

Post renal transplantation obesity in Iraq (Prevalence study)

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Abstract

Background: Obesity is one of the major problems now adays that has been discussed and studied by a-lot of researchers and health care advisors because it is widely distributed and highly complicated into severe co-morbidities and mortality. Obesity may complicate kidney allograft recipient and may lead to graft rejection and affect patient survival.

Methods: There were 170 patients who underwent kidney transplantation, categorized in three categories according to the period of transplantation; before six months, more than six months and less than one year and more than one year. A 23% women and 76% men, 19.7% diabetic patients and 97.6% non-diabetic patients, 2.4% of the patients have cardiovascular diseases and 97.6% don't have CVD. 47.1% of patients are hypertensive while 52.9% are not hypertensive.

Results: Comparison between the mean body mass index before and after transplantation shows there is a statistically significant difference also significant difference between the males values were more than females values. Comparison between waist / ratio before and after transplant to the males and females separately to see if there is any difference between the two genders, the result was the mean of waist / hip ratio of the males is higher than the mean of the females and it can be due to several factors such as hormonal.

Conclusions: The result is too important and identification and control of risk factors that improve patient and graft survival.

Keywords: Obesity, renal transplant, patient survival, grafts survival.

INTRODUCTION

The successful transplantation can extend the lives of people and improve the complication of kidney failure (1). The first renal transplant in Iraq was in the 1970s and just only a few cases were performed in private hospitals, in 1985 the main teaching hospital of the University of Baghdad started the renal transplantation (2). Obesity is the disease of the century which is defined as abnormal or excessive fat accumulation that may impair health. The most basic method to measure the body fat is by body mass index (BMI) by using the weight and the height also can use the waist circumference, waist-to-hip ratio, mid-upper arm circumference and skin fold thickness. The prevalence of obesity increases among those who have already transplanted kidney, and they may probably develop complications and co-morbidity, such as atherosclerosis which may lead to renal transplant rejection, DM, hypertension, and others (3).

Obesity is an important consideration to be taken into account when assessing patient health after renal transplantation or before it as it mentioned in the "impact of obesity and renal transplant outcomes" which suggests that pre-transplant obesity probably causes DGF increased immunologically mediated graft loss and CAN, reduced graft and patient survival and an increased incidence of post-transplant complications {hypertension and post-transplant diabetes mellitus (PTDM)}, which are all likely to hasten the progression of CVD. Despite this, however, transplantation clearly offers a survival advantage compared with remaining on dialysis, even in patients who are obese at the time of transplantation (4). Several studies have investigated the factors that may affect kidney function at 1 year. The factors mentioned are anemia, hypercholesterolemia, immune suppresses, etc. One of these studies showed that donor age, recipient age, and BMI were independent predictors of renal function $>100\mu\text{mol/L}$ at 1 year and the results highlight the difficulty of the management of obesity in renal transplant patients (5).

Likewise, morbidly obese renal transplant recipients incur greater costs and re-admission rates compared with non-obese patients (6).

In some published studies claimed similar outcomes in the overall patients and graft survival results showed different outcome when divided patients into groups; groups A (BMI 30-34.9) and group B (BMI 35 and greater) as regards patients and graft survival, and the result was obese recipients with a BMI of >35 are a high-risk category (7). Some authors searched to determine whether renal transplant recipients with an elevated BMI have worse long-term graft survival, they prospectively studied 92 patients transplanted between April 1999 and July 2000. The result suggests that high weight and BMI are significantly associated with worse graft

survival 3 years post renal trans-plantation (8).

A retrospective study under the name of "impact of body mass index on graft loss in normal and overweight patients: a retrospective analysis of 206 renal transplants" suggests that increasing BMI value, although without categorical variation, may represent an independent risk factor for graft loss (9).

The age is an important additional risk factor for the development of diabetes mellitus in kidney transplant recipients group and it is recommended to follow mainly older patients. Early detection of metabolic abnormalities and dietary and therapeutic intervention in kidney transplant recipients may help to prevent chronic allograft dysfunction. (10)

Single institution series have demonstrated that obese patients have higher rates of wound infection and delayed graft function (DGF), but similar rates of graft survival. Obesity and outcome following renal transplantation journal showed the determination whether obesity affects outcome following renal transplantation. They observed that Donor BMI did not affect overall graft survival ($p > 0.07$). Recipient obesity is associated with an increased risk of DGF and decreased graft survival following renal transplantation (11). Pre-operative obesity has been reported to worsen the outcome of organ transplantation; Impairment of graft function as well as decreased patient and graft survival can contribute to this effect (12). Another article mentioned that moderate to severe obesity patients (BMI 35 kg/m² and over) had a significantly higher risk of DGF, pre-transplant overweight or obesity is associated with an incrementally higher risk of DGF (13).

The World Health Organization estimated that in 2014, over 600 million people met criteria for obesity. In 2011, over 30% of individuals undergoing kidney transplant had a body mass index (BMI) 35 kg/m² or greater. A number of recent studies have confirmed the relationship between overweight/obesity and important co-morbidities in kidney transplant patients. As with non-transplant surgeries, the rate of wound and soft tissue complications are increased following transplant as is the incidence of delayed graft function (14). Overweight and obesity which have a substantial impact on health in the general population, have a similar prevalence in solid organ transplant recipients but carry even more serious ramifications. As this group's use of immunosuppressive medication increases the risk for co-morbidities, e.g. metabolic syndrome and cardiovascular disease, the prevention of additional risk factors is vital (15). A cohort study was performed with 2,491 Chinese adults to investigate the association between the metabolically healthy obesity (MHO) phenotype and incident chronic kidney disease (CKD) they found MHO was significantly associated with

incident CKD (16).

Cardiovascular diseases were investigated in 403 patients who received 464 kidney transplants during the 10-years period. Atherosclerotic complications developed in 15.8 percent during the post-transplant follow up period, multivariate analysis showed that a number of known risk factors (age, sex, diabetes, cigarette smoking, hypertension and serum cholesterol) were independently associated with the post-transplant vascular disease. In addition, the number of acute rejection episodes (all treated with high doses of corticosteroids) was also independently linked to vascular disease. These results suggest that an increased prevalence of known risk factors, and events linked to allograft rejection, explain the high incidence of cardiovascular disease in renal transplant recipient (17).

Post-transplantation diabetes mellitus is defined as diabetes that is diagnosed in grafted patients. It affects 20 to 30 % of kidney transplant recipients, with a high incidence in the first year (18). New-onset diabetes after transplantation (NODAT) affects the graft survival the range of NODAT can change by the control on Modifiable risk factors for NODAT include obesity and the metabolic syndrome, hepatitis C virus and cytomegalovirus infection, corticosteroids, calcineurin inhibitor drugs (especially tacrolimus), and sirolimus. NODAT affects graft and patient survival and increases the incidence of post-transplant cardiovascular disease (19).

SUBJECTS AND METHODS:

The aim of this study is to estimate the prevalence of obesity among kidney transplanted patients.

Design: a cross-sectional study (prevalence study).

Duration: 8 months (from March 2017 to November 2017).

Population Patients who undergo kidney transplantation are included, the patients are divided on the bases of the date of transplantation into three groups: 6 months, 1 year and more than 1 year.

Setting: this a multi-center study, it's carried on patients who are kidney transplanted (graft recipients) in centers mentioned below:

- 1) Ghazi -Al Hariri hospital (In Baghdad)
- 2) Al Karama hospital. (In Baghdad)
- 3) Al Hussein hospital. (In Karbala)
- 4) Genin private hospital (in Baghdad)

Sample size: total sample size is 170 which is consisted of:

- 94 patients from Ghazi Al Hariri hospital
- 40 patients from Al Hussein hospital
- 20 patients from Genin hospital
- 16 patients from Al Karama hospital

Data source: the data were collected using a self-structured questionnaire which was established by the research team and validated by a specialist from community & family medicine.

Data collection: The questionnaire was filled by direct interview using Arabic language form for the patients. During the study period; the researchers introduced themselves to the participants and briefly explain the nature of the study. Then oral consent was obtained from the participants according to Helsinki Law Instruments:

- Weighing machine: for weight calculating.
- Tape measure: for calculation of height, waist and hip circumference.
- Paper questionnaire: for gathering information from the patients.

Questionnaire: the questionnaire includes:

- **Demographic data:** name, age, gender, residence, and occupation.
- **Social history:** smoking & alcohol status exercise.
- **Past medical history:** a history of diabetes mellitus, hypertension, cardiovascular diseases and family history an of chronic kidney diseases.

• **Transplantation:** include date, type, site, and drug intake post-transplantation:

- Date: it's divided into 6 months, 1 year and more than 1 year.
- Type: whether it's the first or second transplant.
- Site: whether the kidney is transplanted in the left or the right side.
- Drugs: which type of drugs does the patient take.
- **Pregnancy history:**
 - Whether she is nulligravida, primigravida or multigravida.
 - A Number of babies.
 - Nature of the labor whether it was natural or Caesarean.
 - Abortion.
- **Body mass index (BMI):** height and weight pre-post transplantation.
- **Waist/hip ratio:** waist and hip circumference.

Measurements: two types of measurements are used to estimate the obesity in this study:

1-Body mass index: is a person's weight in kilograms divided by the square of height in meters. A high BMI can be an indicator of high body fatness; it is used as a screening tool for overweight or obesity. The Weight that is higher than what is considered as a healthy weight for is described as overweight or obese. So, calculating BMI is important in most of the obesity studies; it can be calculated by measuring weight in (kg) and the height in (m2) and decide if whether

Or at risk of obesity according to the values below: (20)

- BMI is less than 18.5 it falls within the underweight range.
- BMI is 18.5 to < 25 it falls within the normal range.
- BMI is 25.0 to < 30 it falls within the overweight range.
- BMI is 30.0 or higher it falls within the obese range.

* Obesity is frequently subdivided into categories:

Class 1: BMI of 30 to < 35

Class 2: BMI of 35 to < 40

Class 3: BMI of 40 and higher

2- **Waist/hip ratio:** Waist circumference is the simplest and most common way to measure "abdominal obesity"-the extra fat found around the middle that is an important factor in health, the waist-to-hip ratio (WHR) is also used to measure abdominal obesity. It's calculated by measuring the waist and the hip (at the widest diameter of the buttocks), and then dividing the waist measurement by the hip measurement. It is a Good correlation with body fat as measured by the most accurate methods and inexpensive at the same time (21).

Waist – to – Hip Ratio (WHR) Norms				
Gender	Excellent	Good	Average	At Risk
Males	< 0.85	0.85-0.89	0.90-0.95	>0.95
Females	<0.75	0.75-0.79	0.80-0.86	>0.86

Ethical issues:

1. Permission would be obtained from Baghdad College of medicine by Administrative request directed to PHCCs to facilitate the task of obtaining the information from participants.
2. Oral consent will be obtained by asking every participant if they want to answer the questions of the questionnaire after a brief explanation of the general purpose of the study and its objectives.

Pilot study: A pilot study was conducted using 4 patients who were excluded from the study sample, to:

- Test the quality of questions, concerning information & language used.
- The time needs to fulfill the questionnaire.

Data analysis: Data were submitted to a statistical package of social science (SPSS) program version (21.0).

Analytic statistics: Chi-square test was used to find if there was

any association between renal transplantation (graft recipients) and obesity with certain demographic data (age, gender, social history, date of transplantation). A P value <0.05 is considered as significant.

RESULTS:

A Total of 170 persons of renal transplanted patients were involved in this study. 40 female who contribute 23% of the sample & 130 male who contribute 76% of the sample, the mean age (38.86 + - 12.21) which range (13-71). When we calculate the BMI of the renal transplanted patients after the transplantation we thought that it differs from the BMI before the operation so we make a cross-table as shown in Table 1.

The Pearson chi-square value is 150.492 and the P value is 0.001 which is less than 0.05, so there is a difference, to make sure of this result, we compared between the means of BMI before/after transplantation: Table 2.

The P value is 0.0001 which is less than 0.05 so we reject the null hypothesis in favor of the alternative hypothesis, there is statistically significant difference between BMI 1 & BMI2, and the scatter diagram is showing this relation obviously (Figure 1).

To be more specific, we calculate the BMI for male and female separately to see if the difference is statistically significant between the two genders: Table 3,4.

This result represents the mean of BMI before/after

transplantation for males which is highly statistically significant, the P-value is 0.0001 less than 0.05, but the p value for the females test is 0.03 which is also less than 0.05 but not as compared to as the males, the table below is for the females test:

We can see the difference clearer in the (Figure 2).

The social history is also has been taken from these patients, they have been asked if they are smoking, 21.2 % of the patients answered " yes" and 78.8 % answered with "no" when they have been asked if they are smoking, and 5.3 % of the patients were drinking alcohol whereas 94.7% were not drinking, then we asked them if they do exercise at least half hour per day the answer was 26.5% "yes" & 37.5 % "No."

The percentage of DM in this study is 19.7% diabetic patients and 97.6% non-diabetic patients, 2.4% of the patients have cardiovascular diseases and 97.6 % don't have CVD.

47.1% of patients are hypertensive while 52.9% are not hypertensive.

Table 5 shows that the mean of waist-hip ratio of the males is higher than female, then we've studied the value of waist-hip ratio of each gender separately:

We can notice that the mean of waist-hip ratio of the males is higher than female maybe due to several factors, such as hormonal factors.

Table (1), cross tabulation between BMI before and after the renal transplantation.

BMI 1 CODING * BMI 2 CODING Cross-tabulation								
		BMI 2 CODING						Total
		underweight	normal	Pre-obesity	obesity class1	obesity class 2	obesity class 3	
BMI 1 CODING	underweight	8	7	3	1	0	0	19
	normal	4	37	28	9	0	0	78
	Pre-obesity	0	3	21	14	2	0	40
	obesity class1	0	2	6	8	2	1	19
	obesity class 2	0	0	1	5	4	2	12
	obesity class 3	0	0	0	0	1	1	2
Total		12	49	59	37	9	4	170

TABLE (2), The comparison between means of BMI before/after transplantation.

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Body mass index before transplantation - Body mass index after transplantation	-2.03252-	4.40429	.33779	-2.69936-	-1.36568-	-6.017-	169	.000

TABLE (3), The mean of BMI before/after transplantation for males

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Body mass index before transplantation - Body mass index after transplantation	-2.22542-	4.53219	.39750	-3.01189-	-1.43896-	-5.599-	129	.000

TABLE (4), The mean of BMI before/after transplantation for females.

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Body mass index before transplantation - Body mass index after transplantation	-1.40558-	3.94809	.62425	-2.66824-	-.14292-	-2.252-	39	.030

TABLE (5) the mean of waist hip ratio

the gender of the patient	Mean	N	Std. Deviation
Male	.990	130	.0785
female	.917	40	.0861
Total	.973	170	.0860

TABLE (6) W.H.RATIO female

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Excellent	2	1.2	5.0	5.0
	Good	1	.6	2.5	7.5
	Average	6	3.5	15.0	22.5
	Risk	31	18.2	77.5	100.0
	Total	40	23.5	100.0	
Missing System		130	76.5		
Total		170	100.0		

TABLE (7) W. H. RATIO male

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Excellent	5	2.9	3.8	3.8
	Good	8	4.7	6.2	10.0
	Average	24	14.1	18.5	28.5
	Risk	93	54.7	71.5	100.0
	Total	130	76.5	100.0	
Missing System		40	23.5		
Total		170	100.0		

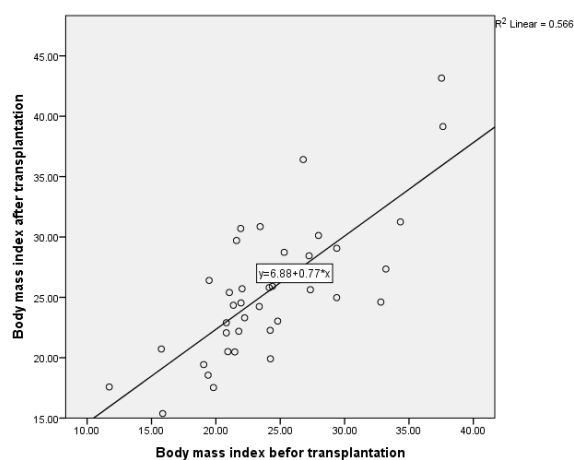


Figure (1), the scatter diagram of the relation between BMI before/after transplantation

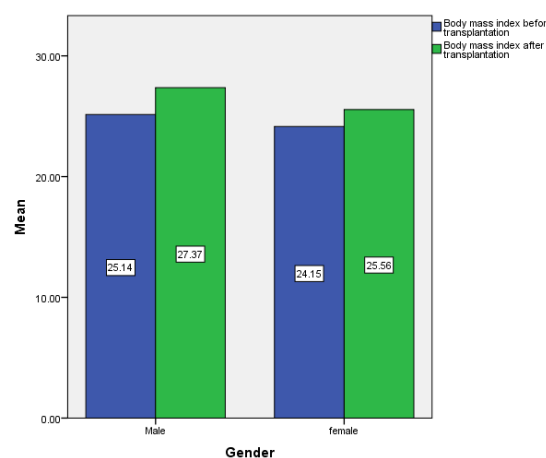


Figure (2), The differences between BMI before /after transplant in both gender.

DISCUSSION

Association between pre-transplant BMI and the risk of DGF was rather linear, incremental. Only a few studies examined the association between BMI and DGF and found conflicting or equivocal results(13).All solid organ transplant recipients seem to be susceptible to gain weight, the organ groups may differ in view of risk factors and consequences. As a subsequent step, the identification of risk factors and correlates associated with post-transplant weight gain is potentially a key element for the development of effective interventions to prevent weight gain following solid organ transplantation (15).

A comparison was made to compare between BMI before & after transplantation, It shows the statistically significant difference (p-

value = 0.0001) This Weight gain after kidney transplantation might be due to many reasons. Patients who once needed many diet restrictions can now eat a greater variety of foods. They also have a better appetite, which is a positive sign of good health. But some medications can make it easier to gain weight, and may also increase the appetite too much. Weight gain can then lead to diabetes and heart disease. So they need to avoid unhealthy lifestyle, (eat less of vegetables, fruits, and whole grains), with high-fat dairy products and meats. Although the exercise is very important for weight reduction, regrettably no more than 26.5 % of all the sample do exercise at least half hour per day.

Male BMI difference before & after transplantation was higher

than female (male 27.37, female 25.56) that could be explained by several Studies had measured the average BMI of people with body fat percentages using formulas that predict body fat percentage, based on Age, BMI and Gender they displayed body fat percentage evidence suggests that Men should have a BMI that is approximately 2.3 kg/m² higher than Women (22).

At the time of data collection, the Waist to hip ratio was calculated by measuring the circumference of an individual's waist and dividing it by the circumference of the individual's hips. This ratio helps the individual determine their risk for certain health-related conditions such as heart disease, diabetes, and other chronic diseases. Individuals with a larger mid-section than hips (or who appear to be apple-shaped) are at greater risk for these conditions because of the fat accumulation in the mid-section.

A study was conducted in Korean population under the title of "Waist Circumference, Not Body Mass Index, is associated with Renal Function Decline in Korean Population: Hallym Aging Study". They found that central obesity was associated with faster renal function decline. Comparing WC of >95 cm in men or >90 cm in women with ≤90 cm in men or ≤85 cm in women, (all p-values for trend <0.05). Waist-to-hip ratio (WHR) and waist-to-height ratio also were associated with renal function decline. There was no significant association of BMI with renal function decline (23) that could be a possible explanation for the WHR outcome that we have found in our study.

The study also shows that male WHR is higher than WHR in females. The circumference of the hips in females is generally larger than the circumference of the waist due to basic female anatomy. This correlation will cause the ratio to be lower (further away from 1) than the ratio for a male. For example, if a female has a 32-inch waist and 40-inch hips they will have a ratio of .80. This represents an acceptable ratio for a female. But, the male anatomy does not typically consist of the larger hips compared to the waist and torso. Therefore, a waist measurement of 32 inches and a hip measurement of 34 inches, which divides to be a ratio of .94, represent a healthy waist to hip ratio for a male (24).

According to questionnaire answers (section social and medical history), most of kidney transplanted patients have co-morbidities that may affect patients and graft survival if not controlled. We observed 19.7% of the patients are diabetic & 47.1% hypertensive. Previous researches have shown approximately same results that morbidly obese RT recipients harbor more co-morbidity during the transplantation period compared to non-obese patients. This is a greater rate of diabetes and CVD. A diagnosis of new-onset diabetes after transplantation (NODAT) carries with it a threat to the renal allograft, as well as the same short- and long-term implications of type 2 diabetes seen in the general population. NODAT usually occurs early after transplantation affects graft and patient survival, and increases the incidence of post-transplant cardiovascular disease.

Cardiovascular diseases also were investigated and showed a number of known risk factors (age, sex, diabetes, cigarette smoking, hypertension and serum cholesterol) were independently associated with the post-transplant vascular disease. In addition, the number of acute rejection episodes (all treated with high doses of corticosteroids) was also independently linked to vascular disease. These results suggest that an increased prevalence of known risk factors, and events linked to allograft rejection, explain the high incidence of cardiovascular disease in renal transplantation.

The patient described had diabetes mellitus, although this was not the cause of CRF. Although the mortality of patients with diabetic nephropathy and ESRF is much higher than for other causes of ESRF, the consequence of coincidental or post-transplant diabetes is much less clear. Post-transplant diabetes mellitus (PTDM) is a complication of immune-suppression, specifically steroids and, to a lesser extent, calcineurin inhibitors. Detrimental effects on

patient and graft survival have been reported within 3 years and a recent study demonstrated a stronger association between CVD and PTDM than with pre-transplant diabetes (25).

CONCLUSION

The identification of risk factors and correlates associated with post-transplant weight gain is potentially a key element for the development of effective interventions to prevent weight gain following kidney transplantation that improve patient and graft survival.

Disclosure

There is no conflict of interest concerning the study.

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