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Original Article

Effect of kidney transplantation on sleep-disordered breathing in patients with End Stage Renal Disease: a polysomnographic study

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ABSTRACT

Background: Sleep-disordered breathing (SDB) is common in patients with end-stage renal disease (ESRD). SDB is associated with comorbidities such as hypertension, diabetes mellitus, and obesity, interplaying with metabolic derangements in the form of uremia, acidosis, and hypervolemia. Renal transplant has been observed to correct most of these metabolic derangements and to control progression of comorbidities. While SDB is highly prevalent among patients in the pretransplant stage, it remains to be seen whether the beneficial aspects of transplant are extended to improvement in SDB in patients with ESRD.

Methods: Eighteen patients undergoing thrice-weekly hemodialysis (HD) for ESRD at the transplant clinic of All India Institute of Medical Sciences (AIIMS), New Delhi, underwent detailed clinical, laboratory, and polysomnographic evaluation. The average number of apneas and hypopneas per hour of sleep, ie, Apnea–Hypopnea Index (AHI), was used to define the severity of sleep apnea. All patients underwent polysomnography (PSG) within 24 h of the last HD and after three months of living-donor transplant.

Results: Of 18 patients, there were 14 males and four females. The median age was 28 years (range 19–50 years). They had already spent a median period of six months (range 3–31 months) on HD before inclusion. The prevalence of SDB (AHI $\geq$ 5/h) was 44.4% (8/18) before transplant, which decreased to 5.6% (1/18) after transplant ($p = 0.016$). The oxygen desaturation index had a median value of 5.8 events/h (range 0.1–35.4) in the pretransplant stage, which decreased to 0 events/h (range 0–6.6) in the post-transplant stage ($p = 0.035$).

Conclusion: There was a significant improvement in the prevalence and severity of SDB after transplant. Whether improvement in SDB is sustained on a long-term follow-up remains to be seen.

1. Introduction

Sleep-disordered breathing (SDB) is defined as repeated interruptions in breathing, which disturb sleep and cause oxygen levels to drop. SDB causes daytime sleepiness, reduced alertness and cognition, and, notably, hypertension and cardiovascular disease [1,2].

The prevalence of SDB in the general population is roughly 6–13%, while the prevalence of sleep disorders in patients with end-stage renal disease (ESRD) is found to be 30–80% [3], with the predominant condition being obstructive sleep apnea (OSA) [4]. The etiology of SDB among patients with ESRD is multifactorial with many contributing factors such as ventilatory instability, upper airway narrowing, older age, edema and comorbidities such as diabetes mellitus [5–9]. Patients with ESRD may also develop SDB through mechanisms that promote upper airway occlusion during sleep. Patients with ESRD are vulnerable to fluid overload that leads to increased extracellular fluid volume in the neck and parapharyngeal structures, which in turn may cause pharyngeal narrowing. A significant increase in neck circumference and pharyngeal resistance was found with only 0.5 L of a fluid shift in healthy patients during recumbency [10]. Another potential cause of pharyngeal narrowing is upper airway dilator muscle dysfunction secondary to neuropathy or myopathy associated with either chronic uremia or the underlying cause of ESRD, such as diabetes mellitus.

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Questionnaires have been developed to assess and screen for SDB in the general population. These include the Pittsburgh Sleep Quality Index [11], the Epworth Sleepiness Scale [12], and the Berlin Questionnaire [13].

However, polysomnography (PSG) performed in a sleep laboratory or with the use of a portable device to assess breathing during sleep in a home setting is the gold standard for studying sleep physiology.

In one study, where home-based unattended PSG was performed, patients on HD were more likely to have severe SDB (>30 respiratory events per hour) compared to the general population [14]. Another study found the prevalence of Sleep Apnea–Hypopnea Syndrome (SAHS) in patients on HD to be 44% [15]. There have been conflicting results regarding the effect of renal transplantation, with two studies [16,17] showing no or minimal improvement in AHI or SDB and two studies showing marked improvement [18,19].

We designed the present study to assess the effect of renal transplantation on SDB in patients with ESRD. We sought to test the hypothesis that there would be an improvement in SDB in patients undergoing renal transplant for ESRD.

2. Material and methods

Patients attending the transplant clinic at the All India Institute of Medical Sciences (AIIMS), New Delhi, were invited to participate in the study. Patients were asked to participate if they were suffering from ESRD, awaiting transplant with an identified living-donor kidney and were on maintenance HD for at least three months.

For participating in the trial, the age of the participant had to be between 18 and 60 years, duration of dialysis at least three months before transplant, and stable graft function for at least three months post-transplantation. Patients were included regardless of their sleep complaints.

Patients with uncontrolled hypothyroidism, taking medications with known effects on sleep physiology such as antihistamines, antidepressants, and anticonvulsants or with major mental illness requiring psychiatric treatment (including those previously diagnosed with anxiety or depression and/or taking medications for those conditions); having comorbidities associated with nocturnal symptoms (congestive heart failure, unstable angina, arthritis, and uncontrolled chronic obstructive pulmonary disease); having a history of pulmonary disease (diagnosed by clinical, radiological, or functional alterations); previously diagnosed and/or treated for sleep disorders such as sleep apnea (SA), periodic limb movement disorder (PLMD), and/or Restless Legs Syndrome (RLS), any upper airway condition including tonsillitis (which could cause airway narrowing); currently consuming alcohol; and who were current smokers were also excluded from the study because our main aim was to study SDB solely attributed to renal dysfunction.

The patients received three sessions of HD per week using volumetrically controlled machines against bicarbonate dialysate. Each session of dialysis aimed at having a urea reduction ratio of $\geq$60. The volume reduction was according to the targeted dry weight of the patient.

All patients, postdialysis, were on their clinically determined "dry weight".

Twenty-five patients were enrolled in the study. They were enrolled irrespective of whether or not they had known sleep-related problems. Written informed consent in the vernacular language of the patient was taken before inclusion.

A detailed history was taken to identify the cause of ESRD, duration of ESRD, duration and frequency of dialysis, and comorbid conditions. A detailed record of medications being taken at the time of enrollment was made.

Laboratory investigations included hemogram, renal function tests, liver function tests, serum calcium, serum phosphate, serum uric acid, intact parathyroid hormone (iPTH), thyroid profile (T3, T4, and TSH), lipid profile, iron profile (total iron-binding capacity, serum ferritin levels, and transferrin saturation), and fasting (FBS) and postprandial (PPBS) blood sugar.

Anthropometric measurements, PSG technique and protocol, and SDB definitions were as described previously by the same author(s) [20,21].

The oxygen desaturation index (ODI) is defined as the number of times per hour of sleep that the oxygen–hemoglobin saturation dropped to 3% or more from baseline.

Socio-economic stratification of the patients was done using the Modified Kuppuswamy scale, updated for the year 2012. In this scale, families are classified as upper class (26–29), upper middle class [16–25], lower middle class [11–15], upper–lower class [5–10], and lower class (<5) according to family income, education, and occupation of the head of the household [22].

After the patients underwent living-donor kidney transplantation, the same protocol was repeated three months after transplantation with stable graft function. Seventeen patients were on tacrolimus, while one patient was on cyclosporine-based immunosuppression in addition to mycophenolate mofetil and steroids (in tapering doses) as other immunosuppressive medications. The protocol of the study was reviewed and approved by the Institute Ethics Committee.

A sample size of convenience was taken owing to the paucity of resources.

The mean and standard deviation (SD) were calculated for data with normal distribution, while median and range were calculated for quantitative variables following a non-normal distribution.

The analysis was performed using STATA version 12.0 (STATA Corporation, College Station Road, Houston, Texas, USA). The categorical variables were expressed as frequencies, while continuous variables with normal distribution were computed using the Student t test. Ordinal variables and variables following non-normal distribution were analyzed using Wilcoxon rank-sum test. The McNemar test was used to compare frequencies. Relationships between variables were analyzed with Pearson correlation when both variables were numerical and normally distributed. Spearman rank correlation was used when numerical variables were not normally distributed. P value < 0.05 was considered statistically significant.

3. Results

Of 25 patients, PSG data were available for 24 patients.

Of the 24 patients, one patient died before transplantation, one was lost to follow-up, and one did not receive a transplant within the period of study. Two patients died within three months of transplant; additionally, and one was too sick to undergo PSG at three months and later succumbed. Thus, 18 patients completed the study, and their results were available for comparative analysis.

Of the 18 patients, 14 (78%) were males and four were (22%) females. The group had a median age of 28 years (range 19–50 years). Mean age of the study population was 28.9 ± 8.9 years. Most of the patients (10/18) were in the lower middle strata of the Kuppuswamy scale.

The cause of renal failure in most of the patients was presumed chronic glomerulonephritis (CGN). Of the 18 patients, 10 had presumed CGN and four had presumed chronic interstitial nephritis (CIN), and of the remaining four patients, one patient each had diabetic nephropathy, hypertensive nephropathy, IgA nephropathy with crescentic glomerulonephritis, and ischemic nephropathy.

Patients had ESRD diagnosed on an average of 15.8 ± 12.6 months before enrollment with a median of 11 months (range

Table 1
Demographics of patients.

Patients (n)	18
Age (in yrs)	
Mean ± SD	28.9 ± 8.9
Median (Min, Max)	28 (19, 50)
Sex (Males/Females)	14/4
Cause of Renal Failure	
CGN	10
CIN	4
Diabetic Nephropathy	1
HT Nephropathy	1
IgAN Crescentic GN	1
Ischemic Nephropathy	1
Duration of CKD (in months)	
Mean ± SD	15.8 ± 12.6
Median (Min, Max)	11 (3, 48)
Time on HD (in months)	
Mean ± SD	9.6 ± 9
Median (Min, Max)	6 (3, 31)
Modified Kuppuswamy SES	
Mean ± SD	13.1 ± 4.9
Median (Min, Max)	12 (7, 24)

Values are expressed as mean ± SD or median (min, max).

3–48 months). They had already spent an average time of 9.6 ± 9 months on HD with a median period of six months (range 3–31 months). The demographics of patients are described in Table 1.

The prevalence of SDB (AHI ≥ 5/h) was 44.4% before transplant which decreased to 5.6% after transplant ($p = 0.016$). Of the eight patients who had AHI ≥5/h, SDB was cured in seven (87.5%). However, the one remaining patient also showed a decrease in AHI (Fig. 1). Median AHI was 1.2 (range 0–28.9) before transplant, which decreased to 0.4 (range 0–7) after transplant ($p = 0.034$). Fifty percent of patients in the pretransplant stage had desaturation index >5/h, while none of the patients in the post-transplant stage had desaturation index >5/h (Fig. 2). Desaturation index had a median value of 5.8 events/h (range 0.1–35.4) in the pretransplant stage, which decreased to 0 events/h (range 0–6.6) in the post-transplant stage ($p = 0.035$) (Table 2).

Total sleep time increased from 437.9 ± 80.5 min to 461.7 ± 61.9 min post-transplant (p > 0.05). There was no significant difference in sleep efficiency, stages of sleep, the number of arousals per hour, baseline oxygen saturation, and decrease in oxygen saturation to less than 90% during sleep between the pre- and post-transplant stages. The PSG findings are shown in Table 2.

All patients (100%) enrolled had hypertension and were on antihypertensive medications in the pretransplant stage. This number decreased to 77.8% after transplant at three months (p = 0.125).

The level of total cholesterol increased from 139.7 ± 21.4 mg/dl to 159 ± 28.8 mg/dl (p = 0.007) in the pre vs post-transplant stages.

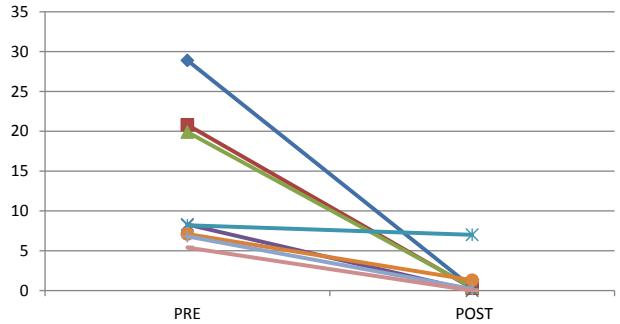

Fig. 1. Apnea–Hypopnea Index in patients with AHI ≥5 pretransplantation (n = 8).

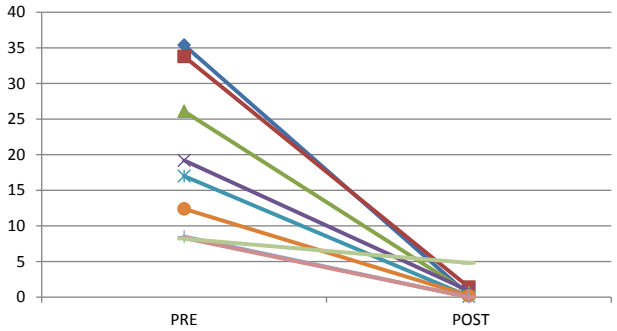

Fig. 2. Desaturation Index in patients with DI > 5 pretransplantation (n = 9).

The increase was largely contributed by triglycerides, which increased from 96.7 ± 26.9 mg/dl to 174.3 ± 55.9 mg/dl (p < 0.001). There was no significant difference in low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels.

Post-transplant, the patients' hemoglobin levels increased significantly from 9.1 ± 2.0 g/dl to 13.4 ± 1.8 g/dl ($p < 0.001$). As anticipated, urea, creatinine, phosphorus, and iPTH levels showed a significant decrease.

Renal function improved significantly post-transplant signifying a successful renal graft. The median urea level was 30 mg/dl, and mean creatinine level was 1.3 ± 0.3 mg/dl post-transplant. All the subgroup patients had stable graft function post-transplant.

All the anthropometric variables measured, ie, body mass index, neck, waist and hip circumference, waist–hip ratio, and fat percentage showed a marginal increase post-transplant, but the differences were not significant. The laboratory and anthropometric findings of patients in the pre- and post-transplant stages are shown in Tables 3 and 4. Analysis of correlation of AHI, desaturation index, and baseline SaO_2 with hemoglobin, TIBC, and serum ferritin is shown in Table 5.

4. Discussion

Our study adds to the literature in several important ways. First, we confirmed a high prevalence of OSA in patients with ESRD as seen in prior reports. Although home sleep testing is increasingly being used in sleep medicine, our use of PSG in the present study is a strength, given the prevalence of insomnia, periodic limb movements, and other conditions in ESRD. Second, we performed this study on people of Indian origin in an under-resourced area with the hope that our efforts will stimulate further research in understudied populations. Third, we observed a major improvement in OSA following renal transplantation. This particular finding has clinical implications regarding potential improvements in symptoms and associated comorbidities. Moreover, the findings may encourage research into mechanisms underlying improvement, which could provide pathophysiological insights into OSA in general.

Sleep disturbances and poor sleep quality have a reportedly high prevalence in patients with ESRD [3]. We could find only four studies that have examined the effect of transplant on SDB in patients with ESRD; three of these studies have been carried out using PSG; one each from Canada (n = 18) [16], Spain (n = 9) [18], and Brazil (n = 34) [17], while one has additionally been carried out using portable ventilation recorder in South Korea (n = 20) [19]. Our sample size (n = 18) is similar to the ones in these studies.

The prevalence of SDB (defined as AHI >5/h) was 44% in the pretransplant stage in our study, which is much lower than that seen by Beecroft et al. [16] (61%, SDB defined as AHI ≥ 10/h) and Lee [20] (60% SDB defined an AHI ≥10/h) and higher than that seen by Rodrigues et al. [17] (26.5%; SDB defined as AHI >5/h). The higher

Table 2
Polysomnographic findings pre and post kidney transplantation.

	Pre-Tx (n = 18)	Post-Tx (n = 18)	p value
Total Sleep Time (min)	437.9 ± 80.5	461.7 ± 61.9	0.134
Sleep Efficiency (%)	90.4 ± 10.8	89.5 ± 6.8	0.737
Stage 1 (%)	20.1 (5.6,55.1)	24.7 (4.4,37.8)	0.112
Stage 2 (%)	42.0 (12.6,62.3)	39.6 (12.6,58.3)	0.267
Slow wave (%)	23.1 (5.4,40.2)	22.4 (8.4,53.9)	0.777
REM (%)	13.2 (3.5,21.2)	12.6 (4.9,24.3)	0.948
AHI (events/h)	**1.2 (0,28.9)**	**0.4 (0,7)**	**0.034**
Arousal Index (events/h)	16.0 (3.7,53.3)	17.0 (2.4,33.2)	0.913
Baseline SaO_2 (%)	96.6 ± 2.4	97.5 ± 1.0	0.191
SaO_2<90% (min)	0.1 (0,510)	1.1 (0,4.8)	0.248
Desaturation Index (median events/h)	**5.8 (0.1,35.4)**	**0 (0,6.6)**	**0.035**
AHI ≥5	**8 (44.4%)**	**1 (5.6%)**	**0.016**
Desaturation index >5	**9 (50%)**	**0 (0%)**	**0.010**

Values are expressed as mean ± SD or median (min, max).
AHI, Desaturation Index reduction were the main objectives of the study.

Table 3
Laboratory findings pre and post kidney transplantation.

	Pre-Tx (n = 18)	Post-Tx (n = 18)	*p* value
Hb (g/dl)	9.1 ± 2.0	13.4 ± 1.8	<0.001
TLC (/cumm)	5900 (4200,10,700)	10,250 (5700,17,000)	<0.001
Urea (mg/dl)	98 (60,220)	30 (14,64)	<0.001
Creatinine (mg/dl)	8.4 ± 2.2	1.3 ± 0.3	<0.001
FBS (mg/dl)	91.6 ± 8.2	92.2 ± 12.2	0.825
PPBS (mg/dl)	110.1 ± 13.3	112.6 ± 16.6	0.570
Bilirubin (mg/dl)	0.6 ± 0.1	0.5 ± 0.2	0.125
AST (U/L)	22 [12 57]	23 [15 68]	0.826
ALT (U/L)	23.5 [9165]	29 [13 83]	0.722
Alkaline Phosphatase (U/L)	182.5 [52 1093]	191 [77,501]	0.845
Total Calcium (mg/dl)	9.0 ± 0.9	9.3 ± 1.0	0.243
Phosphate (mg/dl)	5.6 ± 1.5	3.3 ± 0.9	<0.001
Uric Acid (mg/dl)	5.3 ± 1.2	5.8 ± 1.4	0.103
iPTH (pg/ml)	172 (10,839)	64.6 (39,169)	0.002
T3 (ng/ml)	1.0 ± 0.2	1.0 ± 0.2	0.765
T4 (mcg/dl)	8.1 ± 2.0	7.1 ± 1.4	0.004
TSH (mIU/ml)	3.1 (1.4,7.2)	2.1 (0.7,5)	0.055
Total Cholesterol (mg/dl)	139.7 ± 21.4	159 ± 28.8	0.007
Iron (mcg/dl)	71 (13.5189.8)	87.7 (40,166.9)	0.005
TIBC (mcg/dl)	256.0 ± 57.3	269.5 ± 83.7	0.545
Tfs (%)	28.2 (3.4,93.4)	32.4 (16.7,50.3)	0.12
Ferritin (ng/ml)	212.8 (112,651)	288 (56,851)	0.39
LDL (mg/dl)	80.0 ± 20.0	82.4 ± 22.8	0.640
HDL (mg/dl)	40.2 ± 11.0	41.9 ± 5.9	0.386
VLDL (mg/dl)	19.4 ± 5.3	34.7 ± 11.2	<0.001
Triglycerides (mg/dl)	96.7 ± 26.9	174.3 ± 55.9	<0.001

Values are expressed as mean ± SD or median (min, max).
Hb: Hemoglobin, TLC: Total Leukocyte Count, FBS: Fasting Blood Sugar, PPBS: Postprandial Blood Sugar, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, iPTH: Intact Parathyroid Hormone, TSH: Thyroid-stimulating hormone, TIBC: Total Iron-binding Capacity, Tfs: Transferrin saturation, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very low-density lipoprotein.

prevalence of SDB in the two studies might be due to a higher median age (around 40 years in both the studies) with more comorbidities. In one of the two studies that show higher prevalence (16), even though a higher cutoff of AHI > 10/h is used to classify as an apneic, a higher prevalence could be because only patients suspected of having sleep apnea by the attending nephrologist were referred for further assessment in the pretransplant stage. The median BMI between OSA and non-OSA subjects was comparable in the two studies, showing higher prevalence and suggesting BMI as an unlikely confounder.

Table 4
Anthropometric findings pre and post kidney transplantation.

	Pre-Tx (n = 18)	Post-Tx (n = 18)	*p* value
BMI (kg/m^2)	19.3 ± 2.5	19.9 ± 2.8	0.315
Neck (cm)	33.1 ± 2.8	36.1 ± 12.3	0.316
Waist (cm)	77.9 ± 6.8	81.3 ± 8.9	0.152
Hip (cm)	84.7 ± 5.9	86.1 ± 6.7	0.426
Waist–Hip Ratio	0.9 ± 0.1	0.9 ± 0.1	0.152
Fat (%)	7.4 (2.1,23.4)	9.2 (4.2,25.1)	0.408

Values are expressed as mean ± SD or median (min, max).

There was a significant improvement in the prevalence of SDB after transplant. The present study detected that the median value of AHI was 1.2 (range 0–28.9), which decreased to 0.4 (range 0–7) (p = 0.034), which indicates that in addition to improvement in metabolic parameters there is a significant improvement in SDB after renal transplant. The results are in contrast to the studies by Beecroft et al. [16] and Rodrigues et al. [17], which showed no or minimal improvement in AHI after renal transplant, although the results are similar to those by Jurado-Gámez et al. [18] and Lee et al. [19], which showed significant improvement in AHI post-transplant.

Table 5
Correlation of polysomnographic measures in the pretransplant stage (n = 24).

Polysomnographic Variable	Laboratory Variable	Correlation coefficient	P value
AHI	TIBC	0.636	0.001
Baseline SaO_2	Hb	0.529	0.008
	TIBC	−0.554	0.005
SaO_2 < 90%	Hb	−0.450	0.028
	Ferritin	−0.492	0.015
Desaturation Index	Serum Iron	0.406	0.049
	TIBC	0.698	<0.001

TIB: Total Iron-binding capacity; Hb: Hemoglobin; SaO_2: Oxygen saturation of arterial blood.

The study by Beecroft et al. [16] showed no significant changes in AHI post-transplant (pre vs. post: 20.2 ± 15.1 vs 23.5 ± 21.3), and SDB was cured in only a minority of patients (3 of 11). However, the study group was comprised of an older population (47 ± 13 years in the OSA group and 42 ± 9 years in the non-OSA group) with higher BMI (28.6 ± 4.2 kg/m^2 in the apneic group and 28.2 ± 4.7 kg/m^2 in the non-apneic group) compared to our group. The prior study did not define the exact time interval between transplants and repeat PSG except stating that PSG was repeated several months after successful kidney transplantation. It is likely that post-transplant PSG was performed at varying intervals of time in different participants, as the authors stated that post-transplant PSG in non-responders was performed later than in responders.

The lack of significant decrease in the prevalence of apnea reported by Rodrigues et al. [17] could be because 22 (64.7%) patients noted improvement and 12 (35.3%) patients noted worsening of their AHI post-transplant. The authors observed that there was substantial weight gain after kidney transplantation as BMI increased significantly from 22.3 ± 4.1 kg/m^2 to 24.4 ± 4.2 kg/m^2 post-transplant. Even though there was no association between changes in BMI and AHI, the possible contribution of weight gain after kidney transplantation could not be excluded.

By contrast, Jurado-Gámez [18] observed that AHI improved in eight of the nine patients post-transplant. Even though the sample size was small, the AHI improved significantly in the whole group (10 ± 10.7 events/h pretransplant to 4.9 ± 6.1 events/h post-transplant). This study was similar in most aspects to our study except that the average age and BMI were higher and all allografts were cadaveric.

Lee et al. [19] also observed improved SDB in eight of the twelve patients with OSA. However, they did not use PSG and therefore comparison with our results is challenging.

Our patients also showed a significant reduction in the oxygen desaturation index (ODI) (median 5.8 events/h in the pretransplant group to median 0 events/h post-transplant). Fifty percent of patients in pretransplant stage had desaturation index >5/h which normalized in all patients post-transplant.

Beecroft et al. [16] and Lee et al. [19] did not report ODI. Jurado-Gámez et al. [18] observed a significant decrease from 25 ± 26 dips/h to 12 ± 11.2 dips/h. The study by Rodrigues et al. did not find a significant reduction in ODI post-transplant (2.5 ± 5.5 events/h to 2.1 ± 6.9 events/h).

The age range of our patients (19–50 years) was similar to the other studies. Owing to the limited availability of donor kidneys in our setup, there is a higher probability of a young patient receiving a transplant in view of the better general medical condition and prospective economic benefits of the patient returning to work and earning for their family. Although most of our patients belonged to the lower middle strata of the society, it is likely that the benefits would extend to all sections of the society, provided they are able to afford the treatment and follow-up regularly.

The median time for which patients were on HD in our study was much shorter, ie, six months (range 3–31 months) as compared to the study by Rodrigues et al. [17], where the median time on HD was 16 months. The decision for an early transplant in our patient population may have contributed to better results in terms of decrease in AHI. The only patient for whom SDB was not cured was aged 50 years. It may be argued that the maximal benefit of transplant in SDB occurs in the younger age group.

The 22% decline in the prevalence of hypertension is similar to that reported by Rodrigues et al. [17], where the percentage of patients on antihypertensive medications was reduced by 15% (71%–56%).

Cardiovascular disease is the most common cause of mortality in patients with renal transplant [23,24].

As per the risk factors for increased cardiovascular mortality in post-transplant patients, we observed a decrease in the prevalence of hypertension and AHI, with an insignificant difference in BMI, blood sugar level, and total fat percentage, and a significant increase in the levels of total cholesterol. This finding could be due to the corticosteroids that these patients were receiving as part of the immunosuppressive therapy. Long-term follow-up is required to comment on the sustained decrease in these traditional risk factors because there are studies [25,26] that have shown that there is a progressive weight gain as years pass by after the transplant, which could worsen SDB. Both AHI and desaturation index, as well as baseline SaO_2, were significantly associated with the mentioned parameters. This leads us to believe that improvement in hemoglobin in the post-transplant stage may improve the oxygen-carrying capacity of the blood, which would decrease desaturation index. Improvement in AHI, however, cannot be explained through this mechanism, as improvement in hemoglobin alone cannot improve airflow.

As per the possible mechanism of improvement in SDB after transplant, there was no insignificant increase in BMI, neck, waist and hip circumference, and body fat percentage. This gives us the clue that a combination of upper airway muscle tone improvement due to correction of electrolyte imbalance, improved ventilatory drive due to correction of uremia, and less fluid load may have led to decreased the severity of SDB. As discussed earlier, only 0.5-L fluid load in recumbency is enough to narrow parapharyngeal space [10]. Much of the body weight is accounted for by body fat and not by fluid status; therefore, it may not be reflected as improvement in BMI.

Thus, based on the strengths of our study, we have a reason to believe that SDB improves after renal transplant. Pretransplant PSG was carried out at a time closer to the transplant. There was uniformity in the post-transplant analysis, as repeat studies were performed three months post-transplant on clinically stable patients with stable graft function. Despite the strengths of our study, we acknowledge a number of limitations. First, we had limited sample size. Thus, we are supportive of efforts to study large samples across wider ranges of age and demographics to confirm or refute our findings. Second, we had limited duration of follow-up. By design, we wanted to study the effect of transplantation; hence, we chose a threemonth time period to avoid other secular trends over time, eg, weight gain from glucocorticoids, survivor

effects, progression of underlying neuromyopathy, etc. Nonetheless, we are supportive of long-term studies to assess the durability of our findings and how they might have an effect on important comorbidities. Third, we did not have a true untreated control group because all of our participants underwent renal transplantation. Thus, it is possible that some of our findings may have occurred over time, although we doubt that there was a spontaneous resolution of OSA in the absence of major weight loss. Fourth, as the mean age of participants obtaining a transplant in our study population was 28.9 ± 8.9 years, there may be a selection bias; therefore, the results cannot be generalized to all age groups. The fact that SDB was cured in all except one person, who was aged 50 years, supports this concept, but due to limited representation of this population, we cannot make this a conclusion. It is also obvious that younger people undergoing transplantation have fewer comorbidities and, therefore, may have better outcomes after transplant.

Despite these limitations, we believe that our findings are important.

In summary, we have demonstrated a high prevalence of SDB in Indian patients with ESRD. We have observed major improvement in OSA following renal transplant. Further work will be required to determine if OSA improvement following transplant is a mechanism underlying improvement in daytime symptoms and/or OSA-associated comorbidities.

5. Conclusion

Along with the improvement in renal parameters, there was a significant reduction in the prevalence as well as the severity of sleep-disordered breathing in patients with ESRD after renal transplant.

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Conflict of interest

All authors declare that they have no conflict of interest.

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