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ORIGINAL ARTICLE

Impact of Metabolic Syndrome on Kidney Transplantation Outcome: A Single Centre Experience

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ABSTRACT

Background: To many individuals with end-stage renal disease, kidney transplantation is the best option. Proteinuria and a lower glomerular filtration rate have been linked to metabolic syndrome, implying a connection to chronic kidney disease. The aim of the study is to evaluate the impact of metabolic syndrome on kidney transplantation outcome.

Methods: This cohort study was conducted on 230 kidney transplant recipients in Urology and Nephrology Center, Mansoura University. We classified the included recipients into two groups; with or without metabolic syndrome. Records of all kidney recipients were reviewed for pre-operative details, operative details in addition to post-operative details. In each visit, recipients were subject to full history taking, thorough clinical examination and routine laboratory investigations. Radiological investigations were done as abdominal ultrasound (when indicated) in addition to graft grey scale ultrasound and doppler ultrasound if there is clinical suspicion of acute rejection, acute tubular necrosis, or renal artery thrombosis. Histopathological examination of the graft biopsy was carried out in cases of graft dysfunction.

Results: Both groups were comparable regarding baseline data. Pre-transplant hypertension incidence was higher among the study groups. Tacrolimus was avoided in the study group. Incidence of rejection and other post-transplant medical complications was higher among the study group.

Conclusion: Metabolic syndrome has a negative impact on kidney transplantation outcome. Metabolic syndrome is associated with higher incidence of acute rejection and acute tubular necrosis.

Keywords: Metabolic, Transplantation, Kidney, Nephrology.

INTRODUCTION

To many individuals with end-stage renal disease, kidney transplantation is the best option. In spite of significant advances in brief transplant survival following transplantation throughout the last twenty years, the long-term incidence of transplant rejection remained unchanged **[1].**

Lengthy transplant efficiency benefits either patients or health-care professionals since mortality is less than with regular dialysis and life quality is better. In addition, the cost of transplantation is significantly less than the expense of dialysis on a yearly basis **[2].**

Obesity, dyslipidemia, hypertension, and impaired glucose metabolism are among the clinical and biochemical disorders that make up the metabolic syndrome. Proteinuria and a lower glomerular filtration rate have been linked to metabolic syndrome, implying a connection to chronic kidney disease (CKD). Diabetes mellitus (DM), cardiovascular disease (CVD), and proteinuria are all common following renal transplantation, and have lately sparked a lot of attention in the kidney transplant community **[3].**

Metabolic syndrome has also been linked to CVD and post-transplant diabetes mellitus (PTDM), as well as worsening graft function and graft loss in

kidney transplant recipients. The incidence of metabolic syndrome and its influence on important outcomes following renal transplantation might give helpful information on the syndrome and its risk factors in renal transplant recipients **[4].**

The aim of the study was to evaluate the impact of metabolic syndrome on kidney transplantation outcome.

METHODS

Metabolic syndrome was defined by presence of three out of five critiriea of harmonized definition of Metabolic Syndrome 2020 : Elevated waist circumference: ≥ 102 cm in men ≥ 88 cm in women, blood pressure: systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or hypertension treatment or previously diagnosed hypertension, and fasting blood glucose: ≥ 5.6 mmol/l or treatment for elevated glucose or previously diagnosed Type 2 Diabetes **[5].**

Control group: presence of less than 3 out of 5 critiriea of harmonized definition of Metabolic Syndrome 2020.

Records of all kidney recipients were reviewed for pre-operative details, operative details as ischemia time and time to diuresis; in addition to post-operative details as induction immunosuppressive drugs, maintenance immunosuppressive protocol, frequency of acute and chronic rejection episodes, acute tubular necrosis, post-transplant proteinuria, post-transplantation medical disorders (hypertension, DM, liver impairment, CMV disease, bacterial infection and malignancy), surgical complications (Wound dehiscence, wound infection, hematoma, lymphocele), mean serum creatinine over 5 years post-transplant and condition of the patient at last follow up. In each visit, recipients were subjected to full history taking, thorough clinical examination and routine laboratory investigations. Radiological investigations were done as abdominal ultrasound (when indicated) in addition to graft grey scale ultrasound and doppler ultrasound if there is clinical suspicion of acute rejection, acute tubular necrosis, or renal artery thrombosis. Histopathological examination of the graft biopsy was carried out in cases of graft dysfunction.

Administrative considerations: Written informed consent was obtained from all participants after clear explanation of the study, and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board "IRB") and also from the Urology and Nephrology Center, Mansoura University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

The findings were recorded; tabulated and analyzed using SPSS version 19 for windows. Qualitative data were expressed as frequency and percentage. Student t-test was used to compare symmetrically distributed continuous data. Chi-square test was used to compare categorical data. Fisher-exact test was used to compare categorical data in case of population in 1 group is less than 20. P –value <0.05 was considered statistically significant.

RESULTS

Our study included 230 kidney transplant recipients with male predominance and age ranged from 18 to 55 years old. Obesity prevalence was 29.5%. Metabolic syndrome prevalence among obese patients in our cohort was 37.4%. Obese patients were divided into 2 groups according to presence of metabolic syndrome.

There was no statistically significant difference among both groups regarding demographics and baseline characteristics except that pre-transplant hypertension incidence were higher among the study group ***(p value: 0.001)*** **(table 1).**

In our center, the policy is to accept transplantation up to 5/6 HLA mismatch in one condition that the couple is matched in at least one HLA class II allele. The results regarding degree of HLA mismatch were comparable. Operatie details and surgical complications were comparable. However, incidence of lymphocele was higher among the study group ***(p value: 0.019)*** **(table 2).**

Tacrolimus and mycophenolate mofetil were used more frequent among control group. Being highly

diabetogenic, tacrolimus was avoided among study group.

Acute rejection episodes and acute tubular necrosis incidence was higher among metabolic syndrome group with statistically significant difference ***(p value: 0.001, 0.002 respectively)***. Post-transplant medical complications as hypertension, diabetes, hepatic impairment, bacterial and viral infection had higher incidence among the study group with statistically significant difference **(table 3).** Most of patients were alive with function graft at last follow up. Comparable numbers of population were dead at last follow up either with functioning or failed graft **(table 4).**

DISCUSSION

Obesity prior to transplantation may aggravate post-transplant weight gain and contribute to the occurrence of metabolic syndrome, that had been found in more than half of all common renal transplant recipients in certain studies and is linked to decreased long-term allograft performance **[6]**.

Our study was aiming at evaluating the impact of metabolic syndrome on kidney transplantation outcome. This cohort study was conducted on 230 kidney transplant recipients in Urology and Nephrology Center, Mansoura University. The 230 recipients received renal allo-transplantation during the period between January 2005 and December 2015. We classified the included recipients into two groups with or without metabolic syndrome.

According to Harmonized definition of Metabolic Syndrome 2020, Metabolic Syndrome is defined as having at least three of the following: 1-Elevated waist circumference: ≥ 102 cm in men ≥ 88 cm in women.2-Triglyceride: ≥ 1.7 mmol/l or TG treatment. 3-HDL-C: men < 1.03 mmol/l or women < 1.29 mmol/l or HDL-C treatment. 4-Blood pressure: Systolic ≥ 130 mmHg or Diastolic ≥ 85 mmHg or hypertension treatment or previously diagnosed hypertension. 5-Fasting blood glucose: ≥ 5.6 mmol/l or treatment for elevated glucose or previously diagnosed Type 2 Diabetes **[5].**

Regarding the primary plan for immunosuppression between two groups (with and without metabolic syndrome), there was no statistical significance between two groups except for tacrolimus based and mycophenolate-based plan with P value 0.01 and 0.015 respectively. This was in line with the findings of Xue and colleagues, as we found that patients treated with tacrolimus after renal transplantation were more prone to developing NODAT, that is one of the constituents of metabolic syndrome **[7]**.

By analyzing the rejection episodes between two groups (with and without metabolic syndrome), we found that there was no statistical significance between two groups in chronic rejection but, there was statistically significant difference among acute rejection and acute tubular necrosis with (P value <0.001 and 0.002) respectively. This was similar to the findings of Pagadala and colleagues, as we treat patients with acute rejection by high doses pulse steroid which will increase the risk of post-transplant diabetes mellitus which is a main component of metabolic syndrome **[8].**

Regarding the post-transplant medical complications between two groups (with and without metabolic syndrome), there was no statistical significance between two groups in gastrointestinal complications and malignancy but there was statistically significant difference regarding post-transplant hypertension (P value =0.001), DM (P value <0.001), hepatic impairment (P value =0.021), viral infection (P value =0.021) and bacterial infection (P value=0.001). Wissing and colleagues found a link between metabolic syndrome and the increased prevalence of PTDM, which they explained by a number of risk variables including increased weight, older age, African race, chronic hepatitis C infection, hypomagnesaemia, and genetic susceptibility **[9].**

Dedinska and colleagues found increased incidence of post-transplant hypertension in kidney transplant patients with metabolic syndrome. The same was in our study, as we found that it may be related to cyclosporine protocol that it cause hypertension as it may increase prostaglandin synthesis and decreased water, sodium, and potassium excretion **[10].**

While Pagadala and colleagues had found an increased incidence of viral and bacterial infection

post transplantation that may be contributed to incidence of PTDM this is a part of metabolic syndrome **[8].**

Incidence of post-transplant surgical complications in both groups with or without metabolic syndrome showed no statistically significant difference except for lymphocele which showed statistically significant difference with (P= value 0.019). This was in line with Carvalho and colleagues' findings, and this may be because non-normal weight people had lengthier dissections around their iliac arteries in order to make them more superficial, increasing the chance of lymphatic leakage **[11].**

Regarding serum creatinine follow up over five years and creatinine clearance between two groups (with and without metabolic syndrome), there was no statistical significance. Porrini and colleagues discovered that individuals with metabolic syndrome had a poorer creatinine clearance at baseline and assessment than those without metabolic syndrome **[12].**

In our study as regards the condition of the patients at last follow-up between two groups with and without metabolic syndrome; there was no statistically significant difference with (P value =0.698) and this was not parallel to the results of Dedinska and colleagues who found that metabolic syndrome and its components influences either survival of the patients or performance of the graft in the long term horizon **[10]**.

Our remommendations include careful patient selection with pre-transplantation weight reduction to reduce the rate of early post transplantation complications and to improve long-term outcomes. We recommend that obese renal transplant candidates with a BMI > 35 kg/m2 and with comorbidities or candidates with a BMI > 40 kg/m2 to be carefully assessed for bariatric surgery before transplantation. Our study has powers due to long-duration follow-up. It included all kidney transplant recipients from January 2005 to December 2015.

We had some limitations in our study as being a retrospective one with lack of randomization and also being a single-centre study; thus it may not be possible to generalize our results. All patients in our study were live-donor transplant recipients; therefore, our findings might not apply to the general transplant population which is mainly composed of patients who receive cadaveric renal transplants. The study population is representative of the renal recipients from our geographic area, but may not be representative of other areas with different ethnic composition.

CONCLUSION

Metabolic syndrome has a negative impact on kidney transplantation outcome. Metabolic syndrome was associated with higher incidence of rejection which will by turn increase the use of anti-rejection leading to more worsening of metabolic syndrome. Metabolic syndrome exaggerates the medical post-transplant complications including hypertension, diabetes, hepatic impairment and infections.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest with respect to the authorship and/or publication of this article.

FINANCIAL DISCLOSURES

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TABLES

Table (1): Demographics and baseline characteristics:

	Metabolic syndrome group (86 KTrs) No. (%)	Control group (144 KTrs) No. (%)	P value
Recipient age (years) mean±SD	36.1±10.7	34.4±10.9	0.24*
Recipient sex (Male)	66(76.7%)	117(81.3%)	0.25**
Donor age (years) mean±SD	38.9±10.8	38.9±10.7	0.98*
Donor sex (Male**)**	35(40.7%)	64(44.4%)	0.33**
Consanguinity (Related)	70(81.4%)	125(86.8%)	0.18**
Pre-transplant hypertension	63 (73.3%)	64(44.4%)	***0.001****
Pre-transplant diabetes	2	0	0.29***
Pre-transplant hepatitis infection	11	9	0.08***
Pre-transplant ischemic heart disease	2	0	0.29***
Pre-transplant dialysis	72 (83.7%)	129 (89.6%)	0.13**
BMI proxies:			
Mean blood pressure mean±SD	120±12	87±7.9	***0.008****
Fasting blood glucose mean±SD	6.1±0.38	4.8±0.6	***0.005****
Waist circumference mean±SD	103±9.6	91±9	0.058*
Cholesterol mean±SD	305±64	280±38	***0.0242****
Triglycrides mean±SD	2.1±0.29	1.8±0.24	***0.020****

*Student t-test for continuous data, **Chi-square test, ***Fischer-Exact test

Table (2): Operative details and post-operative surgical complications:

	Metabolic syndrome group (86 KTrs) No. (%)	Control group (144 KTrs) No. (%)	P value
Ischemia time (minutes) mean±SD	54.4±14.38	52.5±14.75	0.33*
Time to diuresis: Immediate Delayed	82 (95.3%) 4 (4.7%)	131 (91%) 13 (9%)	0.167**
Bleeding	2(2.3%)	2(1.4%)	0.480***
Hematomas	1(1.2%)	0(0 %)	0.374***
Lymphocele	4(4.7%)	0(0%)	***0.019******
Wound dehiscence	1(1.2%)	0 (0%)	***0.374******
Renal artery stenosis	0(0%)	1(0.7%)	0.626***
Renal artery thrombosis	3(3.5%)	1(0.7%)	0.148***

*Student t-test for continuous data, **Chi-square test, ***Fischer-Exact test

Table (3): immunosuppressive plans and post-transplant medical complications:

	Metabolic syndrome group (86 KTrs) No. (%)	Control group (144 KTrs) No. (%)	P value
Immunosuppressive plans:			
Steroid-based	45 (52.3%)	79 (54.9%)	0.40*
Cyclosporine-based	26 (30.2%)	23(16%)	0.155
Tacrolimus-based	58 (67.4%)	118 (81.9%)	0.01
Sirolimus-based	2(2.3%)	3 (2.1%)	0.61
Everolimus-based	5 (5.8%)	6 (4.2%)	0.394
Mycophenolate-based	54 (62.8%)	111 (77.1%)	0.015
Azathioprine-based	17(19.8%)	19(13.2%)	0.128
Acute rejection:			
No	54(62.8%)	121(84%)	<0.001*
Hyper-acute	1(1.2%)	6(4.2%)	
Acute cellular rejection	25(29.1%)	15(10.4%)	
Vascular rejection	6(7%)	2(1.4%)	
Acute tubular necrosis	14(16.3%)	6(4.2%)	0.002*
Chronic rejection	1(1.2%)	2(1.4%)	0.68**
Hypertension	86 (100%)	0(0%)	0.001**
Diabetes	12(14%)	3(2.1%)	<0.001**
Hepatic impairment	20(23.3%)	14(9.7%)	<0.005*
Gastrointestinal troubles	3(3.5%)	1(0.7%)	0.148**
Bacterial infection	23(26.7%)	14(9.7%)	0.001*
Viral infection	15(17.4%)	11(7.6%)	0.021*
Malignancy	2(2.3%)	0(0%)	0.139**

*Chi-square test, **Fischer-Exact test

Table (4): condition at last follow up:

	Metabolic syndrome group (86 KTrs) No. (%)	Control group (144 KTrs) No. (%)	P value
Live with functioning graft	70(81.4%)	127(88.2%)	0.69*
Live with failed graft	10(11.6%)	10(6.9%)	
Died with functioning graft	2(2.3%)	2(1.4%)	
Died with failed graft	2(2.3%)	3(2.1%)	

*Chi-square test

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