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Original Research Article

Pulmonary functions in kidney transplant recipients: Single centre observational study

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ABSTRACT

Background: Kidney transplantation in India is steadily increasing with advancement in medicines and surgical expertise. Subjects with kidney disease have spectrum of pulmonary pathologies but little is known regarding status on pulmonary function after kidney transplantation.

Method:149 kidney transplant recipientsbetween 18 to 60 years of age, having stable graft function and more than 6months of post-transplant duration were included in the study. Forced vital capacity (FVC), forced expiratory volume in first second (FEV_1), the ratio of FEV_1/FVC and peak expiratory flow rate (PEFR) were evaluated.

Result: 11 (7.4%) had a restrictive ventilatory impairment, none had obstructive lung function.FEV_1 and FVC were lower among subjects with high waist circumference, over weight and obese. FEV1/FVC ratio were lower in subjects with comorbidities or physical inactivity.

Conclusion: Restrictive lung functions present in few kidney transplant recipients. High waist circumference, over weight, obesity, comorbidity and physical inactivity alters pulmonary functions in kidney transplant recipients.

KEY WORDS: Kidney transplantation,pulmonary function test, anthropometry, physical activity, comorbidity.

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INTRODUCTION

Kidney transplant is a surgical process in which healthy functioning kidney is implanted in the person whose kidneys no longer work effectively. What was an experimental, risky and very limited treatment option fifty years ago is now routine clinical practice in more than 80 countries [1].Kidney transplantation is one of the medical miracles of the 20th century considered the optimal choice of treatment for end stage kidney disease (ESRD) in term of survival, cost-effectiveness and health related quality of life compared to lifelong dialysis therapy [2].Pulmonary complication like fluid retention, pulmonary edema and pleural effusion are common in end-stage renal disease which have shown to alter the lung function [3]. Pulmonary fibrosis, calcification, pulmonary hypertension, and pleural fibrosis have been seen with chronic renal failure [4].

A successful kidney transplant can decrease the deteriorated physical function which is seen in chronic kidney disease population; although the lung functions may not reverse completely even after transplant [5].

The pre-existing comorbidities, chronic use of immunosuppressants, susceptibility to opportunistic infections, metabolic syndrome and sarcopenia may lead to mechanical and hemodynamic changes in the lungs which could pave the way to pulmonary function disorders. Defective diffusion capacity and abnormal spirometric valueshave been reported in many individual transplanted patients in study [6]. Office Spirometry is the most common pulmonary function test which assesses the integrated mechanical function of the lung, chest wall, respiratory muscles, and airways by measuring the total volume of air exhaled from a total lung capacity to maximal expiration till residual volume.

SETTING AND DESIGN

In this single center prospective observational study; the kidney transplant recipients (KTR) from tertiary transplant care center of western India were enrolled between year 2017 and 2019.

Ethical approval: The ethical committee approval(IKDRC-ITS/09/2018, CTRI/ 027245) and participant written informed consent were taken.

Study participants: The KTR; age between 18 to 60 years having GFR > 45ml/min/1.72m^2 and more than 6months of post-transplant duration were included in the study with convenient sampling method. Subjects with history of hospital admission before 3 months of date of evaluation, re-transplant, transplant other than kidney, history of chronic smoking, chronic lung pathology, structural bony pathology, neurological complication, surgical complication like hernia, significant protein urea or oliguria, lymphocele, acute graft failure, active infection.

Procedure: Age, gender, dialysis vintage before transplant (DV) and post-transplant duration (PTD), type of transplant,serum creatinine level were noted. The Modification of Diet in Renal Disease (MDRD) equation was used for calculation of eGFR estimation [7]. Socio-economical categorization was done on basis of modified kuppuswamy socioeconomic scale in to low, upper low, lower middle, upper middle and higher class [8]. Physical Activity was evaluated via international physical activity questionnaire and was categorized as low, moderate or high [9]. Presence of comorbidity were categorized as absent, minimum one or minimum two comorbidities. Body weight was measured to the nearest 0.1kg using a digital scale.Height was measured to the nearest 0.1 cm via wall mount height measurement scale.Objectively measured height and weight were used to calculate BMI [weight in kg) ÷ (height in meter)^2]. The BMI was classified as underweight, normal, overweight or obese [10]. Waist circumference was measured in transverse plane at the midpoint of the line between the costal margin and the iliac crest in the mid axillary line and were categorized as either normal or high as per normative standard for Indian population [10]. For all measurements, the subject stood with feet close together, arms at the side and body weight evenly distributed, and the measurements were taken at the end of a normal expiration. Pulmonary function test was carried out on pre-calibrated desktop spirometer [SpiroUSB(ML-2525), CareFusion®, UK]. Participant was made to sit comfortably and rest of 30 minutes were given before performance of PFT. Subjects were advised to avoid intake of caffeine-containing products for at least 6 h before the test and not to eat a large meal for at least 2 h before spirometry. Maximal expiratory flow volume curves were obtained as per the ATS recommendations. They were instructed to breathe in and out through the mouthpiece as deeply and quickly as possible while a nose clip was applied. The spirometer acquired the forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1), the ratio of (FEV_1/FVC) and peak expiratory flow rate (PEFR). The best performance of the three successful efforts were recorded. Predicted values were based on Knudson et al [11]. Spirometry data were interpreted as per the guideline of ATS [12]and Joint Indian Chest Society guidelines for spirometry [13].

Statistical analysis: Descriptive analyses were used to describe the data. Microsoft excel and graphic user interface to the R statistical analysis online softwarewas used to calculate multivariate analysis [14]. Multivariate analysis of FEV_1 and FVC were performed individually by adjusting various variables like dialysis vintage, post-transplant duration, eGFR, BMI, waist circumference, socioeconomic class with 95% confidence interval and level of significance (p value) was set at <0.05.

RESULTS

149 KTR were analyzed for study. The demographic and kidney transplant related data description has been provided in Table 1 and Table 2 respectively. The result of FVC, FEV_1, PEFR and FEV_1/FVC is shown in Table 3. According to categorization of the lung function 138 individuals (92.6%) had normal pulmonary function, whereas 11 participants (7.4%) had a restrictive impairment, none had obstructive impairment. Using FVC, FEV_1 and FEV_1/FVC as outcome variables, and adjusting for confounding factors, the variables that remained in the model as predictors of lung function were waist circumference and BMI (predictors of FEV_1 and FVC), and physical activity and comorbidities (predictors of FEV_1/FVC). Subjects with -high WC had 0.792L lower FEV_1 compared to the group of normal WC (MVC: -0.792 [-1.08; -0.547], p <0.001,Graph2a). Overweight subjects had on average 0.249L lower FEV_1 compared to subjects with the normal BMI (MVC: -0.249 [-0.447; -0.0588], p = 0.025). FEV_1 of the obese were on average inferior of -0.434L compare to the subjects with normal BMI (MVC:-0.434 [-0.761; -0.161], p = 0.045). There was a statistically significant different FEV_1 depending on all class of BMI (p = 0.023,Graph 2b). FVC of the group high WC was on average inferior of -0.832L to the group normal WC (MVC:-0.832 [-1.07; -0.596], p <0.001,Graph3a). FVC of the overweight subjects were on average inferior of -0.326L to the group of the normal BMI (MVC:-0.326 [-0.526; -0.126], p <0.01,Graph3b). FVC of the obese were on average inferior of -0.475L to FVC of the normal BMI (MVC:-0.475 [-0.890; -0.0587], p = 0.026,Graph3b). Subjects who had minimum two comorbidity were 5.85% lower FEV_1/FVC% than subjects who had no comorbidity. (MVC: -5.85 [-10.4; -1.34], p = 0.011),Subjects who were moderately active were on average superior of 2.96% of FEV_1/FVC% than the subjects who were low active. (MVC: 2.96 [0.148; 5.77], p = 0.039) The other variables like, post-transplant duration, dialysis vintage, GFR and socioeconomic class were not significantly linked to FEV_1 or FVC or FEV_1/FVC.

Table 1: Anthropometric measurements, n=149

Age, yrs; mean±sd	39.9±9.7
Gender; n(%)	
Males	118(79)
Females	31(21)
SE-class; n(%)	
Higher	2(1.3)
Upper middle	70(47)
Lower middle	60(40)
Upper lower	17(11)
Lower	0(0)
Height ,cm; mean±sd	167 ± 5.1
Weight;, Kg; mean±sd	70.5 ± 8.9
BMI; Kg/m^2; mean±sd	24.8±2.4
n(%)	
Under weight	1(0.7%)
Normal	92(62%)
Overweight	48(32%)
Obese	8(6%)
WC; cm; mean±sd	93.2±6.1
n(%)	
N	29 (19%)
High	120 (81%)
TPA; n(%)	
Low	51(34)
Medium	92(62)
High	6(4)

BMI: Body mass index, **WC:** Waist circumference, **TPA:** Physical activity questionnaire

Table 2: Transplant related medical history, n=149.

DV, months; mean±sd	12.6±13.8
n(%)	
<12months	96(64%)
12-24months	27(18%)
>24months	26(17%)
PTD, months; mean±sd	40.2±26.0
n(%)	
< 1 year	8 (5.4)
1 to 3 year	102 (68)
3 to 6 year	27 (18)
>6 year	12 (8.1)
Serum Cr, mg/Dl; mean ±sd	1.1±0.3
eGFR, ml/min/1.73m^2; mean±sd	69.9±8.8
n(%)	
stage 1 : >90	4 (2.7)
stage2: 60 to 89	130 (87)
stage 3: <59	15 (10)
Co-morbidity; n(%)	
HT	60(40.2)
DM	30(20.1)
Hyperlipidemia	5(3.3)
Obesity	8(5.4)

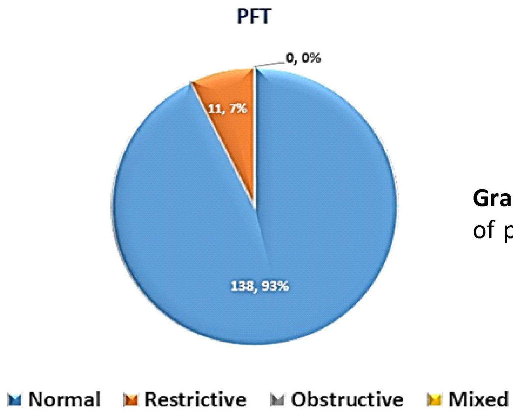
DV: Dialysis vintage, **PTD**: Post transplant duration, **Sr Cr**: serum creatinine, **eGFR**: estimated glomerular filtration rate, **HT**:Hypertention, **DM**: Diabetes mellitus

Table 3: Spiro metric value of pulmonary function; n=149 (mean±sd)

PFT parameter	FVC(L)	FEV_1(L)	PEFR(L/min)	FEV_1/FVC %
Observed value	2.70 ± 0.76	2.96 ± 0.69	283.94 ± 112.66	89.1± 8.08
% predicted	87.71 ± 18.10	89.23 ± 19.77	78.67 ± 22.10	_

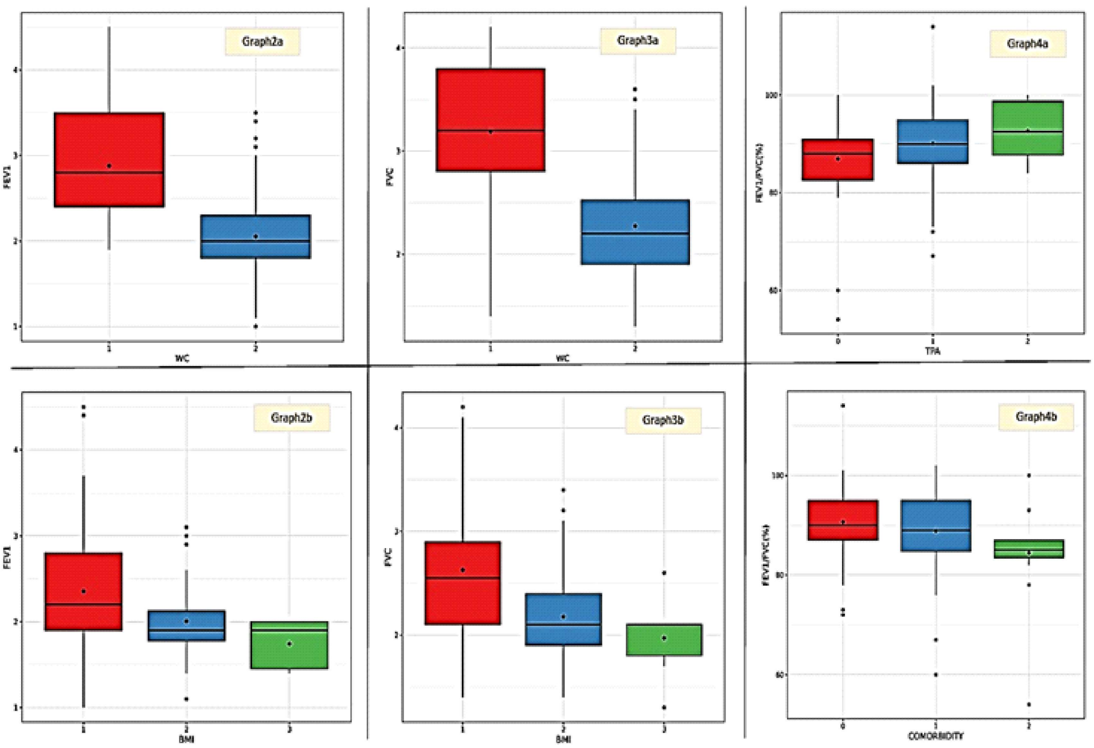
FVC: force vital capacity, **FEV_1**: force expiratory volume in first second, **PEFR**: peak expiratory force rate, **FEV1/FVC:** Ratio of FEV_1 and FVC

Graph 1:



Graph 1: Pie diagram: Distribution of various categories of pulmonary function among participants.

Graph 2:



Graph 2: Box and whisker plot [Graph 1a: FEV_1 between category of normal waist circumference (1), High waist circumference(2); Graph 1b: FEV_1 between category of BMI normal(1), Overweight(2) and Obese(3); Graph 2a: FVC between category of normal waist circumference (1), High waist circumference(2); Graph2b: FVC between category of BMI normal(1), Overweight(2) and Obese(3); Graph3a:FEV_1/FVC between the category of low PA(1), Moderate PA(2), high PA(3); Graph3b: FEV_1/FVC between category of no comorbidity(1), minimum one comorbidity(2), minimum two comorbidity(3).

DISCUSSION

Kidney transplantation in India is steadily increasing with advancement in medicines and surgical expertise. Subjects with kidney disease have spectrum of pulmonary pathologies but little is known regarding status on pulmonary function after kidney transplantation. Present study was aimed to evaluate the same. The mean of all spirometric parameters was normal among participants. According to categorization of the lung function, the result revealed that 38 individuals (92.6%) were categorised as a normal pulmonary function, whereas 11 participants (7.4%) were categorised as a restrictive ventilatory impairment, none of participants was defined as obstructive lung function. These results are in accordance with the result got by Sidhu et al [15], Ö. Karacan et al [16], Kalender B et al [17]in subjects with kidney transplantation.

A restrictive pattern of pulmonary function in kidney disease population had been demonstrated earlier due to fluid retention and pulmonary edema. Bush and Gabriel [18] found restrictive defects persisting in 10 out of 20 patients after renal transplantation. Kalender et al [17]found reduced FVC in 10% in their kidney transplanted population. They proposed that may be due to irreversible pre-transplantation changes. Fairshter RD et al [19] mentioned about persistence of interstitial fibrosis in post kidney transplantation. An involuntary loss of skeletal muscle mass, strength, and function which is termed as 'sarcopenia' is greater with longer dialysis vintage before transplantation [20].

Immunosuppressants and steroids used after transplantation are associated with type 2b fibers myopathy, altered mitochondrial respiration and muscle degeneration [21].Longer the duration after transplant; more the cumulative effect of these medicines [21]. Reduction in respiratory muscle strength has been reported after transplant; as such it was not evaluated in present study [22].However the association of PFT with dialysis vintage or post transplantation duration was not elicited in present study. None of the participant had obstructive defect reported in PFT that suggest that larger airways may not be affected in kidney transplant patients. Similar findings have also been reported by other authors [15]. Present study finding shown variability in lung function in KTR subjects with normal and high waist circumference as well as different category of BMI; which is in line with previous observations seen by Yue Chen et al [23]. The mechanical effects of the intra-abdominal pressure on the diaphragm are likely the main reason for the association of central obesity with compromised lung function. The contributions of increased abdominal mass, restricted outward movement of the muscular abdominal wall, and intrathoracic factors should be considered as a determinants of pulmonary functions. Hypertensionand diabetes are commonly seen in subjects with kidney disease.The association of physical activity and comorbidies that may alter the lung function has been reported earlier [24]. Higher levels of physical activity (PA) have been shown to be related to better clinical outcomes in patients with chronic disease including those with transplant [25]. Beta blockers and ACE inhibitors, which are frequently used in these population, can produce bronchospasm. However that was not observe in present study cohort.

CONCLUSION

Restrictive lung functions present in few kidney transplant recipients. High waist circumference, over weight and obesity reduces FEV1 and FVC. Comorbidity and physical inactivity reduces FEV1/FVC ratio in kidney transplant recipients.

Limitation: The sample was quite heterogeneous and convenient sampling was used, only forced based dynamic lung function were evaluated.

Conflicts of interest: None

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