

Original Article

Risk of Obstructive Sleep Apnea Syndrome in Psoriasis Patients

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Introduction

Psoriasis (Ps) is a chronic, immune-mediated inflammatory disease that is characterized with sharply circumscribed erythematous-squamous plaques. Its prevalence ranges from 1.5% to 5%. Clinically affected individuals can easily be diagnosed through formations of silvery squamous plaques with a chronic course, especially observed on the extensor surfaces of the extremities such as the knees, elbows and hips, and the scalp; and the “Auspitz’s” phenomenon that can be observed upon slightly scratching the squamous part on the plaques, that indicates a disease-specific dermal papillomatosis.^{1,2} Although it was formerly considered to be only a skin disease until a few decades ago, it is now considered as a multisystemic disease.^{3,4} Seventy-three percent of Ps patients have at least one comorbidity⁵ such as arthritis, cardiovascular events, diabetes mellitus (DM), obesity, hypertension (HT), or dyslipidemia.¹ Due to the fact that both psycho-cutaneous effects of Ps and associated disturbances can lead to major vital burden,^{2,4} this can have a great impact on patients’ health-related Quality of life (QoL).^{1,4} In a similar manner, metabolic syndrome (MS) is a multisystemic disease that can be associated

with concurrent disorders such as HT, dyslipidemia, high blood glucose, cardiovascular disorders, uveitis, psychiatric disorders and Crohn’s disease. On the other hand, obstructive sleep apnea syndrome (OSAS) is a common sleep disorder that is observed with a prevalence of 2%–4% in the population and is characterized with complaints of intermittent hypoxia, recurrent awakening and excessive daytime sleepiness that is associated with recurrent partial or complete airway obstruction of the upper respiratory tract. Osteoporosis, chronic obstructive lung disease and OSAS have also been reported as comorbidities found in MS in recent studies.^{6,7} Moreover, OSAS causes an increase in risks of stroke, insulin resistance, type-2 DM, obesity, MS and cardiovascular disorders.^{3,8,10} Because both Ps and OSAS share some comorbidities such as obesity, type-2 DM and cardiovascular diseases, it is increasingly suggested that the two diseases can be due to similar pathogenic mechanisms. However, there are only a few studies that have investigated the relationship between Ps and OSAS. For these reasons, we aimed to research OSAS risk in Ps patients. After the subjects were classified into high and low-risk groups in terms of OSAS risks, they

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were compared with Ps parameters such as demographics, disease severity and duration, QoL and also sleep quality.

Materials and Methods

Study Design

A total of 57 subjects (31 male and 26 female) were enrolled in this study, who were referred to our dermatology clinic between January and July, 2017. They were selected from newly admitted patients to our clinic according to the inclusion and exclusion criteria. After the local Ethics Committee approval and the required written informed consent of the subjects were obtained, they were included in the study. Ps was diagnosed with both clinical and histopathological examinations. Inclusion criteria were as follows: ≥ 16 years of age, clinical and histopathological diagnosis of Ps, enough understanding to be given questionnaires, volunteering to participate, and having no other dermatological disorders. Subjects with cognitive impairment, psychiatric and other dermatological disorders were excluded from the study. Additionally, all subjects were consulted at the ear-nose-throat (ENT) and chest diseases clinics to detect any disorders in the upper respiratory tract (URT) such as acute or chronic viral/bacterial infection, previous surgical URT or chest wall operation, or congenital thoracic deformities that may lead to any obstructive condition. Thus, subjects with any disease were not included in the study. Subject age, gender, smoking and drinking habits, coexistent chronic diseases (DM, HT, heart disease, chronic kidney disease, chronic liver disease, thyroid disease etc) and disease duration were questioned, recorded and eventually evaluated.

Outcome Measures

After heights and weights of subjects were measured, body mass index (BMI) was calculated as weight (kilograms) divided by height (square meters) for an estimate of obesity. Evaluation of obesity was made as non-obese ≤ 29 kg/m², and obese ≥ 30 kg/m². Ps severity was evaluated using Psoriasis Area Severity Index (PASI) scoring which is the golden standard for determine in disease severity in Ps. PASI assesses both severity and expansion of lesions. Minimum score is 0 and maximum score is 72.¹¹ Sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI).¹² The questionnaire evaluates the subjective sleep quality for the past month includes the following 7 components; subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. A total score of ≥ 5 indicates bad sleep quality. This system was tested and validated in the Turkish population by Agargun et al.¹³ QoL of the subjects was evaluated with the Psoriasis Quality of Life Index (PQLI). This psoriasis-specific scale was first developed in our country by Aydemir et al, in 2003, and was integrated to QoL studies associated with Ps, after its validity and reliability were confirmed. The

scale is comprised of 17 questions organized in 3 categories which include disease findings, social and sexual lives of patients, and use of disease (Ps)-specific medication. The questionnaire is entirely composed of yes-no questions and all "yes" answers should further be rated in 4 different severity categories. There is no any cut-off value for this index. As PQLI score increases, QoL is proportionally and adversely impacted.¹⁴ Daytime sleepiness was evaluated with Epworth Sleepiness Scale (ESS). An ESS score of ≥ 10 was considered as daytime sleepiness.¹⁵ Risk of OSAS was evaluated using the Berlin questionnaire (BQ),¹⁶ and this is determined by positive score in at least two of the three categories in this questionnaire.¹⁷ BQ is evaluated in 3 categories. Category-1 assesses frequency and intensity of snoring and witnessed apnea, while Category-2 includes daytime sleepiness questions, and finally Category-3 evaluates the presence or absence of hypertension or obesity. A positive response of ≥ 2 is considered as positive score, and risk indicator in the first two categories, while a positive response of ≥ 1 is considered as positive score in the Category-3. High-risk for OSAS was determined by positive score in at least two of the three categories. According to this determination, subjects divided into two categories as high and low-risk groups. Duration and intensity of disorder, QoL, quality of sleep and daytime sleepiness were assessed in the high and low-risk groups, and compared to these groups.

Statistical Analysis

Acquired data was evaluated with the Statistical Package for Social Sciences (IBM SPSS Statistics, version 18, New York, USA, 2009) for windows. Standard descriptions were used as mean, standard deviation (SD), median (mean) or percentage (%). The normality assumption of the variables was checked using Kolmogorov-Smirnov test. So, independent sample *t* test was used for values which were distributed normal, whereas Mann-Whitney U non-parametric analysis test was used for asymmetric ones. Comparison of qualitative data was evaluated with Pearson's chi-square test and Fisher exact test according to kind of variables. An univariate logistic regression analysis was used for determination of variables in order to predict of risk of OSAS in Ps subjects, whereas a multivariate logistic regression analysis was used for detection of impacts of the determined significant variables. Accuracy rate of multivariate logistic regression analysis were checked with multivariate linear regression analysis. The significance of differences in means and percents was determined using 95% confidence intervals, and a *P* value < 0.05 was considered to be statistically significant.

Results

A total of 57 subjects, who were clinically diagnosed with Ps, were enrolled in the study (26 female, 31 male). General characteristics of the study population are seen in

Table 1. Mean age of the subjects was 46.91 ± 14.23 , with minimum age 21 and maximum age being 73. High-risk was confirmed in 35 subjects (61.40%) according to the BQ, while 22 of them (38.60%) were low-risk. Scores for the three categories of BQ were significantly higher in the high-risk group as compared to the low-risk group (Table 2). Ps subjects had HT, DM, alcohol use and smoking habit, in the rates of 26.3%, 12.3%, 14%, 45.6%, respectively. None of the subjects underwent any systemic therapy for their skin diseases except for topical therapies, and none had used any sleeping drug for the last month. Comparison of OSAS risk groups by the variables such

Table 1. General Characteristics of Subjects

Variables (n = 57)		Min-Max	Mean \pm SD
Age		21-73	46.91 \pm 14.23
Age of females		22-67	45.30 \pm 13.13
Age of males		21-42.9	48.25 \pm 15.18
BMI		21.9-42.9	30.44 \pm 5.02
PASI		1.5-70	19.34 \pm 18.58
PSQI		1-20	7.80 \pm 4.56
PLQI		0-51	19.38 \pm 16.90
Disease duration (y)		1-45	9.16 \pm 8.88
		n	%
Gender	Female	26	45.6
	Male	31	54.4
BQ	<2	22	38.60
	\geq 2	35	61.40

BMI, Body Mass Index; PASI, Psoriasis Area Severity Index; PSQI, Pittsburgh Sleep Quality Index; PLQI, Psoriasis Life Quality Index; BQ, Berlin questionnaire.

Table 2. Comparison of OSAS Groups by BQ Components

BQ Components	High-Risk Mean \pm SD (Median)	Low-Risk Mean \pm SD (Median)	P	95% CI	
				Lower	Upper
Category-1	3.17 \pm 1.15(1)	0.81 \pm 1.06(3)	0.000	0	4
Category-2	2.34 \pm 0.90(0)	0.86 \pm 1.24(2)	0.000	0	3
Category-3	0.45 \pm 0.61(0)	0.04 \pm 0.21(0)	0.003	0	1

OSAS, obstructive sleep apnea syndrome; BQ, Berlin questionnaire. Mann-Whitney U test; $P < 0.05$.

Table 3. Comparison of OSAS Risk Groups by Age, BMI, Study Scales, Disease Duration and Genders

Variables	OSAS (Berlin Questionnaire)		t/U	P	95% CI	
	High-risk Mean \pm SD (Median)	Low-risk Mean \pm SD (Median)			Lower	Upper
Age	47.62 \pm 13.61(49)	45.77 \pm 15.42(45)	0.476	0.633	-5.96	9.67
Women age	47.86 \pm 13.48(53)	41.81 \pm 12.38(44)	1.169	0.254	-16.72	4.63
Men age	47.45 \pm 14.06(49)	49.72 \pm 17.65(47)	-0.394	0.697	-16.61	4.52
BMI	31.80 \pm 5.29(27.8)	28.27 \pm 3.73(31.8)	2.727	0.009**	0.93	6.12
PASI	24.61 \pm 20.66(21)	10.96 \pm 10.45(8)	241.00	0.018*	4.11	23.18
PSQI	9.20 \pm 4.59(9)	5.59 \pm 3.60(5)	3.125	0.003**	1.29	5.92
PLQI	24.00 \pm 18.14(31)	12.04 \pm 11.72(10)	245.00	0.022*	3.23	20.67
ESS	10.94 \pm 6.31(11)	5.95 \pm 4.82(5)	3.167	0.003**	1.83	8.14
Duration	11.10 \pm 10.09(8)	6.09 \pm 5.42(4)	0.230	0.011*	0	7
Gender	No. (%)	No. (%)	χ^2			
Female (n = 26)	11 (50.0)	15 (42.9)	0.278	0.598		
Male (n = 31)	11 (50.0)	20 (57.1)				

OSAS, Obstructive sleep apnea syndrome; BMI, body mass index; PASI, Psoriasis Area Severity Index; PSQI, Pittsburgh Sleep Quality Index; PLQI, Psoriasis Life Quality Index; ESS, Epworth sleepiness scale.

*Independent sample t test, Mann-Whitney U test, Chi-square; * $P < 0.05$; ** $P < 0.01$.

as age, BMI, genders, studied scales and disease duration are seen in Table 3. Mean BMI of subjects was 30.44 ± 5.02 . Mean BMI was 31.80 ± 5.29 for the high-risk group compared to 28.27 ± 3.73 for the low-risk group. In the high-risk group, BMI was significantly high, and they were all obese ($P = 0.009$). Subjects' mean PASI was found as 19.34 ± 18.58 . Mean PASI for the high-risk group was 24.61 ± 20.66 as compared to 10.96 ± 10.45 for the low-risk group. Mean PASI was significantly higher in the high-risk group as compared to the low-risk group ($P = 0.018$). Mean disease duration was 9.16 ± 8.88 years. It was significantly longer in the high-risk group as 11.10 ± 10.09 , compared to 6.09 ± 5.42 in the low-risk group ($P = 0.01$). Mean score for QoL in Ps was 19.38 ± 16.90 . The mean of high-risk group was significantly higher as 24.00 ± 18.14 , compared to 12.04 ± 11.72 in the low-risk group, which was statistically significant ($P = 0.022$).

Risk factors in OSAS patients are seen in Table 4. None of the subjects had any chronic disease except for HT and DM, which both were significantly higher in high-risk group ($P = 0.019$ and 0.036), but there was no significant difference between the groups for alcohol using or smoking ($P = 0.466$ and 0.266). Comparison of PSQI components by OSAS groups are seen in Table 5. According to the PSQI components, subjects' quality of sleep was evaluated based on the total PSQI score. Four people in the high-risk group and 11 people in the low-risk group were characterized with good sleep quality. Mean PSQI of the subjects was 7.80 ± 4.56 . Mean PSQI for the

Table 4. Distribution of Subjects According to OSAS Risk Factors

Risk Factors of OSAS	Berlin Questionnaire		χ^2	P	Odd Ratio	95% CI	
	High-risk, No. (%)	Low-risk, No. (%)				Lower	Upper
HT							
Yes	2.9 (90.1)	13 (37.1.)	5.482	0.019*	5.909	1.18	29.47
No	20 (62.2)	20 (9.9)					
DM							
Yes	7 (20)	0	5.016	0.036*	1.79	1.40	2.28
No	28 (80)	22 (100)					
Alcohol use							
Yes	6 (17.1)	2 (9.1)	0.726	0.466	2.069	0.37	11.31
No	29 (82.9)	20 (90.9)					
Smoking							
Yes	18 (51.4)	8 (36.4)	1.236	0.266	1.853	0.62	5.52
No	17 (48.6)	14 (63.6)					

OSAS, obstructive sleep apnea syndrome; HT, hypertension; DM, diabetes mellitus. Chi-square, *Fisher exact test, $P < 0.05$.

Table 5. Comparison of PSQI Components According to the OSAS Risk Groups

PSQI Components	Berlin Questionnaire		t	P	95% CI	
	High-Risk Mean \pm SD (Median)	Low-Risk Mean \pm SD (Median)			Lower	Upper
Sleep quality	1.91 \pm 0.74 (2)	1.27 \pm 0.76 (1)	3.135	0.003**	0.23	1.05
Sleep latency	1.48 \pm 1.01 (1)	0.77 \pm 0.68 (1)	2.910	0.005**	0.22	1.20
Sleep duration	1.25 \pm 1.14 (1)	0.63 \pm 0.72 (.5)	2.266	0.027*	0.07	1.16
Sleep efficiency	0.65 \pm 1.10 (0)	0.36 \pm 0.78 (0)	1.079	0.285	-0.25	0.83
Sleep disturbances	1.45 \pm 0.61 (1)	1.18 \pm 0.50 (1)	1.771	0.082	-0.03	0.58
Use of sleeping drug	0.94 \pm 0.90 (1)	0.40 \pm 0.50 (0)	2.525	0.014*	0.11	0.95
Daytime dysfunction	1.48 \pm 0.74 (1)	0.81 \pm 0.85 (1)	3.120	0.003**	0.23	1.09

OSAS, obstructive sleep apnea syndrome; PSQI, Pittsburgh Sleep Quality Index. (Independent samples *t* test) * $P < 0.05$; ** $P < 0.01$.

high-risk group was 9.201 ± 4.59 , compared to 5.59 ± 3.60 in the low-risk group. Mean value for all seven PSQI components in the high-risk group was totally higher than the low-risk group. So, sleep quality in the high-risk group was significantly worse as compared to the low-risk group ($P = 0.013$). Higher scores were statistically significant in all components except for habitual sleep efficiency and sleep disturbances. Mean ESS of the subjects was 9.01 ± 6.23 . In the high-risk group it was 10.94 ± 6.31 with a statistically significant daytime sleepiness, whereas it was 5.95 ± 4.82 in the low-risk group ($P = 0.003$). Significance of determinant variables such as gender, age, PASI, disease duration, BMI, PLQI, HT, DM, alcohol consumption, and smoking in prediction of risk of OSAS in Ps subjects are seen in Table 6. According to the analysis, PASI ($P = 0.013$), BMI ($P = 0.014$), PLQI ($P = 0.012$) and HT ($P = 0.030$) had significance in the prediction of OSAS development. From these factors, only PASI and BMI showed significant impacts on the development of OSAS. But, development of OSAS risk more affected from increase in BMI values than increase in PASI values, when all significant variables remain constant (1.25-fold against 1.07-fold) (Table 7). Accuracy rate of the results was detected as 77.2%.

Discussion

In this study, 35 subjects with Ps (61.40%) had high-risk for OSAS. This rate was considerably higher than the prevalence reported by Ardıc et al's study (13.7%) which was a broadly based study performed on the Turkish population using the BQ.¹⁷ Similarly, Karaca et al found frequency of OSAS as 54.5% when they examined 33 Ps patients with polysomnography.¹⁸ Buslau et al evaluated the prevalence in 19 control patients with bronchitis correspondent to the 25 Ps patients in terms of age and gender; they observed a higher apnea hypopnea index in Ps patients, along with a high prevalence of OSAS.¹⁹

Ps is a chronic inflammatory skin disease that is accompanied by many disorders. The presence of a strong correlation was reported between Ps and obesity, with obesity being the most important element of MS indeed.²⁰ Ps and obesity are chronic inflammatory events. Fatty tissue secretes many cytokines like tumor necrosis factor-alpha (TNF- α) and many adipokines like leptin and adiponectin. TNF- α causes insulin resistance by increasing the production of free fatty acids, decreasing adiponectin synthesis and disrupting insulin signals.²¹ The amount of TNF- α has been found to be significantly more in the skin and joints of Ps patients in comparison to unaffected

Table 6. Significance of Variables in Prediction OSAS Risk

Variables	B	SE	Wald	df	Sig	Exp(B)	95% CI
Gender	-0.288	0.546	0.277	1	0.598	0.750	0.257–2.188
Age	-0.009	0.019	0.233	1	0.629	0.991	0.954–1.029
PASI	-0.053	0.021	6.219	1	0.013*	0.948	0.910–0.989
Duration	-0.102	0.053	3.680	1	0.055	0.903	0.814–1.002
BMI	-0.170	0.069	6.031	1	0.014*	0.844	0.737–0.966
PLQI	-0.048	0.019	6.267	1	0.012*	0.953	0.918–0.990
HT	1.766	0.820	4.694	1	0.030*	5.909	1.185–29.478
DM	20.962	15.191	0.000	1	0.999	1.269	0.00–0.00
Alcohol	0.727	0.867	0.704	1	0.402	2.069	0.378–11.310
Smoking	0.617	0.558	1.224	1	0.269	1.853	0.621–5.526

Univariate logistic regression analysis.

PASI, Psoriasis Area Severity Index; BMI, body mass index; HT, hypertension; PLQI, Psoriasis Life Quality Index. B, beta. This is the coefficient for the constant (also called the “intercept”) in the null model. SE, standard error. It is around the coefficient for the constant. Wald, chi-square test that tests the null hypothesis that the constant equals 0. *df*, degrees of freedom for the Word. Sig, significance value of independent variable. Exp(B), exponentiation of B(Beta) coefficient, which is an odds ratio.

Table 7. Impact Levels of Significant Variables in OSAS Risk Development

Variables	B	SE	Wald	Sig	Exp(B)	95% CI
Constant	-7.441	2.556	8.475	0.004	0.001	
PASI	0.067	0.023	8.100	0.004	1.069	1.021–1.119
BMI	0.226	0.081	7.723	0.005	1.254	1.069–1.471

Multivariate logistic regression analysis.

PASI, Psoriasis Area Severity Index; BMI, body mass index, B, beta. This is the coefficient for the constant (also called the “intercept”) in the null model. SE, standard error. It is around the coefficient for the constant. Wald, chi-square test that tests the null hypothesis that the constant equals 0. Sig, significance value of independent variable. Exp(B), exponentiation of B(Beta) coefficient, which is an odds ratio.

people.^{22,23} This suggests that obesity in Ps plays a key role in increasing the risk of MS and DM alongside cardiovascular diseases.^{24,25} On the other hand, OSAS is associated with cardiovascular risk factors and obesity.^{26,27} The relationship between OSAS and Ps can be explained by their sharing of similar comorbidities like obesity and cardiovascular risk factors. In OSAS, URT is inflamed, and presence of systemic inflammation is observed with elevated TNF- α , interleukin-6 and C-reactive protein levels along with an increase of oxidative stress.²⁸ Although Ps is known to impair sleep leading to insomnia, its association with Ps and OSAS is controversial. However, it is well-known that the prevalence of OSAS is higher in obese patients and the prevalence of obesity is increased in patients with Ps.²⁹ Yang et al found that the respiratory disturbance index was greater in patients with Ps than controls, and deep sleep was decreased.³⁰ Buslau and Benotmane showed the recovery of skin lesions of the three Ps patients who also had OSAS during positive airway pressure treatment.¹⁹ Their study results suggested a significant relationship between the two diseases, and that positive airway pressure treatment becomes effective in treatment of Ps by alleviating inflammation and improving sleep quality.²⁶ Due to the fact that disease severity of our Ps patients is significantly higher in the lower sleep quality group than the higher sleep quality group, our results support the above mentioned studies in terms of severe Ps patients who have high-risk for developing OSAS. When Papadavid et

al evaluated 35 Ps patients with polysomnography, they showed that OSAS was not associated with Ps severity and QoL. However, they showed that OSAS was related to disease duration in women in the sub-group analysis.³¹ The QoL of our patients was evaluated with PQLI which is unlike the questioner in Papadavid et al’s study. Because our index belonged to only Ps patients, but not to all skin diseases, we thought that the answers of our subjects to questions was only about their disease. Because specific QoL questionnaires may change according to the disease state, this difference may lead to important differences in final evaluations of disease-specific QoL. We observed that Ps duration was significantly longer in the high-risk group. In a study conducted by Karaca et al, Ps patients were evaluated with polysomnography, and patient groups with and without OSAS were assessed for Ps severity, disease duration and dermatological QoL, but they did not obtain any significant difference between the groups.¹⁸ In the present study, we evaluated high and low-risk groups for risk of OSAS with BQ, and statistically significant differences were detected between high and low-risk groups in terms of Ps severity, disease duration and QoL. When we look at the significance of determinant variables such as gender, age, PASI, disease duration, BMI, PLQI, HT, DM, alcohol consumption, and smoking in prediction of risk of OSAS in Ps subjects, we detect that PASI, BMI, PLQI and HT had significance in prediction of OSAS development. However, only PASI

and BMI showed significant impact on development of OSAS. Moreover, development of OSAS risk was slightly more affected by increase in BMI values relative to increase in PASI values (1.25-fold against 1.07-fold).

The presented study has some limitations such as a relatively low number of subjects, representing only a single center, lack of a control group, and absence of equal number of subjects in each OSAS group. Additionally, although polysomnography is the gold standard for the exact diagnosis of OSAS,³² we could not verify our results with polysomnography. Moreover, it has been stated that some sleep apnea questionnaires presents moderate diagnostic utility in detecting OSAS, especially in women.³² However, our detected significant differences between the OSAS groups is pointing to considerably high decrease in sleep quality in patients with severe Ps compared to the less severe group. Given the shared common chronic inflammatory pathogenesis in these two diseases, we think that the obtained results should not be surprising at all. Moreover, being that severity and duration of the Ps were high in the high-risk OSAS group suggests the need for a polysomnography evaluation for exact diagnosis for OSAS because OSAS is one of the very important cardiovascular risk factors. Our results supported the previously suggested bidirectional relationship between Ps and development of OSAS risk. For these reasons, we also think that OSAS may be a new comorbidity in Ps patients, which is recently being considered as a chronic inflammatory disease, or vice versa. Therefore, future studies need to be conducted on broad-based populations and along with polysomnographic evaluations. In conclusion, the risk of OSAS evaluated with BQ was found to be 61.40%. This rate was considerably higher than the prevalence of previously determined OSAS which was calculated in the Turkish population (13.7%). Determining higher PASI, longer disease duration and higher PQLI scores in the high-risk OSAS group support a positive correlation between severity of Ps and disturbance of sleep quality.

Authors' Contribution

Conception/Design of study: VKI, BT. Data acquisition: VKI, BT. Data analysis/interpretation: VKI, BT, HAD, AS. Drafting manuscript: VKI, BT, MA, HDA, AS. Critical revision of manuscript: VKI, BT, MA, HDA, AS. Final approval and accountability: VKI, BT. Technical or material support: VKI, BT, MA, HDA, AS. Supervision: VKI, BT, HDA, AS.

Conflict of Interest Disclosures

The authors declare that there is no conflict of interest which could be perceived as prejudicing the impartiality of the research reported.


Ethical Statement

Required ethical committee approval was obtained from local ethical committee (Approval code:2018.11.1.08.108).

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