To Study Cardiac Sympathetic Autonomic Dysfunction in Patients with Metabolic Syndrome

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Abstract: *Introduction: Autonomic neuropathy in metabolic syndrome can cause disturbances in the function of cardiovascular, gastrointestinal, and genitourinary systems. Cardiac autonomic neuropathy results from damage to the autonomic nerve fibers to the heart. Metabolic syndrome and its association with cardiovascular autonomic neuropathy is an overlooked but important subject and known to be associated with a disability in coping with daily activities, a wide spectrum of cardiovascular problems and predicting cardiovascular mortality . Materials and methods: A case control study at a tertiary healthcare hospital. The study was conducted. A total 50 cases were included in the study satisfying the inclusion criteria , 50 subjects of age and sex matched; not satisfying IDF criteria of metabolic syndrome were selected for the study as control. Results: In present study of 100 samples the distribution of prevalence of cardiac sympathetic dysfunction differs significantly between two study groups (P-value<0.05). Significantly higher proportion of subjects from Cases group(16 out of 50 - 32%) had higher prevalence of dysfunction compared to the subjects from Controls group (6 out of 50 - 12%) (Pvalue<0.05). Conclusion: Metabolic syndrome unfavorably affects the cardiac autonomic function by causing sympathovagal imbalance with augmented sympathetic activity.*

Keywords: metabolic syndrome, autonomic dysfunction, sympathetic dysfunction, cardiac

1. Introduction

Metabolic syndrome and its association with cardiovascular autonomic neuropathy is an overlooked but important subject and known to be associated with a disability in coping with daily activities, a wide spectrum of cardiovascular problems and predicting cardiovascular mortality [1]. Metabolic syndrome (MetS), also known as the cardio metabolic syndrome, is a medical disorder that consists of a complex combination of abdominal obesity, hypertension, impaired glucose tolerance and dyslipidemia [2, 3]. Compared with healthy population, people with MetS have a five-fold greater risk of developing type 2 diabetes [4], twice as likely to develop CVD [5], three times as likely to have a heart attack or stroke [6].

The exact pathogenesis of cardiovascular autonomic neuropathy associated with metabolic syndrome is not fully understood and it is likely that cardiovascular autonomic neuropathy is of multifactorial origin [7]. Thus, there is a special interest to investigate cardiovascular autonomic neuropathy in obese patients, pre-diabetic conditions and in risk groups of Type 2 diabetes, such as in persons with impaired glucose tolerance, most of whom also have the metabolic syndrome.

Heart rate variability (HRV) is a non – invasive test which is used to detect the cardiac autonomic functions and it predicts mortality from cardiovascular disease [8]

Autonomic dysfunction is a broad term that describes any disease or malfunction of the autonomic nervous system. Autonomic neuropathy in metabolic syndrome can cause disturbances in the function of cardiovascular, gastrointestinal, and genitourinary systems. Cardiac autonomic neuropathy results from damage to the autonomic nerve fibers to the heart and the earliest indicator of cardiac autonomic neuropathy is a decrease in heart rate variation (HRV) during deep breathing [9-11]. Cardiac autonomic dysfunction caused by metabolic syndrome, includes postural orthostatic tachycardia syndrome (POTS), inappropriate sinus tachycardia (IST), neuro-cardiogenic syncope (NCS). Clinical features of autonomic neuropathy in metabolic syndrome are not often seen, although it has been suggested that subclinical signs may be present. As per current knowledge, prevalence of cardiovascular autonomic neuropathy has not been systematically examined in persons with metabolic syndrome and only few studies have evaluated autonomic dysfunction or its correlates within this high-risk group.

2. Materials and Methods

A case control study at a tertiary healthcare hospital. The study was conducted after formal approval from institutional ethics committee. Cases and controls as mentioned below: CASES- A total 50 cases were included in the study satisfying the inclusion criteria i.e. age >20 years, of both sex and satisfying criteria of International Diabetic Federation (IDF) attending IPD (In Patient Department). CONTROLS- 50 subjects of age and sex matched; not satisfying IDF criteria of metabolic syndrome were selected for the study as control. Informed consent was taken from all the patients and complete secrecy of information was maintained.

Inclusion criteria:
Patients aged between > 20 years of both sex
International Diabetic Federation (IDF) criteria for metabolic syndrome

Exclusion criteria:
Not willing to participate in the study
Hypo and Hyperthyroidism

Nephrotic syndrome
Coronary heart disease
Pregnancy
Chronic renal failure
Polycystic ovary syndrome liver disease/ Ascites due to any cause
Cushing's disease
Taking medications known to influence lipid profile, B.P., cardiac autonomic function and plasma glucose.

3. Methodology and data collection

Data were collected from the participants after giving detailed explanation about the procedure and their cooperation and willingness was obtained with written informed consent. The diagnostic criteria for metabolic syndrome were according to the new International Diabetes Federation (IDF) criteria.

According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:
1) Central obesity (defined as waist circumference* with ethnicity specific values) (For Indian: Male ≥ 90 cm & Female ≥ 80 plus any two of the following four factors
2) Raised TG level : cm) ≥ 150 mg/dL
3) Reduced HDL C holesterol :< 40 mg/dL (1.03 mmol/L) in males & < 50 mg/dL (1.29 mmol/L) in females
4) Blood Pressure: Systolic BP ≥ 130 or Diastolic BP ≥ 85 mm Hg or treatment of previously diagnosed hypertension
5) Raised Fasting Plasma Glucose (FPG) (FPG) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes If above 5.6 mmol/L or 100 mg/dL

All subjects underwent anthropometric assessment such as measurement of height, weight, body mass index (BMI), waist circumference (WC), and measurement of blood pressure using standard protocols and automated electronic devices. Height and weight were recorded to the nearest 1 cm and 0.1 kg while participants were wearing light indoor clothing without shoes. BMI was calculated as weight divided by height squared (kg/m2).

Complete hemogram with total leucocyte count and differential leucocyte count ☐ Urine routine and microscopic examination ☐ Blood glucose levels fasting and post prandial ☐ Kidney function tests blood urea and Serum creatinine ☐ Liver function tests

Profile including serum triglycerides, serum cholesterol, high density lipoprotein-C, and low density lipoprotein-c. ☐ T3, T4, TSH if indicated

Cardiac autonomic functions were assessed by the following cardiac autonomic function tests
1. Deep breathing test:
2. Valsalva maneuver
3. Sustained handgrip test
4. Cold pressor test
5. Active Standing (Orthostatic Test)
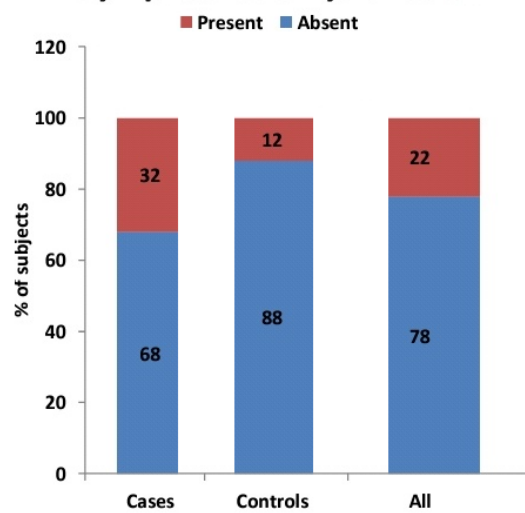
Graph 16: Distribution of prevalence of cardiac sympathetic dysfunction across two study groups.

Criteria for labeling patients with autonomic dysfunction:

A **normal** test was defined as heart rate variation during deep breathing ≥15 beats/min and deep breathing expiratory to inspiratory R-R ratio (E: I ratio) ≥1.21, Valsalva ratio ≥1.21, Sustained handgrip test DBP ≥16 mm of mercury, Cold pressor test DBP ≥10, SBP response to standing ≤10 mm of mercury and 30:15 ratio R-R ratio on standing ≥1.04.

An **abnormal** test was defined as heart rate variation during deep breathing <10 beats/min and (E: I ratio) <1.21, Valsalva ratio <1.21, Sustained handgrip test DBP ≤10 mm of mercury, Cold pressor test DBP <10, SBP response to standing ≥30 mm of mercury and 30:15 ratio R-R ratio on standing ≤1.0 respectively [129].

Resting Heart Rate: Normal- 60 to 100 beats/min. Abnormal: > 100 beats/min (for parasympathetic dysfunction) or < 60 beats/min (for sympathetic dysfunction)

Patients were defined as having dysfunction of both PNS and SNS [129] if: 1. Valsalva ratio was abnormal. 2. The result of any test of PNS test was abnormal and that any test of SNS was borderline. 3. The result of any test of PNS and SNS was abnormal.

Table 24: Distribution of parameters of cardiac sympathetic dysfunction across two study groups

Parameters		Cases (n = 50)		Controls (n = 50)		All (n = 100)		P-value
		n	%	n	%	n	%	Cases Vs Controls
Resting Heart Rate	Normal	42	84.0	46	92.0	88	88.0	0.218^{NS}
	Abnormal	8	16.0	4	8.0	12	12.0	
Handgrip Test	Normal	41	82.0	48	96.0	89	89.0	0.025*
	Abnormal	9	18.0	2	4.0	11	11.0	
Cold Pressor Test	Normal	45	90.0	47	94.0	92	92.0	0.461^{NS}
	Abnormal	5	10.0	3	6.0	8	8.0	
Orthostatic Test	Normal	44	88.0	49	98.0	93	93.0	0.050*
	Abnormal	6	12.0	1	2.0	7	7.0	
Cardiac Sympathetic Dysfunction	Absent	34	68.0	44	88.0	78	78.0	0.016*
	Present	16	32.0	6	12.0	22	22.0	

Values are n (% of subjects), P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. * P-value$\leq$0.05, ***P-value<0.01, NS-Statistically non-Significant.

4. Results

In present study of 100 samples the distribution of prevalence of cardiac sympathetic dysfunction differs significantly between two study groups (P-value<0.05). Significantly higher proportion of subjects from Cases group (16 out of 50 - 32%) had higher prevalence of dysfunction compared to the subjects from Controls group(6 out of 50 - 12%) (Pvalue<0.05).

It was found that there was significant correlation between occurrence of sympathetic dysfunction and metabolic syndrome.

5. Discussion

Among patients of metabolic syndrome, prevalence of cardiac sympathetic dysfunction was 32% and in control group it was 12%. Similarly prevalence of parasympathetic cardiac dysfunction in patients with metabolic syndrome was 36% and in control group it was 12%.

6. Conclusion

Metabolic syndrome unfavorably affects the cardiac autonomic function by causing sympathovagal imbalance with augmented sympathetic activity.

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