EVALUATION OF RETINAL NERVE FIBRE LAYER THICKNESS AND OPTIC NERVE HEAD PARAMETERS IN OBSTRUCTIVE SLEEP APNOEA PATIENTS

By

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DISCLAIMER

I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been duly acknowledge.

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Abstrak

Pengenalan

“Obstructive sleep apnea (OSA)” atau sindrom tidur berapnea adalah masalah gangguan pernafasan ketika tidur yang boleh membahayakan nyawa. Sindrom ini melibatkan gangguan pernafasan separa (hypopnoea) dan gangguan pernafasan total (berhenti bernafas atau apnoea) berlanjutan sekurang-kurangnya 10 saat ketika tidur. Akibatnya berlaku kekurangan oksigen dalam darah. OSA seringkali menyebabkan masalah gangguan saraf (“NAION”, “bengkak saraf optik”, glaukoma) dan juga masalah salur darah tersumbat (CRVO). Pemeriksaan tomografi koheran optikal (OCT) boleh mengukur ketebalan saraf lapisan retina dan parameter sarah optik yang berkemungkinan mengalami perubahan disebabkan penyakit OSA.

Objektif

Tujuan kajian ini adalah untuk membandingkan perubahan ketebalan saraf retina dan perubahan pada parameter saraf optik antara pesakit OSA dan subjek kawalan. Analisa mengkaji perkaitan anatara perubahan pada parameter tersebut dengan tahap keterukan penyakit tersebut.

Bahan dan kaedah

Satu perbandingan kajian "cross-sectional" telah dijalankan di Hospital Universiti Sains Malaysia yang melibatkan seramai 54 orang pesakit OSA dan 54 orang subjek kawalan. Pemeriksaan mata secara menyeluruh dilakukan sebelum pesakit menjalani

ujian imbasan tomografi koheren optikal (OCT). Untuk analisa statistik, kaedah "Chi square, Fisher exact test, Independant t-test, dan analisa regressi dan korelasi digunakan.

Keputusan

Terdapat penipisan ketara pada ketebalan lapisan saraf retina di kalangan kumpulan pesakit OSA berbanding subjek kawalan, ($p=0.008$ pada purata saraf dan $p<0.001$ pada saraf quadrant atas). Analisis regressi menunjukkan perkaitan secara linear negatif yang signifikan antara ketebalan lapisan saraf retina dengan tahap penyakit OSA ($R= 0.293$, $p=0.030$, $r= -0.293$ pada kuadran atas, $R=0.292$, $p=0.032$ $r= -0.292$ pada kuadran nasal). Tiada perbezaan ketara antara parameter saraf optik antara OSA dan subjek kawalan dan tiada hubungan yang signifikan ditemui antara parameter-parameter tersebut dengan tahap penyakit OSA.

Kesimpulan

Pesakit OSA mempunyai lapisan saral retina yang lebih nipis dari subjek kawalan dan perubahan ini mempunyai perkaitan yang signifikan dengan keterukan penyakit tersebut.

Kata Kunci: Sindrom tidur berapnea (OSA), index apnea/hypopnea (AHI index), Ketebalan lapisan saraf retina (RNFL thickness), Parameter kepala saraf optik (ONH).

ABSTRACT

Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder which can be life threatening characterized by partial (hypopnoeas) and complete pauses (apnoeas) in breathing lasting at least 10 seconds during sleep. As a result, the blood oxygen saturation may fall, with resulting in a hypoxia state. OSA has been associated with ocular conditions such as non-arteritic anterior ischemic optic neuropathy (NAION), papilloedema, glaucoma and central retinal vein occlusion. Optical Coherent Tomography (OCT) can measure the retinal nerve fibre layer (RNFL) thickness and optic nerve head (ONH) parameter changes that can result from the disease.

Objective

The aim of this study was to compare the changes of RNFL thickness and ONH parameters in patients with OSA and control group. We also analyzed the relationship between these parameters with the severity of OSA.

Material and methods

A comparative cross-sectional study was conducted in Hospital Universiti Sains Malaysia involving 54 samples who was diagnosed to have OSA based on overnight polysomnography (PSG) and 54 control subjects. A complete ocular examination was performed. RNFL thickness and ONH parameters were measure using the OCT. Independent t-test, chi square, Exact Fisher test, correlation and regression analysis

were use in the statistical analysis.

Results

There were statistically significant thinning of the RNFL of the OSA group compared to control. In obstructive sleep apnoea group (OSA), mean of average RNFL thickness was 93.87µm, SD= 9.17, p=0.0008 (p<0.05) while superior RNFL thickness was 113.59µm, SD=16.29, p= <0.001 (<0.05). The changes in RNFL thickness has fair significant linear relationship with the severity of the disease particularly involving superior RNFL with R=0.293, R2= 0.087 r= -0.293 p=0.030 (p<0.05), and nasal RNFL R=0.292, R2=0.085, r= -0.292 p=0.032 (p<0.05). Optic nerve head parameters had no significant difference from control and there was no significant direct linear relationship of all the optic nerve head parameters with the severity of the disease. However, the RNFL thickness was confounded by dyslipidaemia.

Conclusion

OSA patients have significantly thinner in average and superior RNFL layer compared to control. There was fair significant direct linear relationship of RNFL thickness with the severity of the disease.

Key Words: Obstructive sleep apnoea (OSA), Retinal nerve fibre layer (RNFL) thickness, optic nerve head (ONH) parameters , Apnoea/hypopnoea index (AHI)

Chapter 1:

Introduction

1.1 Obstructive Sleep Apnoea

Obstructive sleep apnea syndrome (OSA) is characterized by repetitive episodes of upper airway obstruction that occur during sleep, usually associated with a reduction in blood oxygen saturation (American Academy of Sleep Medicine 2005). It is a chronic disorders which is common in overweight middle-aged men and women.

This sleep-related breathing disorder can be life threatening. When the throat muscles relax during sleep, soft tissue in the throat tend to collapse and block the upper airway. This condition results in partial (hypopnoeas) and complete pauses (apnoea) in breathing that last at least 10 seconds during sleep. As a consequence, the blood oxygen saturation may fall, with oxygen levels decreasing by as much as 40 percent or more in severe cases (Medicine, 2014).

Chronic oxygen deprivation subsequently results in activation of the sympathetic pathway, vascular endothelial dysfunction, increased oxidative stress, inflammation, increased platelet aggregatability, and metabolic dysregulation. These factors could contribute to the initiation and progression of vascular diseases (Glacet-Bernard et al., 2010), in which OSA has been shown to be associated with increased risk of coronary artery disease, heart failure, stroke, hypertension and arrhythmia.

The diagnosis of OSA is made by polysomnographic monitoring. It consist of monitoring of sleep by electroencephalography, electrooculography, electromyography, airflow, and respiratory muscle effort, and should also include measures of electrocardiographic rhythm and blood oxygen saturation. Changes in cardiac rhythm, particularly bradytachycardia, frequently occur with the apneic episodes. The arterial oxygen saturation level falls during the apneic episode and rises to baseline levels at the termination of the apneic episode. Carbon dioxide

values in the blood are usually only transiently elevated, but sustained elevations can be seen in some patients. Diagnosis of OSA was made with the presence of apnoea hypoapnoea episodes of 5 or more in an hour of sleep.

1.2 Prevelance of Obstructive Sleep Apnoea

In Western populations, the prevalence is around of 4% for men and 2% in women but produced variable result among Asian studies range from 3.57% to 15.5% (Puvanendran et al., 1999, Kim et al., 2004, Sharma et al., 2006, Asaoka et al., 2010). Various study had been done and the above prevalence were taken from community studies using questionaires to evaluate the risk for OSA but the diagnosis were still made via a polysomnogram study. In many studies, prevalence of OSA in men were higher compared to women. Quintana-Gallego in a clinical studies suggest that possible reason for this discrepancy in the clinical and epidemiological studies is that the clinical significance and the potential of morbidity for having a high AHI in the general population is lower in females. Less women involved in out-of-home employment compared to man, hence the symptoms less recognised. Another reason, however, is that sociocultural factors or differences in clinical expression of this disorder would result in less and later consultations of women, or alternatively their clinical picture could be less recognized by primary care physicians and therefore OSA may be underdiagnosed (Quintana-Gallego et al., 2004).

Pillar reported higher indexes of depression and anxiety in women irregardless of age groups and AHI levels without clear association between these symptoms and OSA in the female group. Furthermore, the presentation of women with non-specific symptoms, in addition to the classic symptoms, which could make physicians turn to other diagnostic possibilities especially psychiatric reason instead of OSA (Pillar and Lavie, 1998).

1.3 Obstructive Sleep Apnoea And Ocular Disease

1.3.1 OSA and Glaucoma

Many researcher had came out with studies associating glaucoma and OSA. Sergi reported higher prevalence of normal tension glaucoma (NTG) in OSA patients compared with a control (Sergi et al., 2007), while another study documented a relative risk for NTG in OSA is 3.34 (Bilgin, 2014). Tsang et al. reported that moderate to severe OSA was associated with a higher incidence of visual field defects and glaucomatous changes in the optic nerve (Tsang et al., 2006). Moghimi reported that OSA patients had reduction in the retinal nerve fiber layer (RNFL) thickness and were at higher risk to develop glaucoma and (Moghimi et al., 2013). Bendel, in a cross-sectional case series involving hundred patients of moderate and severe OSA estimated the prevalence of glaucoma in their group of OSA, which is as high as 27% (Bendel et al., 2007).

1.3.2 OSA and Non-Arteritic Ischaemic Optic Neuropathy (NAION)

Based on specific questionnaires among non-arteritic ischaemic optic neuropathy (NAION) patients, subjects were 2.5 times likely to report symptoms and characteristics consistent with OSA as compared to control (Li et al., 2007). However, in a more recent study using polysomnography (PSG) and controlled for age, sex and risk factor for NAION, OSA found as contributing factor but not a risk factor for NAION (Arda et al., 2012). Palombi, in study involving patients referred for NAION found that despite classical risk factor associated with NAION; diabetes mellitus and hypertension, it was found that the prevalance of OSA in their

studies even higher than the two classical risk factors (diabetes mellitus 49%, hypertension 26%, OSA 89%). Their study found almost similar finding by Mojon (2002), hence concluded that NAION is more commonly associated with OSA compared to diabetes mellitus and hypertension (Palombi et al., 2006).

1.4 RNFL and ONH Changes in OSA

NAION and glaucoma are both optic neuropathies. Their structural changes include retinal nerve fibre layer (RNFL) changes and optic nerve head (ONH) parameters changes. Studies have come out to associate these changes with the severity of OSA by using optical coherence tomography (OCT) as a more objective assessment. Recurrent repeated episode of apnoea during sleeping subsequently result in hypoxemia, hypercapnia, haemodynamic, humoral, and neuroendocrine responses affect the circulation of the optic nerve (Mannarino et al., 2012). Kergoat et al. reported that the retinal ganglion cells are particularly sensitive to normal perfusion and a decrease in oxygen saturation (2006). Another possible mechanism for thinning of the RNFL in patients with OSAS is that hypoxia and hypercapnia causes vasodilation leading to increases in intracranial pressure. This indirectly disturbs cerebral perfusion and the blood flow to the optic nerve. Intracranial pressure was found to increase by apnea episodes occurring during sleep in OSA patients but was found to be normal in those patients during the day (Jennum et al., 1989). Repetitive episode of hypoxia and reperfusion in OSAS can result in inflammation and oxidative stress (Jelic et al., 2008). Oxidative by-products are increased in OSA and are declined with CPAP therapy. Elevated markers of oxidative stress in OSA include xanthine oxidase and lipid peroxides were found accompanied by a decrease in antioxidant capacity (Ramar & Caples, 2011).

Casas et al. found that OSA patients had thinner RNFL and increased in ONH area and volume. She suggested the possibility of neuronal degenaration in the optic nerve as previously observed in other neurodegenerative disease (Casas et al., 2013). However, there are also other studies that do not found significant different in the thickness of RNFL in OSA compared to control (Nowak et al., 2011, Adam et al., 2013). Purvin in a case series published postulated that the various result of RNFL thinning may be contributed by the fact that subclinical papilloedema occur in OSA, hence swelling of the nerve fibre layer may occur in early part of the disease, therefor did not show decrement of the RNFL (Purvin et al., 2000).

1.5 Rationale of Study

Obstructive sleep apnoea had been linked to various ocular diseases, mainly that causes optic neuropathy such as glaucoma and non arteritic optic neuropathy. This study aim to prove that there is significant effect of obstructive sleep apnoea on the optic nerve that is not clinically evident yet, in which could possibly later progress to optic neuropathy. If this study can prove that significant thinning of the retinal nerve fibre layer as well as changes occur in the optic nerve head parameters as the disease progress, this will suggest that subtle changes of optic neuropathy do occur in these group of patients, which may not be recognised earlier until patient already suffered from optic neuropathy. Ocular diseases such as glaucoma and NAION have been shown to associate with OSA, Therefore suggesting that this sussceptible group should routinely get an eye examination to prevent the development of the conditions leading to optic neuropathy. The regular eye check up should also include the optical coherent tomography as an adjuct to the clinical examinations to detect a more subtle changes before it become clinically obvious. OCT can measure the thickness of the RNFL and ONH parameters before a more obvious clinical symptoms and sign of optic neuropathy occur, hence may provide a more

objective measurement of the RNFL thickness and ONH parameters during screening and follow up on obstructive sleep apnoea patients who are at risk of developing the disease.

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CHAPTER 2:

OBJECTIVES

2. OBJECTIVES

2.1 General Objective

To study the retinal nerve fibre layer thickness and optic nerve head (ONH) parameters in obstructive sleep apnoea patients

2.2 Specific Objectives

2.2.1 To compare the mean of retinal nerve fibre layer thickness in obstructive sleep apnoea patient and control

2.2.2 To correlate between retinal nerve fibre layer thicknes and AHI in obstructive sleep apnoea patients

2.2.3 To compare the mean of the optic nerve head (ONH) parameters of obstructive sleep apnoea patient and control

2.2.4 To correlate between the the optic nerve head (ONH) parameters and AHI of obstructive sleep apnoea patients

CHAPTER 3:

MANUSCRIPT

TITLE : EVALUATION OF RETINAL NERVE FIBRE LAYER THICKNESS AND

OPTIC NERVE HEAD PARAMETERS IN OBSTRUCTIVE SLEEP APNOEA PATIENTS

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Running head : RNFL and ONH , OSA.

ABSTRACT

Objective: To study the retinal nerve fibre layer thickness and optic nerve head parameters in obstructive sleep apnoea patients and their relationship with severity of the disease. **Methods:** A cross-sectional, hospital-based study. 54 obstructive sleep apnoea (OSA) subjects and 54 controls were recruited. Candidate that fulfil the criteria with normal ocular examinations then proceed with SD-Cirrus OCT examinations. Optic nerve head (ONH) parameters and retinal nerve fibre layer (RNFL) thickness were evaluated. Apnoea/Hypopnoea Index (AHI) of the obstructive sleep apnoea group were obtained from the medical record. **Results:** In OSA, mean of average RNFL thickness was 93.87µm, SD= 9.17, P=0.008 (P<0.05) while superior RNFL thickness was 113.59µm, SD=16.29, p= <0.001 (P<0.05). RNFL thickness fairly correlate with severity of the disease (AHI), superior RNFL with R=0.293, R2= 0.087, P=0.030 (P<0.05), and nasal RNFL R=0.292, R2=0.085, P=0.032. No significant difference and correlation observed on ONH parameters. **Conclusion :** The mean of the average and superior RNFL thickness were significantly lower in the OSA group compare to control. Regression analysis showed RNFL thickness having significantly linear relationship with the apnoea/hypopnoea index (AHI), specifically involving the superior and nasal quadrant.

Keywords : ONH , RNFL, OSA, AHI.

INTRODUCTION

Obstructive sleep apnoea syndrome (OSA) is characterized by repetitive episodes of upper airway obstruction that occur during sleep, usually associated with a reduction in blood oxygen saturation [1]. The prevalence in Asian populations ranges from 3.57% to 15.5% [2-5].

Over the past two decades various studies have found the link between OSA and systemic diseases such as heart failure [6], diabetes mellitus [7], cognitive impairment [8], and ocular diseases; non arteritic anterior ischaemic optic neuropathy (NAION) [9-11], glaucoma [12-15], retinal vein occlusion [16] and, central serous chorioretinopathy [17,18]

Chronic oxygen deprivation in OSA may results in activation of the sympathetic pathway, vascular endothelial dysfunction, increased oxidative stress, and inflammation, which may contribute to the initiation and progression of vascular diseases [16]. It is postulated that there is a reduction of ocular perfusion pressure and decreased oxygenation to the optic nerve, causing ischaemia particularly to the sensitive ganglion cell layer resulting in optic neuropathy in OSA patients [19].

Optical coherence tomography (OCT) provides measurement of the thickness of the retinal nerve fibre layer (RNFL) and optic nerve head (ONH) parameters. RNFL thickness and ONH changes may reflect the changes that occur due to hypoxia in OSA. It was found that RNFL thinning was observed in OSA patients [20, 21]. Theoretically, the severity of OSA will result in thinner RNFL and ONH parameter changes based on the severity of the hypoxia [20]. However, there are also studies that have not been able to demonstrate the difference in the RNFL and ONH parameters changes in OSA [22,23].

Our study aimed to compare the difference between mean RNFL thickness and ONH parameters in OSA patients and control. We also examined the potential relationship between RNFL thickness and ONH parameters and severity of OSA. We were also taking into consideration other factors that can also contribute to RNFL thinning; age, gender, obesity and smoking, which has not much been addressed in previous studies.

MATERIAL AND METHODS

This observational cross-sectional study was conducted between May 2015 and February 2017. This study obtained ethical approval from the Human Research Ethics Committee, Universiti Sains Malaysia (USM/JEPeM/15050160) and was conducted in accordance with the Declaration of Helsinki for Human Research.

Patient Selection

Recruitment of OSA patients was conducted in the Department of ORL-HNS Hospital Universiti Sains Malaysia. A total of 54 OSA patients were recruited. Both newly diagnosed OSA and known cases on treatment with continuous positive airway pressure therapy (CPAP) were recruited. OSA was diagnosed based on apnoea/hypopnoea index (AHI) on polysomnogram. AHI of ≥ 5 events/ hour was diagnosed of having sleep apnoea. The severity of OSA was divided into mild (AHI 5-15), moderate (16-30), and severe (>30). The control group consists of 54 individuals presented to Ophthalmology clinic without history of sleep apnoea. Only OSA patients and control subject who have best corrected visual acuity of at least 6/12 using the Snellen chart and clear ocular media with refractive error of not more than +/- 6.0

dioptre were included in this study. Subject who had a pre-existing optic neuropathy, retinopathy, maculopathy, history of trauma or previous ocular surgery, and systemic disease of neurological and demyelinating diseases were excluded. All participants who consented to take part in the study undergo thorough ocular examinations and fundus evaluation via slit lamp biomicroscopy (Topcon Corp, Japan). Intraocular pressure measurement were performed to rule out ocular pathology, which would have precluded participation in the study. Intraocular pressure was assessed with air-puff tonometer to ensure minimal manipulation to the cornea surface in order to prevent artifact on the OCT images. All participants were then subjected for OCT examinations for the right eye.

Optical coherence tomography (OCT)

OCT examinations was performed using Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA) using the fast RNFL scan protocol. The tests were performed by a single and well trained operator . Only the test or repeated test that yielded signal strength of $\geq$ 6/10 was taken for interpretations to ensure accuracy of the results. Measurement were taken on right eye which include average RNFL thickness, rim area, disc area, average cup/disc ratio, vertical cup/disc ratio, cup volume and RNFL thickness in 4 quadrant (superior, inferior, nasal and temporal).

Statistical analysis

Data analysis was performed using the SPSS statistical package version 22 (SPSS, Chicago, IL,USA). Descriptive analysis was used for the mean values and SD. All values will be tested for normal distribution in both groups. For demographic data, they will be tested for comparison of age, race and gender. The Student t-test, Pearson Chi-Square and Fisher's exact test were used to analyse the demographic data. All P-values of <0.05 were considered statistically significant.

Independent t-test were used to compare the means of optic nerve head parameters and retinal nerve fibre layer thickness between study group and control. P value of < 0.05 was considered as significant. Pearson correlation were use to determine the correlations of optic nerve head parameters and retinal nerve fibre layer thickness and the AHI in the obstructive sleep apnoea group. The strength of association was determined and P value of <0.05 was considered significant. General guidelines for assigning strength of association by Cohen (1988) will be used.

Coefficient Value	**Strength of Association**
0.1 < r < 0.3	Small / weak correlation
0.3 < r < 0.5	Fair/ moderate correlation
R > 0.5	Large / Strong correlation

Result

There were a total of 108 participants. Among them 71 were male while 37 of them were female. The age of the participants ranged from 22 to 78 years. OSA patients have higher body mass index (BMI), more medical comorbidities and less number of active smoker compared to control subjects (Table 1).

Table 1: Demographic data of obstructive sleep apnoea subjects and control

	OSA N=54	Control N=54	P Value
Mean Age (Mean, SD)	45.69 (11.41)	42.54 (13.13)	0.186[a]
Sex (n, %)			0.839[b]
Male	35 (32.4)	36 (33.3)	
Female	19 (17.6)	18 (16.7)	
Race (n, %)			0.750[b]
Malay	48 (44.4)	49(45.4)	
Chinese	6 (5.6)	5 (4.6)	
Mean BMI (Mean, SD)	33.04 (6.29)	25.94 (3.22)	<0.001[a]
Smoking Status (n, %)			0.003[c]
Non-Smoker	50 (46.3)	37 (34.3)	
Smoker	4 (3.7)	17 (15.7)	
Medical Problem (n, %)			
Diabetes Mellitus	9 (7.4)	8 (8.3)	0.792[b]
Hypertension	19 (17.8)	11 (10.3)	0.075[b]
Dyslipidaemia	18 (16.8)	10 (9.3)	0.069[b]
Heart Disease,	2 (1.9)	0(0.0)	0.150[b]

a Independent t test

[b]Pearson Chi-square test

[c] Fisher's Exact Test

The mean RNFL values of OSA patients and controls are shown in Table 2. We observed a

significant difference in the mean of average RNFL thickness with P =0.008 and superior thickness with P= <0.001 between the control and study group.

Table 2: Comparing mean of retinal nerve fibre layer thickness of right eye in obstructive sleep apnoea patient and control

RNFL Thickness (µm)	OSA (N=54) Mean (SD)	Control (N=54) Mean (SD)	t	Means Difference	Confidence Interval 95%		df	P value*
					Lower	Upper		
Average	93.87(9.17)	98.96 (10.50)	2.686	5.093	1.333	8.852	104.12	0.008*
Superior	113.59(16.29)	125.76(14.93)	4.047	12.167	6.206	18.127	105.20	<0.001*
Inferior	123.06(17.79)	126.80(16.02)	1.148	3.741	-2.719	10.200	104.87	0.253
Nasal	69.65(9.61)	71.04(11.21)	0.691	1.389	-2.595	5.373	103.59	0.490
Temporal	67.87(14.20)	72.09 (12.78)	1.624	4.222	-0.932	9.376	104.85	0.107

Independent t-test

Multivariate analysis (MANCOVA) was performed to look into the possibilities of diabetes mellitus, hypertension and dyslipidaemia becoming covariates affecting our results.

Table 3: Multivariate analysis of covariant (MANCOVA) of right eye RNFL thickness in Obstructive Sleep Apnoea Subject and Control.

Effect	Value	F	Hypothesis df	Error df	Partial Etan Square	Significance
Age	0.910	0.901	10.00	91.00	0.900	0.536

BMI	0.950	0.477	10.00	91.00	0.500	0.901
Smoking	0.841	1.722	10.00	91.00	0.159	0.088
Diabetes Mellitus	0.921	0.705	10.00	91.00	0.072	0.718
Hypertension	0.901	0.996	10.00	91.00	0.099	0.453
Dyslipidaemia	0.827	1.900	10.00	91.00	0.173	0.055

The MANCOVA analysis showed that the age, body mass index, smoking, diabetes mellitus, hypertension and dyslipidaemia were not the confounder affecting the thickness of retinal nerve fibre layer in our study.

Table 4: Comparing mean of optic nerve head parameters of right eye in obstructive sleep apnoea patient and control

ONH Parameters	**OSA (N=54) Mean (SD)**	**Control (N=54) Mean (SD)**	**t**	**Means Difference**	**Confidence Interval 95%**		**df**	**P value***
					Lower	**Upper**		
RNFL Symmetry(%)	87.07 (8.18)	83.67 (9.92)	1.947	3.407	-6.879	0.640	102.30	0.054
Rim Area	1.303(0.214)	1.346 (0.232)	1.002	0.043	-0.042	0.128	105.34	0.319
Disc area	2.023(0.331)	2.123(0.421)	1.373	0.100	-0.044	0.244	100.46	0.173
Average CDR	0.567(0.108)	0.563(0.163)	0.146	0.004	-0.567	0.049	91.870	0.884
Vertical CDR	0.522(0.119)	0.524(0.162)	0.061	0.002	-0.053	0.056	97.40	0.952
Cup Volume	0.170(0.119)	0.214(0.155)	1.636	0.436	-0.009	0.096	106.00	0.105

Independent t-test

There were no significant difference between mean of optic nerve head parameters of obstructive sleep apnoea subjects and control.

Table 5 shows that there was a significantly fair negative correlation between AHI and RNFL thickness among the subject in the OSA group in the superior R= 0.295, R2= 0.087,r= -0.295, p= 0.030 ($p<0.05$) and nasal quadrant R=0.292, R2= 0.085, r= - 0.292, p=0.032 ($p<0.05$). However, none of the optic nerve head parameters had significant linear relationship with the AHI among subjects in the OSA group.

Table 5: Correlation between the retinal nerve fibre layer thickness of right eye and apnoea/hypopnoea index (AHI) in the obstructive sleep apnoea patients

	R	**R^2**	**F**	**r**	**P value***
RNFL Thickness					
Average	0.228	0.052	2.845	-0.228	0.980
Superior	0.295	0.087	4.962	-0.295	0.030*
Inferior	0.043	0.002	0.097	-0.043	0.756
Nasal	0.292	0.085	4.852	-0.292	0.032*
Temporal	0.102	0.010	0.548	-0.102	0.463
ONH Parameters					
Rim Area	0.029	0.001	0.043	0.029	0.836
Disc Area	0.248	0.062	3.410	0.248	0.070