Original Article

Prevalence of Metabolic Syndrome in renal transplant recipients — a single centre experience

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Abstract

Objective: To determine the prevalence of metabolic syndrome (MS) in renal transplant recipients (RTR) using the modified Asian National Cholesterol Education Programme-Adult Treatment Panel III (NCEP-ATP III) criteria.

Methods: A cross-sectional study was conducted on 200 RTRs between January 2008 - August 2008. All were more than six months post transplant and above 18 years of age. Subjects with pre-transplant diabetes or New Onset Diabetes Mellitus after renal transplantation, with overt infections, dyslipidaemia or on lipid lowering medication and taking immunosuppressive drugs of the target organ inhibitor group as rapamycin, were excluded. The prevalence of MS was determined using the (NCEP-ATP III) criteria modified for Asians which includes waist circumference, triglycerides, HDL cholesterol, blood pressure and fasting blood glucose.

Results: Of the 200 recipients studied, 87 (43.5 %) had MS. There were 58 (39.4 %) males and 29 (54.7 %) females which shows female predominance. The mean age of the MS group was more then that of the non MS group ($p<0.0001$). Hypertension and New Onset Diabetes Mellitus were prevalent more in MS group ($p<0.001$ and $p<0.0001$ respectively). Mean serum creatinine was higher in MS group but there was no significant difference.

The prevalence of MS was 4.5% in the first twelve months, with a rise in this figure to 41.3% between one to five years after transplantation.

Conclusion: There is a high prevalence of MS in Renal Transplant Recipients specifically after one year of transplantation (JPMA 59:533; 2009).

Introduction

Metabolic Syndrome (MS) represents a constellation of metabolic derangement including central obesity, glucose intolerance, hyperinsulinaemia, low high density lipoprotein (HDL) cholesterol, high triglycerides (TG) and hypertension (HTN).[1] It represents a complex interaction among various genetic, environmental and metabolic factors interconnected by energy homeostasis pathways. Obesity is considered the phenotypic hallmark of MS that contributes to insulin resistance, hyperinsulinaemia and dyslipidaemia.

The prevalence of MS is continuously increasing in the general population[2] but its prevalence and consequences after renal transplantation are not well established. It has been universally recognized that MS is a known cardiovascular risk factor in the general population[3] and cardiovascular disease (CVD) is the leading cause of mortality in renal transplant recipients.[4] A community based population study demonstrated that established CVD risk factors are associated with the development of new onset kidney disease.[5]

Recently, both obesity and MS have been suggested to participate in the pathogenesis of renal disease[6] as well as chronic allograft nephropathy.[7] Another study showed that MS is a prominent risk factor for New Onset Diabetes Mellitus (NODM), chronic graft dysfunction, graft loss and patients death in RTR.[8] These reports suggest that MS may be a risk factor of renal dysfunction and CVD not only in general population but also in RTR. In addition, in the general population, the prevalence of MS differs widely among ethnic groups and according to the definition of MS used.[9] As the original cut-off values for abdominal obesity in the NCEP definition was considered inappropriate for the Asian population and the number of subjects who actually met these criteria was extremely low,[10] so experts modified the cut-off limits for Asians.[11]

To the best of our knowledge there is no published study on the prevalence of MS in the Pakistani RTR. The present study investigated the prevalence of MS in renal transplant Recipients using the modified Asian (NCEP-ATP III) criteria.

Methods

This was a cross-sectional study on 200 living-related primary renal transplant recipients, conducted at Sindh Institute of Urology and Transplantation (SIUT) between January 2008 and August 2008. The selection criteria were, age more than 18 years and the period of transplantation more than six months.

Patients with pre-transplant diabetes or NODM developing within six months of transplant, dyslipidemia diagnosed and treated with lipid lowering drugs prior to transplant, were excluded. Patients with overt infection or on immunosuppressive drugs of the target organ inhibitor group as rapamycin, were also excluded.

For analysis purposes, recipients were stratified into two categories with / without MS based on modified NCEP- ATP III criteria for Asians.[11] All recipients were on triple immunosuppressive therapy with either tacrolimus or cyclosporine, azathioprine or mycophenolatemofetil and prednisolone. As all were more than six months post transplant, they were taking the maintenance dose of steroids (i.e.0.07-0.1/mg/kg/day of prednisolone). All patients gave informed consent for participation in the study, which had already been approved by the Ethical Review Board of SIUT.

Diagnostic criteria for MS:

The diagnosis of MS was made according to the National Cholesterol Education Program- Adult Treatment Panel III (NCEP ATP III) criteria.[11,12] The five thresholds used were:(i) serum Triglyceride (TG) level >150mg/dl or specific treatment for this lipid abnormality, (ii) serum high density lipoprotein (HDL) — cholesterol level <40mg/dl in men or <50mg/dl in women or specific treatment for this lipid abnormality, (iii) systolic blood pressure (SBP) more than 130 mmHg and diastolic blood pressure (DBP) more than 85 mmHg or use of antihypertensive medication, (iv) fasting plasma glucose level >100 mg/dl or use of antidiabetic medication, and (v) Waist girth >90 cm for men and >80 cm for women (modified NCEP- ATP III criteria for Asians).

Subjects who had three or more of the risk factors were judged as having MS (MS group), and subjects who had two or less risk factors were judged as not having MS (non-MS group).

Measurements:

Subjects were called at 8:00am after a 12-14 hour overnight fast and blood samples were drawn to determine serum creatinine, triglycerides, HDL cholesterol and plasma glucose concentrations. Blood pressure was reported as the average of three automated measurements taken at 3-minutes intervals.

Hypertension was defined by (i) the administration of antihypertensive agents and/or a history of this disorder; (ii) a systolic blood pressure more than 130 mmHg; or (iii) a diastolic blood pressure more than 85 mmHg.

NODM was defined as a fasting glucose of more than 126mg/dl on two occasions at any time after transplantation or associated with use of oral hypoglycemic agents and/or insulin, in patients with no prior history of diabetes. Weight was measured by the weighing machine which was daily calibrated by a weight of 5 kg, with the subject in light clothing. Height was measured by a scale fitted on the wall and the subject standing without shoes. BMI was calculated by the formula weight in kg / height in m2.

Waist circumference was determined by using a non-stretchable measuring tape midway between the iliac crest and costal margin.

Blood samples were processed on auto - analyzer for estimating HDL, TG, Serum creatnine and blood sugar.

The data was entered in the SPSS Software (Statistical package for the Social Sciences, version 10.0).All data were presented as the mean +/- SD. Differences between groups were compared with Student's t-test. Chi- square was used to compare categorical variables. A p value of < 0.05 was considered statistically significant.

Results

Table-1 shows the demography and transplant characteristics of renal transplant recipients with/ without MS. Using modified (Asian) NCEP ATP III criteria, a total of 87 (47.5%) of 200 patients had MS. The mean age group of the MS group was older than that of the non- MS group ($p < 0.0001$).HTN and NODM were prevalent in MS group ($p < 0.001$ and $p<0.0001$ respectively). Body mass index

Table-1: Demographic and Transplant Characteristics of patients with/without Metabolic Syndrome by modified (Asian) NCEP-ATP III Criteria.

	Metabolic Syndrome N=87 (43.5%)	Non-Metabolic Syndrome n=113 (56.5%)	P value
Age (years)	38.52 +/- 10.83	31.35 +/- 9.30	<0.0001
Male/Female	58/29	89/24	NS
NODM (No.)	18	2	<0.0001
S. Creatinine (mg/dl)	2.06 +/- 1.70	1.76 +/- 1.05	NS
Time from Transplant (Months)	63.56 +/- 42.99	58.36 +/- 42.99	NS
BMI (wt in kg/ht in Meter square)	24.24 +/- 4.54	20.86 +/- 3.54	<0.0001
Calcineurine Inhibitor CYA (No.)/TAC (No.)	81/4	63/2	NS
Waist Circumference (cm)	94.06 +/- 10.16	81.50 +/- 9.36	<0.0001
Triglyceride (mg/dl)	36.98 +/- 9.96	45.95 +/- 14.69	<0.0001
HDL Cholesterol (mg/dl)	36.98 +/- 9.96	45.95 +/- 14.69	<0.0001
Systolic Blood Pressure	125.38 +/- 19.6	130.43 +/- 94.33	NS
Diastolic Blood Pressure (mm Hg)	79.77 +/- 11.30	77.96 +/- 9.24	NS
Fasting Glucose (mg/dl)	95.80 +/- 24.394	85.29 +/- 8.08	<0.0001
Hypertension (No.)	86	96	0.001

NODM: New Onset Diabetes Mellitus; CyA: Cyslosporine; TAC: Tacrolimus; BMI: Body Mass Index; HDL: High Density Lipoprotien.

Table-2: Percentage of patients with Metabolic Syndromes in different years post transplant (%).

	Total N=200	Non-Metabolic Syndrome n=113	Metabolic Syndrome n=87
> 6 months - 1 years	27	20.35%	4.59%
1-5 years	85	43.36%	41.37%
> 5 years	66	31.80%	34.48%
> 10 years	22	8.84%	13.70%

(BMI) and WC of the MS group greater than that of non-MS group (p=<0.001). Serum triglyceride and fasting blood glucose levels of the MS group were higher than the non-MS group (p<0.0001). Serum HDL cholesterol level of the MS group was lower than that of non-MS group (p<0.0001). Other clinical variables did not differ significantly.

The prevalence of MS in different time frames post-transplant can be seen in Table-2. In the period between 6 months and 1 year the prevalence was 4.5 % whereas this figure rose to 41.37% between one and five years after transplantation.

On analysis of the components of MS, the most common was HTN and least common was hyperglycaemia. Central obesity was significantly more frequent in females (62% vs 40%, p< 0.005). Although hyperglycaemia was more prevalent in males, but was statistically not significant. There was no significant gender difference in the occurrence of other MS components (Table-3).

Table-3: Crude Prevalence of Metabolic Syndrome and its components as defined by Modified (Asians) NCEP-ATP III Criteria.

	Crude Prevalence (%).			
	Total (n=200)	Men (n=147)	Women (n=53)	P value
Central Obesity	92	40.1	62	0.005
Low HDL Cholesterol	117	55.7	66	0.196
High TG	59	28.5	32	0.634
Hypertension	182	92.5	86.7	0.214
Hyperglycaemia	36	21	9.4	0.059
Metabolic Syndrome	87	39.4	54	0.05

HDL: High Density Lipoprotein; TG: Triglyceride.

Discussion

The prevalence of MS in the general population differs widely among ethnic groups and according to diagnostic criteria used. MS among the US general population was found to be 24.1% - 27%[2] according to the original NCEP ATP III criteria. In contrast, the prevalence of MS among Japanese general population was 12.4% by the original NCEP ATP III criteria.[13] Recently, De Varies et al.[7] reported the prevalence of MS among Netherland renal transplant patients using the Original NCEP ATP III criteria. Their study was the first application of a consensus definition of MS to the kidney transplant population.

They reported that 383 (63%) out of 606 Caucasian renal transplant patients had MS. Armstrong et al[4] observed that 45 out of 90 Australian RTRs (50%) had MS by applying the original NCEP ATP III criteria. Porrini et al[8] found that 37.7% of Spanish RTRs had MS by using the modified criteria. These reports suggested that MS is more prevalent in renal transplant recipients as compared to the general population. But there was only a slight difference in the prevalence of MS between Japanese general population and renal transplant patients.[14] This discrepancy may be due to difference in life style, eating habits, or the prevalence and degree of obesity between Japanese and Caucasian population. RTRs are perhaps more compliant to dietary intervention for reducing post - transplant obesity or in using medication for hypertension and dyslipidaemia.

The prevalence of MS among Chinese general population was only 15.1%[9] and a recent study showed that MS was found in a higher percentage in Chinese RTRs as compared to the general population (32%).[15]

Our study showed the prevalence of MS in 43.5% RTRs, by applying the modified NCEP ATP III criteria. Comparing this figure with those of the general population, the results of a single center study were used which reported 35.2% MS among patients attending an outdoor clinic of a teaching hospital[16] according to the original NCEP ATP III criteria and not the modified criteria for Asians. The results of a community based survey in an urban population of Pakistan, using modified NCEP ATP III criteria showed MS to be 49%.[17] This prevalence rate is slightly higher than our study results, probably because the survey subjects were in good health Another probable explanation can be because of the comparatively smaller sample size of our RTRs. These reports suggested that the prevalence of MS in our general population and RTRs is almost the same and overall there is a high prevalence.

Our study revealed that MS was more prevalent in female patients (54.7% Vs 39.4%) which was consistent with the Chinese study[15] and the Spanish study.[8] In contrast both Japanese[14] and Netherland[7] studies showed a male preponderance. This proves that the gender predisposition of MS in RTRs may differ widely among ethnic groups similar to the general population.[9]

In our study, NODM was present more in MS group, which was consistent with the previous report by Porrini et al.[8] Obesity and dyslipidaemia, the components of MS are associated with insulin resistance, the core defect of type 2 diabetes, leading to higher figures of NODM in this

population. Recently two studies from China[15] and Japan[14] also showed a higher prevalence of NODM in MS group.

In our study, body mass index (BMI) and waist circumference (WC) of the MS group were significantly greater than those in the non-MS group. This proves that obesity is a major component of MS in RTRs similar to the general population.

It has been reported recently that MS is a risk factor for renal dysfunction in the general population.[5] Another study showed that MS is a prominent risk factor for chronic graft dysfunction, graft loss and patient's death in RTR.[8] Although the present study is a cross-sectional study, it was observed that mean serum creatinine in MS group was higher than non-MS group but was statistically insignificant. This was consistent with the studies published from China[15] and Japan.[14] There is no single explanation how MS is associated with impaired renal function. Obesity can contribute to renal dysfunction in many ways: excess excretory load, renal sodium retention, hyperinsulinaemia, insulin resistance, or renal lipotoxicity.[18] Obesity may cause worsening of proteinuria in RTRs.[4] Another possibility is that all components of MS directly damage the kidney through renal or systemic atherosclerosis. MS is closely associated with atherosclerotic cardiovascular disease in the general population[3] but there is no evidence that MS is linked to atherosclerotic cardiovascular disease directly in RTR.

In conclusion, the study revealed a high prevalence of MS in RTR especially after 1 year post transplant .

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