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ORIGINAL ARTICLE

MAGNITUDE OF METABOLIC SYNDROME AND ASSOCIATED FACTORS AMONG RENAL TRANSPLANT RECIPIENTS: EXPERIENCE FROM A NEW CENTER, ADDIS ABABA

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ABSTRACT

Introduction: Metabolic syndrome is a cluster of risk factors for cardiovascular diseases. It is also common in renal transplant recipients and is associated with increased risk of graft dysfunction and cardiovascular mortality. Its magnitude is not known in our Ethiopian patients.

Objective: The study is conducted to determine the magnitude of metabolic syndrome and associated factors among renal transplant recipients.

Methods: Analytical cross-sectional design was used. Eighty-seven Ethiopian renal transplant recipients having follow-up at St. Paul Hospital's Millennium Medical College Kidney Transplant Centre were studied from May to July 2018. A structured data collection format was used to collect data. Contextualized "WHO STEPS Instrument for Non-communicable Diseases Risk Factor Surveillance" was utilized for collecting data on behavioral risk factors, biophysical measurements and laboratory tests. The diagnosis of metabolic syndrome was made according to the revised National Cholesterol Education Program-Adult Treatment Panel III criteria. Data were described by frequencies, percentage and mean (\pm SD). Comparative analysis between variables was done using bivariate and multivariate logistic regression. Statistical significance of the prediction was declared at p -value < 0.05 with 95% confidence interval.

Results: Majority 64 (73.6%) of the cases were male patients. Most of them were young with mean (\pm SD) age of 35.8 (\pm 11.9) years. Hypertension was the commonest component of metabolic syndrome accounting for 49 (56.3%) of cases. The magnitude of metabolic syndrome was 34.5%. Only central obesity (P value = 0.046; AOR 39.1 (95% CI 1.1, 141) and hyperglycemia ($P=0.031$; AOR 25.1 (95%CI 1.3, 467.8) were significantly associated with metabolic syndrome.

Conclusion: The magnitude of metabolic syndrome was high in our kidney transplant recipients. However, only waist circumference and hyperglycemia were found to have significant association with metabolic syndrome. Comprehensive preventive strategies should be implemented for management of metabolic syndrome to minimize its impact.

Key Words: Metabolic syndrome, renal transplant, Diabetes Mellitus, Hypertension, Dyslipidemia, Central Obesity.

INTRODUCTION

Metabolic syndrome (MS) is a cluster of risk factors for cardiovascular disease (CVD) that has drawn more clinical attention. It comprises multiple risk factors including abdominal obesity, hypertension, hyperglycemia and dyslipidemia that can occur in different combinations. Different expert panels have provided various definitions for MS to enable a clinical

diagnosis and treatment of patients at risk of associated complications (1-3). Metabolic syndrome is one of the major public health issues globally. World-wide, the prevalence of MS ranges from 10% to 50%. The International Diabetes Federation (IDF) believes that this cluster of factors is driving the twin global epidemics of type 2 diabetes and cardiovascular diseases (4-6).

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Lifestyle changes such as dietary habits, sedentary life and consumption of energy-dense foods that have occurred over the years has led to an epidemic of abdominal obesity, which in turn resulted in dramatic increase in the prevalence of metabolic syndrome. Obesity and obesity mediated MS has been paralleled by escalation in the incidence of chronic kidney disease (CKD) (7, 8). MS is also common in renal transplant recipients. MS has been shown to be an independent risk factor for chronic allograft dysfunction, graft failure, new-onset diabetes, and cardiovascular disease. The development or worsening of obesity plays a central role in the development of metabolic syndrome after kidney transplantation. Risk factors specific to transplant recipients include the duration of pre-transplant dialysis and post-transplant immunosuppression and weight gain. Immunosuppression also plays an important role in the pathogenesis of the individual components of the metabolic syndrome. They should be designed to limit exacerbation of components of the metabolic syndrome (9-15).

The metabolic syndrome is emerging as a significant surveillance target following kidney transplantation. Control of body mass index (BMI), blood glucose and lipid levels, as well as blood pressure, is required to prevent the consequences of the metabolic syndrome. Patients with metabolic syndrome or components of metabolic syndrome need to have complete clinical evaluation and optimal management including screening and treatment of risk factors, comorbidities and expected complications. There are internationally accepted standards of clinical care for such patients. Efforts toward promoting lifestyle modification including healthy diets, physical activity, and blood pressure control must be undertaken (8, 10, 16-21).

Since renal transplantation service was established only two and half years ago, the magnitude of MS in transplant patients in Ethiopia is not known. A better understanding of the magnitude and impact of metabolic syndrome in our transplant patients would help in prevention, early detection, and management of the syndrome as well as its detrimental sequelae of cardiovascular morbidity and mortality.

PATIENTS AND METHODS

A cross-sectional study was conducted from April 15 to July 15, 2018 at St. Paul's Hospital Millennium Medical College (SPHMMC) Kidney Transplant Centre, in Addis Ababa, Ethiopia. The transplant center was established in September 2015, under the Federal Ministry of Health, in collaboration with University of Michigan. The transplant center has a multidisciplinary team involving nephrologists, transplant surgeons, nephrology fellows, a vascular access surgeon, interventional radiologists, psychiatrists, nurses, and other supportive staffs.

A total of 83 patients have been transplanted. Additional 37 patients who were transplanted abroad are also having post-transplant care and follow up in our transplant outpatient clinics. Out of the total (N= 120) patients currently having regular post-transplant treatment and follow in our transplant center, 87 sampled adult (age ≥ 18 years) patients who came for their regular follow-up during the study period were included in the study whether they were transplanted in our center or abroad. Those who were transplanted within three months before the study period were excluded.

Variables of interest for data collection were patients' socio-demographic characteristics, behavioral risk factors; clinical characteristics including BP, weight, height, waist circumference; and laboratory tests including FBS, lipid profile and serum creatinine. A structured data collection format was used to collect data. For collecting data on behavioral risk factors for metabolic syndrome, we used the "*WHO STEPS Instrument for Non-communicable Diseases Risk Factor Surveillance*" with modification and contextualization (22). Data were collected using patient interview, clinical evaluation, and laboratory tests. Data collection tools were standardized and pretested. Data collectors were nephrology fellows and transplant nurses. They were trained by the principal investigator on the objective of the study, the instruments of data collection, and the process of data collection. Laboratory tests were performed by a trained laboratory technologist.

To ensure data quality, the questionnaire, prepared in English, was translated into Amharic and back to English for checking language consistency. Pre-testing was conducted on four patients. Accordingly, gaps and ambiguity were clarified by further discussion, including demonstration and practical session on patient interviewing and anthropometric measurements. Weighing scales and BP measurement apparatus were used for biophysical measurements. They were checked and calibrated every morning and after each measurement for functionality and consistency. Standard laboratory procedures were implemented. The principal investigator assisted and supervised the data collection process.

The collected data was checked for completeness and consistency by crosschecking with the source documents when it was needed. Then it was coded and entered in to study database using EPI Info Data software version 3.1. Then, the data was exported to Statistical Package for Social Science (SPSS) version 21 program for analysis. Continuous observations were expressed as means while categorical observations were described by frequencies and percentages.

Bivariate analysis was done first to select candidate independent variables for the multiple logistic regressions. For those variables whose p-value were > 0.25 on bivariate analysis, multiple logistic regression analysis was done to identify independent predictors of MS. Statistical significance of the prediction was declared at p-value < 0.05 with 95% confidence interval.

Ethical clearance was obtained from SPHMMC ethical review committee. Objectives of the study and procedures of data collection were explained to the study subjects and they gave informed written consent. During the interview, all patients were given a brief description about MS components. They were also advised on preventive strategies.

Patients were diagnosed to have MS if they fulfilled the updated NCEP-ATPIII criteria; i.e. if they have any three of the following five criteria (1-3):

- Waist circumference ≥ 94 cm for male; and ≥ 80 cm for female;
- Systolic BP > 130 mmHg or diastolic BP > 85 mmHg or being on treatment for HPN;
- FBS ≥ 100 mg/dl or being on treatment for DM;
- Fasting HDL ≤ 40 mg/dl for male or ≤ 50 mg/dl for female or being on treatment for dyslipidemias;
- Fasting Triglyceride level ≥ 150 mg/dl or being on treatment for dyslipidemias.

Healthy lifestyle was defined as fulfilling all the following criteria (17-20):

Healthy Diet:

- Regular consumption of fruits and vegetables (daily consumption of at least three servings of vegetables and fruits);
- High intake of cereals, whole grains, poultry, fish, low-fat dairy foods, and vegetable oil;
- Low intake of high calorie foods and fats (butter, fatty meat, honey, sweets, and saturated fat); and
- Low sodium intake (i.e., ≤ 2.4 gm per day);

Healthy physical activity:

- A minimum of 150 min per week of moderate-intensity physical activity continuously done at least for 10 minutes; AND

No habit of cigarette smoking or alcohol drinking.

Graft dysfunction: was defined as stable creatinine level ≥ 1.5 mg/dl at three months or more after transplantation.

RESULTS

Among 120 post renal transplant patients having regular follow up and treatment in our transplant center, 87 were sampled and involved in the study.

Sociodemographic characteristics: Men accounted for 64 (73.6%) of the study sample. The mean age was 35.8 (± 11.9) years, with 78.2% of patients under the age of 45 years (Table 1 and Figure 1).

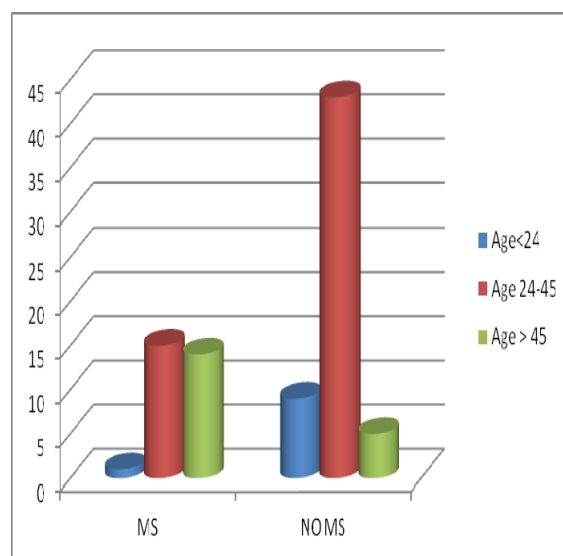


Figure 1: Distribution of metabolic syndrome by age, among transplant recipients at St. Paul's Hospital's Millennium Medical College Transplant Center, July 2018.

Table 1: Socio-demographic characteristics of renal transplant recipients, on follow up at SPHMMC* national transplant center, July 2018.

Sociodemographic Characteristics	Category	Frequency	Percentage (%)
Age	<24 years	10	11.5
	24-45	58	66.7
	>45	19	21.8
Sex	Male	64	73.6
	Female	23	26.4
	Illiterate	1	1.1
Educational status	Can read and write	3	3.4
	Primary Education	10	11.5
	Secondary Education	29	33.3
	Tertiary Education	44	50.6
Occupation	Non-government employee	8	9.2
	Self employed	34	39.1
	Student	6	12.6
	unemployed	30	14.9
Marital status	Single	37	32.5
	Married	46	52.9
	Divorced	3	3.4
	Widowed	1	1.1
Residence	Addis Ababa	63	72.4
	Elsewhere in Ethiopia	24	27.6

Behavioral risk Factors

Diet: Fifty four (62.1%) patients eat three times servings of fruits at least three days a week. The majority, 83 (95.4%), eat 3 times servings of vegetables at least three days a week. All of the patients knew that salt is harmful for health; and 70 (80.5%) of patients consume too little amount of salt in their diet occasionally. Similarly, 72 (82.7%) patients don't use high caloric or fatty diet like fatty meat, butter or sweets. Most, 67 (77%), patients use vegetable oil for cooking while only 18 (20.7%) patients use small amount of butter occasionally. Thirty six (41.4%) patients always consume home prepared meals. Only 14 patients consume more than three meals per week prepared outside home.

Smoking and alcohol: None of the patients currently smoke cigarettes nor drink alcohol. Only 9 (10.3%) patients have past history of smoking. The mean number of cigarettes they used to smoke was 12 per day for a mean duration of 132 (+/- 5.4) months.

Similarly, only 33 (37.9%) have past history of alcohol drinking for a mean duration of 118.6 (+/- 4.7) months.

Mostly they used to drink beer; on average 3-4 bottles of beer per day three days a week. All of them quit smoking and drinking while diagnosed with CKD.

Exercise: Most, 85 (97.7%), of the patients do moderate intensity exercise like walking for at least 150 minutes per week. The mean duration of exercise was 48.6 (+/- 15.7) minutes at least three days a week. Most, 48 (55.2%) of them, do exercise on daily basis. The mean duration spent by patients while sitting or reclining was 5 (+/- 1.6) hours a day with only 8 patients sitting or reclining for ≥ 8 hours (Table 2).

Table 2: Frequency of behavioral risk factors for MS among transplant recipients having treatment follows up at SPHMMC national transplant center, July 2018.

Behavioral Risk Factors	Category	Frequency (N)	Percentage (%)
Current smoking	Yes	0	0.0%
	No	87	100.0%
Currently alcohol drinking	Yes	0	0.0%
	No	87	100.0%
Past history of smoking	Yes	9	10.3%
	No	78	89.7%
Past history of alcohol drinking	Yes	33	37.9%
	No	54	49.1%
Doing moderate intensity exercise like walking for at least 150minutes per week	Yes	85	97.7%
	No	2	2.3%
Consumption of Fruits*	Yes	54	62.1%
	No	33	37.1%
Consumption of Vegetables**	Yes	83	95.4%
	No	4	4.6%
Consumption of fatty foods or high calorie diets	Yes	15	17.3%
	No	72	82.7%

*Patients eat 1-3 times servings of fruits at least 3days a week.

**Patients eat 1-3 times servings of vegetables at least 3 days a week.

Transplant characteristics: Most patients, 64 (73.6%), were transplanted at our transplant center. The rest were transplanted abroad. The underlying cause of the renal failure was not known for a larger proportion of patients, 37 (42.5%). Of the known causes, HPN and DM accounted for 24 (27.6%) and 14 (16%), respectively. Five of the patients were transplanted before starting dialysis. For the rest the mean (\pm SD) duration of dialysis was 12.6 (\pm 11.0) months. The mean (\pm SD) duration since transplantation was 16.6 (\pm 15.5) months.

All of the patients were on maintenance doses of triple immunosuppressive therapy comprising of tacrolimus, mycophenylate mofetil (MMF) and prednisolone except two who were taking cyclosporine instead of tacrolimus and another two taking azathioprin instead of MMF. Only 11 (12.6%) of the patients had graft dysfunction.

Magnitude of Metabolic Syndrome and its Components

Hypertension (HPN): HPN was the commonest component of metabolic syndrome. Forty nine (56.3%) patients were on treatment for HPN of which 33 (67.3%) have good control of their HPN. Eight of the patients became hypertensive after transplantation.

Hyperglycemia: A total of 23 (26.4%) patients have hyperglycemia of which 19 (82.6%) are already diagnosed with DM and on treatment. At base line, only 14 patients had DM as an underlying cause of the renal failure.

Central Obesity: Most, 69 (79.3%) of the patients had normal BMI while only 15 (17.2%) were overweight. Twenty five (28.7%) patients were found to have central obesity with a mean waist circumference of 96cm.

Dyslipidemia: The commonest form of dyslipidemia was low high density lipoprotein (HDL) level occurring in 29 (33.3%) patients followed by high triglyceride, high low density lipoprotein (LDL), and high total cholesterol level each accounting for 25 (28.7%), 21 (24.1%), and 20 (23%) respectively. However, only 3 patients were on lipid lowering treatment.

Magnitude of metabolic syndrome and its components is shown in Figure 2.

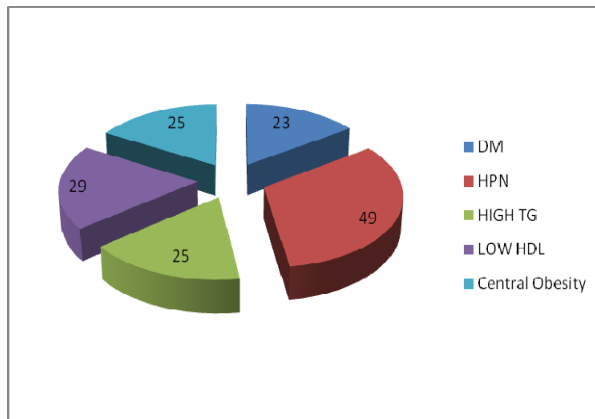


Figure 2: Frequency of Components of metabolic syndrome among transplant recipients having treatment follow up at SPHMMC national transplant center, July 2018.

Magnitude of Metabolic syndrome: According to revised NCEP-ATP III criteria 30 out of 87 patients were found to have metabolic syndrome making the prevalence 34.5%.

Factors associated with MS: Age, past history of smoking, BMI, waist circumference, HPN, DM, dyslipidemia, and creatinine level showed statistically significant association with MS when analyzed with binary logistic regression (P value <0.05).

However, with multiple logistic regression analysis only central obesity (P value=0.046; AOR 39.1 (95%CI 1.1, 141) and hyperglycemia/DM (P=0.031; AOR 25.1(95%CI 1.3, 467.8) were significantly associated with Metabolic syndrome (Table 3).

Table 3: Multivariate logistic regression of components of metabolic syndrome among transplant recipients on follows up at SPHMMC* Transplant Center, July 2018.

Category of Independent Variables		With Outcome Variable (MS)		Without Outcome Variable (No MS)		COR (95% CI)	AOR (95% CI)	P Value
		No	(%)	No.	%			
Waist Circumference	Normal	8	9.2%	54	62.1%	1.0	1.0	0.046
	Above normal	22	25.3%	3	3.4%	49.5 (12.0,204.0)	39.1 (1.1, 141)	
HPN	Yes	4	8.7%	19	41.3%	4.63 (0.48, 45.1)	0.26 (0.012,5.66)	0.391
	No	1	2.2%	22	47.8%	1.0	1.0	
DM	Yes	11	12.6%	53	60.9%	22.9 (6.5, 80.6)	25.1 (1.3, 467.8)	0.031
	NO	19	21.8%	4	4.6%	1.0	1.0	
Low HDL	Yes	10	11.5%	48	55.2%	10.67 (3.8, 30.2)	15.4 (0.867, 273)	0.62
	NO	20	23.0%	9	10.3%	1.0	1.0	
High Triglycerides	Yes	11	12.6%	51	58.6%	14.7(4.8,45.3)	1.47 (0.007, 290.7)	0.886
	NO	19	21.8%	6	6.9%	1.0	1.0	

DISCUSSION

Consistent with other literatures, a majority of our patients (73.6%) were males (23-26). Our patients were younger, with the mean age of 35.8(\pm 11.9) years compared to findings of other similar studies. This can be explained by relatively younger age of our CKD patients and by our transplant center's highly selective criteria.

Even though, most of the patients eat fruits (62.1%) and vegetables (83%) with their diet, the frequency of consumption and the variety are below what is recommended by literature (7, 10, 22, 26). As patients were advised to avoid certain fruits and raw vegetables, particularly during the early months following transplantation, for fear of contamination and food- drug interaction, they tended to continue avoiding fruits and vegetables for several months. Unavailability of a dietician or nutritionist in the center might have contributed to this over-precaution.

Most of our patients restrict or avoid salt (80.5%) and fatty foods or high caloric diets (82.7%), matching recommendations from other studies and WHO for risk reduction for chronic non communicable diseases (7, 10, 12, 22). None of the patients currently smoke cigarettes or drink alcohol. Most (97.7%) of the patients do moderate intensity exercise like walking for a mean duration of 48.6 minutes. The mean duration spent by patients while sitting or reclining was 5hours a day with only eight patients sitting or reclining for \geq 8hrs. These risk reduction behaviors are also in line with literature and WHO recommendations (7, 10, 12, 22).

Of the known underlying causes, HPN and DM accounted for larger proportion of cases consistent with findings worldwide. HPN was the most common component of MS accounting for 56.3% of cases. This finding is comparable with the findings of other similar studies done on MS elsewhere (9, 14, 23-29). Most, 69 (79.3%), of the patients had normal BMI. However, 25 (28.7%), of the study subjects had central obesity. MS was diagnosed in 21(84%) of them. This was expected as central obesity is considered to play a major role in the development of MS. This finding is comparable with the findings of other similar studies (9, 12, 14, 30).

Twenty three (26.4%) patients had hyperglycemia, of which 19 (21.8%) were already diagnosed with DM and were on treatment. At base line, only 14 patients had DM as an underlying cause of the renal failure.

This means nine (10.3%) patients have developed hyperglycemia after transplantation five of which had already started treatment for new onset diabetes after transplantation (NODAT). This can be as a result of the immunosuppressive regimens. This finding is comparable with the findings of other similar studies done on MS elsewhere (9, 14, 15, 23-29).

The frequency of dyslipidemia ranged from 33.3% for low HDL to 23% for total cholesterol level. As expected, the dyslipidemia mostly overlapped with central obesity. This is also in line with other similar studies (9, 14, 15, 23-29). Only 11 (12.6%) of the patients had graft dysfunction. The mean duration of stay since transplantation was 16.6 months. This is a shorter duration when compared to other studies (10, 25, 28). These can be justified by our center being established only two and half years back.

The magnitude of metabolic syndrome in our patients was found to be 34.5%, similar to the findings of other studies from Europe (34.2%) (9, 28); Iraq (32.5%) (24) ; and Iran (32%) (9). However, the prevalence of MS in our patients was higher compared to finding of other similar studies from Japan (28.8%) and China (25.3%) (25, 31). This might be because these studies used NCEP-ATP III criteria modified for Asians who are known to have lesser obesity. On the other hand, the prevalence of MS was higher than ours in some other similar studies from Pakistan (43.5%) (26); Brazil (44.8%) (27); and Saudi Arabia (52.8%) (24). This can be justified by our patients being younger compared with relatively older patients in the other studies which is known to increase the risk of MS. It can also be as a result of different study populations of the other studies with higher prevalence of obesity.

Among the independent variables, age, past history of smoking, BMI, waist circumference, HPN, DM, dyslipidemia, and creatinine level showed statistically significant association with MS when analyzed with binary logistic regression [$P < 0.05$]. However, with multiple logistic regression analysis only waist circumference (P. value = 0.046; AOR 39.1 (95%CI 1.1, 141.8) and hyperglycemia or being on treatment for DM ($P = 0.031$; AOR 25.1 (95%CI 1.3, 467) were significantly associated with MS. These findings are also in line with findings of other similar studies(10, 14, 15, 24-26, 28, 29, 31).

The strength of the study is being original in our setup and addressing an important clinical problem. However, the study is underpowered by a small size and by short period of post-transplant follow up of most patients. This study can be used as a basis for further large-scale studies on prevalence of MS and associated factors in CKD patients or in the community at large.

Conclusion

Almost all of patients on our series didn't have many of the behavioral risk factors, except relatively lower number of daily servings of fruits and vegetables. The prevalence of MS was high in our transplant recipients. Only waist circumference and hyperglycemia were found to have significant association with MS. Comprehensive preventive strategies should be strengthened for optimal management of our transplant patients so that complications of MS could be averted.

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Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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