/HDL cholesterol ratio (>3.5) when compared with the non-obese and obese hypertensive subjects [37].

In the present study newly diagnosed Hypertensive subjects have the prevalence of ischemia and conduction disturbance in IGT was 30.0% and 23.0% respectively. The prevalence of LVH among IGT patients was 66.7% which was statistically highly significant. Cardiovascular disease is the most common cause of disability and death among subjects with NIDDM. The atherosclerotic process begins during the prediabetic phase characterized by impaired glucose tolerance, hyperinsulinemia and insulin resistance [38].In ARIC study it was reported that person with NIDDM or borderline glucose intolerance have stiffer arteries than their counter parts with normal glucose tolerance and that the decreased elasticity is independent of artery wall thickness. The joint effect of elevated glucose, insulin and triglycerides can have a considerable impact on arterial stiffness and play an important role in the early pathophysioloy of macrovascular disease in NIDDM. Caballero et al reported that abnormalities in vascular reactivity and biochemical markers of endothelial cell activation are present early in individuals at risk of developing type 2 diabetes [39].Lind et al found that left ventricular wall thickness to be significantly related to blood pressure, fasting insulin level and hematocrit level and inversely related to insulin sensitivity. In study, it was concluded that left ventricular wall thickness to be closely associated with insulin resistance [40].Abnormal glucose tolerance is a strong risk factor for future cardiovascular events after myocardial infarction since it is common and possible to detect even during the hospital phase it may be a target for novel secondary preventive

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efforts [41].Qing et al in their studyconcluded that baseline IGT was independent risk predictors for cardiovascular morbidity and mortality and for total mortality, which was not confounded by the subsequent development of overt diabetes [42].

The following conclusions of present study were drawn-the prevalence of abnormal glucose tolerance test was high in hypertensive subjects, especially those who have moderate to severe hypertension, elderly population, females, higher cholesterol level, abnormal WHR, have history of habitual addiction, non-vegetarian dietary habits, have urban life style are indulged in sedentary jobs, have a family history of diabetes and have ECG abnormalities (left ventricular hypertrophy). So testing for IGT should be carried out frequently in these individuals.

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