

Metabolic Syndrome and its correlates in Type 2 Diabetes Mellitus

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Abstract

Insulin resistance and/or diabetes are an integral component of metabolic syndrome. Diabetes with metabolic syndrome is associated with an increased risk for cardiovascular morbidity and mortality. Concurrence of the two poses an increased risk of diabetic microvascular complications; though few studies have not shown a positive correlation. Hence the study was carried out to investigate the association between the two entities. This hospital based cross-sectional study was carried out at a tertiary care centre. Consecutive type 2 Diabetics meeting the inclusion criteria were included in the study. Detail history, clinical examination (anthropometry, screening for diabetic complications) and laboratorial investigations were done in all study subjects. Data was analyzed using Chi square and student's 't' test. Total 59 type 2 Diabetic subjects were included in the study. 86.44% patients had metabolic syndrome. Significantly more patients with MS had coronary heart disease ($p=0.0011$), whereas the microvascular complications were not significantly different in the two groups ($p>0.05$). 86.44% diabetic subjects amongst the study group had MS. Presence of MS in type 2 diabetes is a risk indicator of coronary heart disease. Chronic microvascular complications occur in diabetics irrespective of the presence of MS.

Keywords: Type 2 Diabetes, Metabolic Syndrome, Complications.

Introduction

The metabolic syndrome (MS) is a distinct pathobiological entity characterized by Insulin resistance, hypertension, atherogenic dyslipidemia (high Triglycerides and/or low HDL cholesterol) and central obesity. Since the time it was first described, various definitions have been proposed and revised from time to time.⁽¹⁻³⁾ Insulin resistance/hyperinsulinemia remains the core biologic entity in all the definitions.⁽⁴⁾ MS with or without Diabetes is a predictor of coronary heart disease (CHD); the simultaneous presence of both the entities predisposes the individual for increased CHD risk and premature mortality.⁽⁵⁻⁷⁾ Furthermore, presence of MS in diabetic patients is a risk indicator of chronic microvascular complications.^(5-6,8-10) There are, however few studies which have shown a negative association between presence of MS and microvascular complications in diabetics.⁽¹¹⁻¹²⁾ Thus detection of MS in type 2 diabetes can be used as a simple, safe and non-invasive tool to predict CHD and/or microvascular complications.

Hence the present study was undertaken to determine the rate of occurrence of MS in type 2 Diabetes and to investigate the association of MS with the various complications in Diabetes.

Material and Methods

The present study was a hospital based cross-sectional study carried out at a tertiary care centre, initiated after approval by the Institutional Ethics Committee. Consecutive type 2 Diabetic subjects willing to participate in the study were included in the study after informed consent. Detailed history and clinical examination was done in all the study subjects.

Patients already receiving lipid lowering drugs and unwilling to participate were excluded. Patients with clinical suspicion of hypothyroidism were also excluded.

The various parameters studied were duration of Diabetes, weight, height, BMI, waist circumference, waist: hip ratio, blood pressure, HBA1c, fasting lipid profile, fundus examination and urine for proteinuria. Weight (in Kg) was recorded in light clothes without shoes, waist circumference was measured mid-way between the lower costal margin and, hip circumference was measured as the greatest distance at the hip. Hypertension was defined as blood pressure more than 130/85 mm Hg or already on treatment of hypertension. Waist circumference ≥ 90 cm in males and ≥ 80 cm in females; WHR ≥ 0.90 in males and ≥ 0.85 in females was considered abnormal. Fasting and Post meal:-done by GOD/POD method (with the kit manufactured by Bio In-vitro Diagnostic Pvt. Ltd. Fasting lipid profile was done in all subjects after an overnight fast of 8-10 hours. HDL - Cholesterol and HDL-cholesterol sub fractions were measured by serial precipitation Method of (Nilson and Ekiman, 1977) using dextran sulphate and Magnesium chloride. Triglyceride levels were measured by GPO-POP method.

All subjects were screened for CHD, Diabetic retinopathy, Diabetic nephropathy and Diabetic neuropathy. CHD was diagnosed based on history of chest pain and/or ECG changes suggestive of ischemia/infarction. Fundus examination was done in all patients by a trained Ophthalmologist to detect proliferative and/or non-proliferative Diabetic retinopathy. Neuropathy was defined as presence of clinical symptoms and signs of neuropathy (hyposthesia/anesthesia/absent ankle

jerks). Nephropathy was diagnosed by doing urine analysis by dipsticks. MS was diagnosed according to IDF criteria.⁽³⁾ Since all the patients were diabetics, MS was diagnosed if they had any two of the following – increased waist circumference (> 90 cm in males, >80 cm in females), hypertension (>130/85 mm of Hg), increased triglycerides (>150 mg) and reduced HDL cholesterol (< 40 in males, <50 in females). Data was analyzed using Chi square and student's 't' test.

Results

Total 59 diabetic subjects meeting the inclusion criteria were included in the study. There were 33 males and 26 females; the male: female ratio was 1.27:1. Maximum (69.49%) subjects were in the age group 50-69 years, irrespective of the gender (Table 1).

Table 1: Age and gender distribution of study subjects

| Age(years) | Gender (n=59) | | Total (n/%) |
|------------|---------------|------|-------------|
| | Female | Male | |
| <40 | 0 | 1 | 1(1.69) |
| 40-49 | 5 | 6 | 11(18.64) |
| 50-59 | 12 | 10 | 22(37.29) |
| 60-69 | 7 | 12 | 19(32.20) |
| ≥70 | 2 | 4 | 6(10.17) |
| Total | 26 | 33 | 59(100) |

51 (86.44%) of the 59 subjects had MS. The proportion of subjects with MS increased upto 60 years after which a decline in the number was seen (Table 2). The duration of diabetes in the study group ranged from newly detected diabetics upto 15 years. None of the subjects had duration more than 15 years. An attempt was made to compare the presence of MS with the

duration of diabetes and it was found that the proportion increased with an increase in the duration of diabetes (76.67%, 90.91% and 100% patients with duration less than 5, 5-10 and more than 10 years respectively) (Table 3).

Table 2: Distribution of study subjects according to presence of MS

| Age (years) | MS (n=59) | |
|--------------|--------------|---------------|
| | Absent (n/%) | Present (n/%) |
| <40 (n=1) | 1(1.69) | 0(0) |
| 40-49 (n=11) | 2(3.39) | 9(15.25) |
| 50-59 (n=22) | 3(5.08) | 19(32.20) |
| 60-69 (n=19) | 1(1.69) | 18(30.51) |
| ≥70 (n=6) | 1(1.69) | 5(8.47) |
| Total () | 8(13.56) | 51(86.44) |

Table 3: Distribution of diabetic subjects with MS according to duration of Diabetes

| DM Duration (years) | MS | |
|---------------------|--------------|---------------|
| | Absent (n/%) | Present (n/%) |
| 0-5 (n=30) | 7(23.3) | 23(76.67) |
| 5.1-1 (n=11) | 1(9.09) | 10(90.91) |
| 10.1-15 (n=4) | 0(0) | 4(100) |
| Total (n=59) | 8(100) | 51(100) |

On studying the various characteristics of subjects with and without MS, significant differences were found only for systolic blood pressure (p=0.009), and triglycerides (p=0.017). Glycated hemoglobin (p=0.062) and systolic blood pressure (p=0.073) also showed significant difference though it failed to reach statistically significant proportions (Table 4).

Table 4: Mean values of various characteristics in study subjects with and without MS

| Parameter | MS | Mean value | Standard deviation (±) | Standard Error mean | t value | p value |
|--------------------------|---------|------------|------------------------|---------------------|---------|---------|
| Age (years) | Present | 57.69 | 8.901 | 1.246 | 1.494 | 0.141 |
| | Absent | 52.38 | 12.094 | 4.276 | | |
| Duration of DM (years) | Present | 4.22 | 3.443 | 0.482 | 1.469 | 0.147 |
| | Absent | 2.38 | 1.923 | 0.680 | | |
| BMI (Kg/m ²) | Present | 23.74 | 2.7603 | 0.3865 | 1.826 | 0.073 |
| | Absent | 21.81 | 2.928 | 1.0352 | | |
| WHR | Present | 0.956 | 0.0827 | 0.01158 | 1.322 | 0.191 |
| | Absent | 0.914 | 0.0835 | 0.0295 | | |
| SBP(mm of Hg) | Present | 137.18 | 13.654 | 1.912 | 2.686 | 0.009 |
| | Absent | 123.25 | 13.477 | 4.765 | | |
| DBP(mm of Hg) | Present | 84.35 | 8.330 | 1.166 | 84.35 | 8.330 |
| | Absent | 76.75 | 7.851 | 2.776 | | |
| FBS (mg/dl) | Present | 192.51 | 151.004 | 21.145 | 0.454 | 0.652 |
| | Absent | 167.88 | 55.355 | 19.571 | | |
| PMBS(mg/dl) | Present | 257.49 | 75.947 | 10.635 | - | 0.208 |
| | Absent | 296.75 | 111.378 | 39.378 | | |

| | | | | | | |
|------------------------|---------|--------|--------|--------|-------|-------|
| HbA1c | Present | 8.51 | 1.286 | 0.180 | - | 0.062 |
| | Absent | 9.50 | 1.852 | 0.655 | 1.903 | |
| Total cholesterol (mg) | Present | 178.73 | 37.397 | 5.237 | - | 0.618 |
| | Absent | 185.88 | 38.294 | 13.539 | 0.501 | |
| HDL cholesterol (mg) | Present | 42.41 | 7.108 | 0.995 | - | 0.135 |
| | Absent | 47.13 | 13.506 | 4.775 | 1.517 | |
| TG (mg) | Present | 164.10 | 49.357 | 6.911 | 2.454 | 0.017 |
| | Absent | 120.38 | 21.948 | 7.760 | | |
| LDL cholesterol (mg) | Present | 87.59 | 37.721 | 5.282 | 0.767 | 0.446 |
| | Absent | 98.50 | 35.096 | 12.408 | | |

BMI – Body mass Index, WHR – Waist: Hip ratio, SBP – Systolic blood pressure, DBP – Diastolic blood pressure, FBS – Fasting blood sugar, PMBS – Post meal blood sugar

The association between the presence of diabetic complications and MS was studied and it was found that the presence of MS was a significant indicator of only CHD (p value = 0.0011) whereas MS was not significantly associated with other diabetic complications like diabetic nephropathy, neuropathy and retinopathy (p value 0.99, 0.478 and 0.99 respectively)(Table 5).

Table 5: Table showing association of MS with diabetic complications

| Complications | | MS | | 'P' value |
|---------------|----------------|--------------|----------------|-----------|
| | | Absent (n=8) | Present (n=51) | |
| Nephropathy | Absent (n=41) | 6 | 35 | 0.99 |
| | Present (n=18) | 2 | 16 | |
| Retinopathy | Absent (n=48) | 7 | 41 | 0.99 |
| | Present (n=11) | 1 | 10 | |
| Neuropathy | Absent (n=46) | 5 | 41 | 0.478 |
| | Present (n=13) | 3 | 10 | |
| CHD | Absent (n=57) | 57 | 0 | 0.0011 |
| | Present (n=2) | 0 | 2 | |

Discussion

The present study reveals a very high rate (86.44%) of occurrence of MS. Though the reported prevalence of MS in general population is 19.5%,⁽¹³⁾ its prevalence in type 2 diabetes is much higher. Similar high prevalence rates have been described by previous studies. Song et al found a prevalence rate of 93.1% by IDF criteria and 90.1% by NCEP ATP III criteria.⁽¹⁴⁾ Other studies have observed a varying rate from 66.2% to 73.3%.^(5,9,15) Varying definitions of MS and different ethnicities are the probable causes of this wide variation in the prevalence rates.

In the present study, the proportion of diabetic subjects with MS decreased with increasing duration. Raman R et al observed a similar trend but observed a

gender difference (only males were noted to have this trend).⁽⁹⁾ Shimajiri et al⁽⁸⁾ and Ghani et al⁽¹⁶⁾ also noticed a decreased prevalence of MS with increased duration of diabetes. The possible reason for this trend was suggested to be decreased BMI as a result of successful interventions for lifestyle modification. However Song et al⁽⁵⁾ and Bonadonna et al⁽¹⁴⁾ in their study found positive relation between duration of disease and prevalence of MS.

Amongst the various complications of diabetes, MS was found to be significantly associated with only CHD (p=0.0011) whereas its presence was not found to be significantly associated with microvascular complications (p>0.05). Significant positive correlation of MS with CHD has been shown in previous hospital as well as population based studies.^(5,7,17-18) MS being a congregation of various cardiometabolic risk factors confers an increased risk for CHD. As for the microvascular complications, no significant association between MS and the complications was observed in the present study. This observation is similar to that observed by earlier studies.⁽¹¹⁻¹²⁾ However many other studies have shown a positive correlation between the two.^(5,7-10,18)

Conclusion

In the present hospital based study, 86.44% diabetic subjects had MS. MS did not show significant correlation with duration of diabetes. Whereas MS in type 2 diabetes does not predict microvascular complications, it is a risk indicator of CHD. Since CHD is a major cause of morbidity and mortality in type 2 diabetes, early suspicion and intervention in the form of modification of the various risk factors responsible for CHD would be beneficial to the patients. Diabetics with MS should be screened for the presence of MS and focused and robust counseling for lifestyle modification in this subset of population is needed.

Limitations

The present study is a hospital based study. However, its small sample size is undoubtedly its major limitation. Further, the definitions of various diabetic

complications probably underestimate the prevalence of these complications.

References

1. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 1988;37:1595–1607.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486–2497.
3. Alberti KG, Eckel RH, Grundy SM. Harmonizing the MS: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-1645.
4. Paresh D, Ahmad A, Ajay C, Priya M, Rajesh G. MS :A Comprehensive Perspective Based on Interactions Between Obesity, Diabetes, and Inflammation. *Circulation* 2005,111:1448–1454.
5. Metascreen Writing Committee, Bonadonna RC, Cucinotta D, Fedele D, Riccardi G, Tiengo A: The MS is a risk indicator of microvascular and macrovascular complications in diabetes: results from Metascreen, a multicenter diabetes clinic-based survey. *Diabetes care* 2006,29:2701-07.
6. Cheng Y, Zhang H, Chen R, Yang F, Li W. Cardiometabolic Risk Profiles Associated with Chronic Complications in Overweight and Obese Type 2 Diabetes Patients in South China. *PLoS ONE* 9(7): e101289.
7. Isomaa B, Henricsson M, Almgren P, Tuomi T, Taskinen MR, Groop L. The MS influences the risk of chronic complications in patients with type II diabetes. *Diabetologica* 2001,44:1148-54.
8. Abdul-Ghani M, Nawaf G, Nawaf F, Itzhak B, Minuchin O, Vardi P. Increased prevalence of microvascular complications in type 2 diabetes patients with the MS. *Isr Med Assoc J* 2006,8:378-82.
9. Raman R, Gupta A, Pal SS. Prevalence of MS and its influence on microvascular complications in the Indian population with Type 2 Diabetes Mellitus. *Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS, report 14). Diabetology and MS* 2010 2:67. doi:10.1186/1758-5996-2-67.
10. Pang C, Jia L, Hou X, Gao X, Liu W, Bao Y, et al. The Significance of Screening for Microvascular Diseases in Chinese Community-Based Subjects with Various Metabolic Abnormalities. *PLoS ONE* 2014;9(5):e97928. doi:10.1371/journal.pone.0097928.
11. Iwasaki T, Togashi Y, Ohshige K. Neither the presence of MS as defined by the IDF guideline nor an increased waist circumference increased the risk of microvascular nor macrovascular complications in Japanese patients with type 2 Diabetes. *Diabetes Res Clin Pract* 2008;79(3):427-32. doi: 10.1016/j.diabres.2007.10.035.
12. Carole AC, Christine CJ, Retnakaran R. Impact of the MS on Macrovascular and Microvascular Outcomes in Type 2 Diabetes Mellitus United Kingdom Prospective Diabetes Study 78. *Circulation* 2007;116:2119-2126.
13. Sawant A, Mankeshwar R, Shah S, Raghavan R, Dhongde G, Raje H, et al. Prevalence of metabolic syndrome in urban India. *Cholesterol* 2011;2011:920983.
14. Song SH and Hardisty CA. Diagnosing metabolic syndrome in type 2 diabetes: does it matter? *Q J Med* 2008; 101:487–491. doi:10.1093/qjmed/hcn034.
15. Jacob B, George AT, Antony TP, Jose R, Sebastian SR. Prevalence of metabolic syndrome in newly detected type 2 diabetes mellitus. *Academic Medical Journal of India* 2015 Mar 29;3(1):8-12.
16. Shimajiri Y, Tsunoda K, Furuta M, Kadoya Y, Yamada S, Nanjo K, et al. Prevalence of metabolic syndrome in Japanese type 2 diabetic patients and its significance for chronic vascular complications. *Diabetes Res Clin Pract* 2008,79:310-7.
17. Cheng Y, Zhang H, Chen R, Yang F, Li W. Cardiometabolic Risk Profiles Associated with Chronic Complications in Overweight and Obese Type 2 Diabetes Patients in South China. *PLoS ONE* 2014; 9(7): e101289. doi:10.1371/journal.pone.0101289.
18. Bonora E, Targher G, Formentini G, Calcaterra F, Lombardi S. The Metabolic Syndrome is an independent predictor of cardiovascular disease in Type 2 diabetic subjects. Prospective data from the Verona Diabetes Complications Study. *Diabet Med* 2004;21:52–58.