Arab Journal of Nephrology and Transplantation. 2012 Sep;5(3):141-4

Original Article

AJNT

Prevalence of the Metabolic Syndrome in Renal Transplant Recipients

Ibrahim M. Elkehili[1*], Ahmed B. Kekli[1], Ali M. Grera[2]

1. Nephrology Department, National Heart Center, Tripoli, Libya

2. Community Department, Faculty of Medicine, Tripoli University, Tripoli, Libya

Abstract

Introduction: The cause of the metabolic syndrome (MS) is incompletely understood but represents a complex interaction between genetic, environmental, and metabolic factors, clearly including diet, and level of physical activity. The prevalence of MS is continuously increasing in the general population. Recently it has been found that MS is also common in renal transplant recipients (RTRs). The aim of this study was to determine the prevalence and characteristics of MS in a group of Libyan renal transplant recipients, using two different diagnostic criteria.

Methods: This study was conducted at the Nephrology Department of the National Heart Center, Tripoli, Libya. We determined the prevalence of MS in a group of renal transplant recipients using both the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria and the International Diabetes Federation (IDF) criteria. All patients were more than six months post transplantation. Patients with Pre-transplant diabetes mellitus were excluded from the analysis.

Results: By using the NCEP-ATP III criteria 26 out of 91 patients (28.6%) had the metabolic syndrome. MS was commoner in females than males, affecting 12 out of 35 females (34.3%) and 14 out of 56 males (25%). Using the IDF criteria the metabolic syndrome was diagnosed in 23 patients (25.3%). In this group of patients the most common component of the metabolic syndrome was high blood pressure and the least common was impaired glucose tolerance and diabetes.

Conclusions: The prevalence of MS in our renal transplant patients is high, affecting females more than males.

* Corresponding author; P.O. Box No. 80112, Tripoli, Libya; E mail: elkhili57im@hotmail.com

Key words: International Diabetes Federation; Metabolic Syndrome; NCEP-ATP III; Renal Transplant Recipients

The authors declared no conflict of interest

Introduction

The Metabolic syndrome (MS) was originally described in 1988 as «syndrome X» by Reaven *et al [1]*. The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) [2] defines MS clinically by the presence of any three of the following five traits: abdominal obesity, elevated fasting glucose level (reflecting insulin resistance), elevated blood pressure (BP), elevated serum triglyceride level and low HDL cholesterol level. The International Diabetes Federation (IDF) criteria define MS by the presence of central obesity plus any two of the remaining criteria used in the ATPIII/NECP classification.

The cause of the metabolic syndrome is not completely understood but it represents a complex interaction between genetic, environmental, and metabolic factors, clearly including diet [3, 4] and level of physical activity [4, 5]. The prevalence of MS is continuously increasing in the general population [6]. Recently, it has been found that MS is also common in renal transplant recipients (RTRs) [7]. The Metabolic syndrome is associated with a two-fold increase in the risk for cardiovascular disease (CVD), CVD mortality, myocardial infarction, and stroke as well as a 1.5 fold increase in the risk of all-cause mortality [8, 9]. Renal transplant recipients (RTRs) have about four-times higher mortality after the first year compared with the general population [10]. CVD events represent the single most frequent cause of death in RTRs accounting for 35-50% of all-cause mortality and

Table 1: Prevalence of different components of the metabolic syndrome in the study population

	Total (n = 91)	Men (n = 56)	Women (n = 35)
Central obesity	46	36	63
Hypertension	58	60	54
High TG	44	48	37
Low HDL-Cholesterol	33	25	46
Hyperglycemia	29	34	23
MS (NCEP-ATP III criteria)	28.6	25	34.2
MS (IDF criteria)	25.3	30.4	21.4

TG: triglyceride; HDL: high density lipoprotein; MS: metabolic syndrome; NCEP-ATP: National Cholesterol Education Program Adult Treatment Panel III; IDF: International Diabetes Federation

they occur at least twice as often as in the background population [10-14].

A community based population study demonstrated that established CVD risk factors are associated with the development of new onset kidney disease [15]. Recently, both obesity and MS have been suggested to participate in the pathogenesis of renal disease [16] as well as chronic allograft nephropathy [7]. Another study showed that MS is a prominent risk factor for new-onset diabetes mellitus , chronic graft dysfunction, graft loss and patient death in RTRs [17]. These reports suggest that MS may be a risk factor for renal dysfunction and CVD not only in the general population but also in RTRs. The present study investigated the prevalence of MS in a group of Libyan renal transplant recipients using the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and the International Diabetic Federation (IDF) criteria.

Methods

This study was conducted at the Nephrology Department of the National Heart Center, Tripoli, Libya. We included a total of 91 live related and non-related renal transplant recipients, all of whom were more than 6 months post transplantation. Patients with pre-transplant diabetes mellitus were excluded. Patients were receiving combination therapy with cyclosporine or tacrolimus, azathioprine or mycophenolate mofetil along with prednisolone at a dose of 0.07 to 0.1/mg/kg/day. All patients gave informed consent for participation in the study.

After 10-12 hours over night fast, blood samples were taken for determination of glucose, creatinine, triglyceride (TG), and high density lipoprotein (HDL) cholesterol by auto-analyzer (Cobas Integra 400 plus, Roche). Waist circumference was determined by using a non-stretchable measuring tape midway between the iliac crest and costal margin.

According to NCEP ATP III criteria, the diagnosis of MS was made when three or more of the following criteria were fulfilled [18]: (i) serum TG level $\geq$ 150 mg/dl or specific treatment for this lipid abnormality, (ii) serum HDL cholesterol level < 40 mg/dl in men or < 50 mg/dl in women or specific treatment for this lipid abnormality, (iii) systolic blood pressure (SBP) $\geq$ 130 mmHg and/or diastolic blood pressure (DBP) $\geq$ 85 mmHg or use of antihypertensive medications, (iv) fasting plasma glucose level >100 mg/dl or use of anti-diabetic medications, and (v) waist girth > 102 cm for men and > 88 cm for women. According to the International Diabetes Federation criteria [19], subjects with central obesity (defined as waist girth > 102 cm for men and > 88 cm for women) plus any two of the remaining four criteria were considered to have MS.

The statistical Package for Social Sciences version 14 for windows (SPSS Inc, Chicago, IL, US) was used for statistical analysis. Continuous data were expressed as means and standard deviations and categorical data as percentages. Continuous variables were compared by the independent t-test and categorical data by the Chi squared test. P value < 0.05 was considered statistically significant.

Results

By using the NCEP-ATPIII criteria 26 of 91 patients (28.6%) had the metabolic syndrome. It was diagnosed in 12 out of 35 females (34.3%) and 14 out of 56 males (25%) indicating female predominance. The mean age of the MS group was more than that of the non-MS group (46 ± 12 versus 40 ± 11years respectively; P = 0.03). Mean serum creatinine level was not different between the two

groups (1.2 ± 0.5 versus 1.4 ± 0.8 mg/dl respectively; P = 0.04).

By using IDF criteria, MS was diagnosed in 23 patients (25.3%), the prevalence was 31.4% in the females and 21.4% in the males. Table-1 shows the prevalence of different components of the metabolic syndrome. The most prevalent component of the metabolic syndrome was elevated blood pressure and the least common was elevated fasting plasma glucose level.

Discussion

Among the numerous current definitions of the MS (World Health Organization, European Group for the Study of Insulin Resistance, American Association of Clinical Endocrinologists, and the IDF), the one proposed by the NCEP-ATPIII is most widely Used [2]. The criteria were modified in 2005 by the American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHBI) [20].

In the general population the prevalence of MS differs widely among ethnic groups and according to diagnostic criteria used [21-23]. De Varies *et al* showed that the prevalence of MS among renal transplant patients using the original NCEP ATP III criteria was 63% [7]. The Australian study on renal transplant patients using the same criteria revealed 50% prevalence of MS among these patients [24]. Porrini *et al* found that 37.7% of Spanish RTRs had MS by using the modified criteria [17]. These reports suggested that MS is more prevalent in renal transplant recipients as compared to the general population with ethnic variation.

Obesity is common in renal transplant recipients and is associated with worsening cardiovascular parameters and proteinuria progression [24]. The metabolic syndrome is a prominent risk factor for new-onset diabetes mellitus [17]. It has been reported that MS is a risk factor for renal dysfunction in the general population [15] and a prominent risk factor for chronic graft dysfunction [7, 17, 25, 26]. Our study did not show significant difference in serum creatinine levels between MS and non-MS patients.

Our results showed that the prevalence of MS differed according to the criteria used; it is slightly lower by using the IDF than the NCEP ATP III criteria (25.3% versus 28.6%). By using the NCEP ATP III criteria the prevalence of MS in our patients is consistent with the results of Ozdemir *et al* [25]. Some studies reported higher prevalence [7, 27, 28] while other investigators showed less prevalence [26, 29, 30] compared to our results. This may be due to ethnic variations. MS in this study was more prevalent in females compared to males, which is consistent with the results shown by the Chinese study [31] and by Elahi *et al* [27]. In contrast, the results of the Japanese study [30] showed that the prevalence of MS was more common in males than females. The most common component of metabolic syndrome was high blood pressure which is similar to the results of the Chinese study [31] and Elahi *et al* [27]. The least common component was impaired fasting glucose and diabetes mellitus which is consistent with the results shown by Elahi et al [27]. On other hand, the Chinese study results [31] showed that low high density lipoprotein-cholesterol level was the least common component.

Conclusion

The prevalence of MS in our renal transplant patients is high, affecting females more than males.

References

1. Reaven GM: Role of insulin resistance in human disease. Diabetes. 1988; 37: 1595–1607.

2. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): 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) final report. Circulation. 2002;106: 3143–421.

3. McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW, Jacques PF. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. Diabetes Care. 2004;27: 538–46.

4. Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas J, Tousoulis D, Toutouza M, Toutouzas P, Stefanadis C. Impact of lifestyle habits on the prevalence of the metabolic syndrome among Greek adults from the ATTICA study. Am Heart J. 2004;147: 106–12.

5. Lakka TA, Laaksonen DE, Lakka HM, Männikkö N, Niskanen LK, Rauramaa R, Salonen JT. Sedentary lifestyle, poor cardiorespiratory fitness and the metabolic syndrome. Med Sci Sports Exerc. 2003;35: 1279–86.

6. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. Adults. Diabetes Care. 2004;27(10): 2444-9.

7. de Vries AP, Bakker SJ, van Son WJ, van der Heide JJ, Ploeg RJ, The HT, de Jong PE, Gans RO. Metabolic syndrome is associated with impaired long term renal

allograft function; not all component criteria contribute equally. Am J Transplant. 2004; 4(10): 1675-83.

8. Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. Am J Med. 2006;119: 812-19.

9. Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, Rinfret S, Schiffrin EL, Eisenberg MJ. The Metabolic Syndrome and Cardiovascular Risk A Systematic Review and Meta-Analysis. J Am Coll Cardiol. 2010;56:1113-32.

10. Arend SM, Mallat MJ, Westendorp RJ, van der Woude FJ, van Es LA. Patient survival after renal transplantation; more than 25 years follow-up. Nephrol Dial Transplant 1997;12: 1672−9.

11. Lindholm A, Albrechtsen D, Frodin L, Tufveson G, Persson NH, Lundgren G. Ischemic heart disease−major cause of death and graft loss after renal transplantation in Scandinavia. Transplantation 1995;60: 451−7.

12. Foley RN, Parfrey PS. Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. J Am Soc Nephrol 1998;9 Suppl 12: S16−23.

13. Ojo AO, Hanson JA, Wolfe RA, Leichtman AS, Agodoa LY, Port FK. Long-term survival in renal transplant recipients with graft function. Kidney Int 2000;57: 307−13.

14. van Dijk PC, Jager KJ, de Charro F, Collart F, Cornet R, Dekker FW, Grönhagen-Riska C, Kramar R, Leivestad T, Simpson K, Briggs JD. Renal replacement therapy in Europe: The results of a collaborative effort by the ERA−EDTA registry and six national or regional registries. Nephrol Dial Transplant 2001;16(6): 1120-29.

15. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D. Predictors of new-onset kidney disease in a community based population. JAMA 2004;291: 844-50.

16. El-Atat FA, Stas SN, McFarlane SI, Sowers JR. The relationship between hyperinsulinemia, hypertension, and progressive renal disease. J Am Soc Nephrol 2004;15: 2816-27.

17. Porrini E, Delgado P, Bigo C, Alvarez A, Cobo M, Checa MD, Hortal L, Fernández A, García JJ, Velázquez S, Hernández D, Salido E, Torres A. Impact of metabolic syndrome on graft function and survival after cadaveric renal transplantation. Am J Kidney Dis 2006;48(1): 134-42.

18. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. American Heart Association; National Heart, Lung, and Blood Institute. Definition of metabolic syndrome: Report of the National Heart, Lung and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004;109: 433-8.

19. Alberti KG, Zimmet P, Shaw J. IDF Epidemiological Task Force Consensus Group. The metabolic syndrome - a new worldwide definition. Lancet 2005;366: 1059-62.

20. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112: 2735–52.

21. Morales DD, Punzalan FE, Paz-Pacheco E, Sy RG, Duante CA. Metabolic syndrome in the Philippine general population: prevalence and risk for atherosclerotic cardiovascular disease and diabetes mellitus. Diab Vasc Dis Res. 2008 Mar;5(1):36-43.

22. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: Findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287: 356–9.

23. Al-Nozha M, Al-Khadra A, Arafah MR, Al-Maatouq MA, Khalil MZ, Khan NB, Al-Mazrou YY, Al-Marzouki K, Al-Harthi SS, Abdullah M, Al-Shahid MS, Al-Mobeireek A, Nouh MS. Metabolic syndrome in Saudi Arabia. Saudi Med J. 2005 Dec;26(12):1918-25.

24. Armstrong KA, Campbell SB, Hawley CM, Nicol DL, Johson DW, Isbel NM. Obesity is associated with worsening cardiovascular risk factor profiles and proteinuria progression in renal transplant recipients. Am J Transplant 2005;5: 2710-18.

25. Ozdemir FN, Karakan S, Akgul A, Haberal M. Metabolic syndrome is related to long-term graft function in renal transplant recipients. Transplant Proc. 2009 Sep; 41(7):2808-10.

26. Faenza A, Fuga G, Nardo B, Donati G, Cianciolo G, Scolari MP, Stefoni S. Metabolic syndrome after kidney transplantation. Transplant Proc. 2007 Jul-Aug;39 (6):1843-46.

27. Elahi T, Akhtar F, Ahmed E, Naqvi R. Prevalence of metabolic syndrome in renal transplant recipients-a single centre experience. J Pak Med Assoc. 2009 Aug;59 (8): 533-36.

28). Luan FL, Stuckey LJ, Ojo AO. Abnormal glucose metabolism and metabolic syndrome in non-diabetic kidney transplant recipients early after transplantation. Transplantation. 2010 Apr 27;89 (8):1034-9.

29. Kishikawa H, Nishimura K, Kato T, Kobayashi Y, Arichi N, Okuno A, Fujii N, Kyo M, Takahara S, Ichikawa Y. Prevalence of the metabolic syndrome in kidney transplantation. Transplant Proc. 2009 Jan-Feb; 41(1):181-3.

30. Naganuma T, Uchida J, Kinoshita Y, Kuroki Y, Takemoto Y, Yoshimura R, Sugimura K, Nakatani T. The prevalence of metabolic syndrome in Japanese renal transplant recipients. Nephrology (Carlton) 2007; 12: 413-17.

31. Cheung CY, Chan HW, Liu YL, Chan YH, Wong HS, Chak WL, Choi KS, Chau KF, Li CS. Prevalence of metabolic syndrome in Chinese renal transplant recipients. HKMJ. 2008; 14(5):379-84.