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ORIGINAL ARTICLE

Disorders of the Sleep-Wake Cycle in Blindness

Troubles du cycle veille-sommeil dans la cécité

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ABSTRACT

BACKGROUND: **Alteration of the intensity of light reaching the pineal gland through the visual pathway affects the sleepwake cycle in humans.**

OBJECTIVE: **To determine the prevalence, types and severity of sleep-wake disorders in the blind and their relation to the degree and cause of blindness.**

METHODS: **One hundred and seventy consecutive blind patients were included in the study. The patients were interviewed and administerd the Montgomery Asberg Depression Rating Scale (MADRS) and the Pittsburg Sleep Quang Index (PSQI) questionnaire. Information collected included age, sex, visual loss parameters, type and degree of sleep-wake disorder.**

RESULTS: **A total of 138 (81.2%) blind patients had sleepwake disorders with significant disorder found in 84(49.4%). The mean PSQI ± SD were 8.4 ± 2.91, 9.6 ± 3.3 and 8.0 ± 2.7 globally, no light perception group and the remaining blind patients respectively. The commonest type of sleep-wake disorder was day time nap [112(65.9%)]. Forty-one (46.1%), 33(58.9%), 8(80.0%), 2(100%) and 0(0.0%) of those that had cataract, glaucoma, optic atrophy, uveitis and others respectively had moderate and/or severe sleep-wake disorder. The relationship between degree of blindness and prevalence and severity of sleep-wake disorder was very significant statistically (p = 0.008 and 0.002 respectively). The relationship between causes of blindness and prevalence and degree of sleep-wake disorder was statistically significant (p=0.009 and 0.007 respectively).**

CONCLUSION: **This study has shown that the prevalence of sleep-wake disorders in the blind is high and a strong relationship exists between visual loss and the sleep-wake cycle in humans. WAJM 2010; 29(3): 163–168.**

Keywords: **Circadian rhythm, sleep-wake cycle, disorders, blindness, melatonin.**

RÉSUMÉ

CONTEXTE: *Modification de l'intensité de lumière qui atteint la glande pinéale par la voie visuelle affecte la sleepwake cycle chez les humains.*

OBJECTIF: *Déterminer la prévalence, le type et la gravité des troubles du sommeil-éveil chez les aveugles et leur relation à la le degré et la cause de cécité.*

MÉTHODES: *Cent soixante-dix consécutifs aveugles patients ont été inclus dans l'étude. Les patients ont été interrogés et administerd l'Asberg Montgomery Échelle d'évaluation de la dépression (MADRS) et le sommeil Pittsburg Quang Index (PSQI) questionnaire. Les renseignements recueillis âge, le sexe, les paramètres de la perte visuelle, le type et le degré de trouble du sommeil-éveil.*

RÉSULTATS: *Un total de 138 (81,2%) patients aveugles avait sleepwake troubles de troubles importants dans 84 (49,4%). La moyenne ± SD PSQI étaient de 8,4 ± 2,91, 9,6 ± 3,3 et 8,0 ± 2,7 globalement, aucun groupe perception de la lumière et le reste aveugle patients, respectivement. Le type de veille-sommeil désordre était sieste pendant la journée [112 (65,9%)]. Quarante et un (46,1%), 33 (58,9%), 8 (80,0%), 2 (100%) et 0 (0,0%) de ceux qui avait la cataracte, le glaucome, l'atrophie optique, uvéite et d'autres respectivement, avaient modérée et / ou graves troubles du sommeil-éveil. La relation entre le degré de cécité et de la prévalence et la gravité des troubles du sommeil-éveil est très important statistiquement (p = 0,008 et 0,002, respectivement). La relation entre les causes de la cécité et de la prévalence et le degré de trouble du sommeil-éveil était statistiquement significative (p = 0,009 et 0.007 respectivement).*

CONCLUSION: *Cette étude a montré que la prévalence de troubles du sommeil-éveil chez les aveugles est élevé et une forte relation existe entre la perte de vision et le cycle veille-sommeil dans humains.* ***WAJM 2010; 29 (3): 163–168.***

Mots-clés: *rythme circadien, le cycle veille-sommeil, les troubles, la cécité, la mélatonine.*

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Abbreviations: ANOVA, Analysis of Variance; **MADRS,** Montgomery Asberg Depression Rating Scale; **PSQI,** Pittsburg Sleep Quang Index; **SCN,** Suprachiasmatic Nucleus; **VA,** Visual Acuity.

INTRODUCTION

The loss of the ability to see is a serious physical and emotional condition, which prevents the afflicted individual from functioning adequately within the society.

Sleep, like many physiological functions follows a circadian rhythm which is controlled by a complex group of biological processes that serves as an internal clock. This clock called the suprachiasmatic nucleus (SCN) is a pair of pinhead-sized brain structure located in the hypothalamus above the chiasm. Environmental factors known collectively as zeitgebers also influence the sleep-wake cycle. Light is one of the most important of these factors that influence the sleep-wake cycle.[1–3] Light that reaches the retina photoreceptors travel along the optic nerve to the SCN and from there, signals travel to several brain regions including the pineal gland which responds by switching off production of the hormone melatonin. In darkness, the level of melatonin increases, making people feel drowsy.

Melatonin, a naturally occurring hormone found in most animals including humans,[4] is important in the regulation of the circadian rhythms of many biological functions.[5] Oral administration of melatonin has been found to synchronize sleep-wake cycles.[6,7]

The biological functions of melatonin are due to activation of melatonin receptors.[8] Disorders of the sleep wake cycle are related to the timing of sleep within the 24 hour day.

Some studies have demonstrated that visual loss may be associated with disorders of the sleep-wake cycle.[9–11] Also reports of graded inhibition of melatonin levels by light of different intensity[12] suggest a reduction in the input of signals to the SCN by any degree of visual loss. Therefore, subjects with severe loss of vision are expected to have a higher prevalence or greater severity of sleep disorders than others. The recognition of sleep-wake disturbances in the visually handicapped is very important since a disturbed sleep cycle may aggravate the problem. Chronic insomnia is associated with an increased risk of depression,[13] anxiety,[13] excess disability,[14] increased use of health care resources[14] and reduced quality of life.[15]

This study set out to determine the prevalence, types and severity of sleep disorders in the blind and their relation to the degree and cause of blindness.

To our knowledge, this study is the first to provide data on disorders of the sleep-wake cycle in the blind in Nigeria if not Africa as a whole.

SUBJECTS, MATERIALS, AND METHODS

This was a hospital based study done in a Teaching hospital located in Osogbo, the capital of Osun state, Nigeria. It was approved by the ethical review committee of the Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria.

Osun State, situated in the Southwest region of Nigeria is bordered in the West and North West by Oyo state, in the east by Ondo State and in the South by Ogun State. It has an estimated population of about 3.3 million.[16]

The hospital is the only state owned teaching hospital in the vicinity and serves as referral centre for all the state owned General hospitals. Also, it is situated in a strategic site where it receives catchments from all the surrounding states, and the entire nation as a whole.

In this study, an individual with a presenting visual acuity of less than 3/60 (Snellen's 6m scale) in the better eye, with glasses, if worn is regarded as blind.[17]

All consecutive clinic patients seen by the consultant between April 2005 and June 2007 who presented with visual acuity (VA) poorer than 3/60 in the better eye with correction if worn were included in the study. Excluded were patients with other conditions that might contribute to sleep disorders such as affective disorders and those who take sedatives and stimulants. The Montgomery Asberg Depression Rating scale (MADRS)[18] was used to identify subjects with affective disorders. In this study, a score of 7 or greater was considered as indicating significant depression.[18–20]

After an informed consent, subjects were interviewed and each had full ophthalmological examination. Two assisting nurses, who had been trained to understand the purpose of the study, assessed the VA and administered the MADRS[18] and Pittsburg Sleep Quality Index (PSQI) questionnaire.[19,21] All interviews were based on the past one month before presentation.

A separately prepared questionnaire was used to collect information which included age, sex, visual loss parameters (visual acuity, duration and rapidity of blindness), type of sleep disorder (interrupted sleep, short sleep, daytime naps and increased sleep latency) and cause of blindness. All data except the age, sex, VA, MADRS and PSQI were collected by the ophthalmologist.

As part of the process of grading the degree of blindness, VA was assessed with glasses if worn, using an illuminated Snellen's chart placed at a distance of six meters away from the patient. Only patients whose visual acuities were worse than 3/60 in the better eye were regarded as blind. These were then tested further by using the hand and pen torch to assess their VA. Depending on the degree of visual loss, they were divided into two categories: no light perception and blind but with light perception or better. This classification was to see the effect of light and its absence on sleep disorders.

The duration of visual loss was recorded in weeks, months or years but changed to months for analysis while the rapidity was categorized into progressive and sudden types. Sudden loss of vision implied anything from instantaneous loss of vision to loss over the course of a week. Progressive loss of vision on the other hand connoted visual loss that was gradually becoming worse over a period of weeks or even years.

For the purpose of this study, interrupted sleep meant those who were woken up by something during the night such as urination; short sleep meant those who slept for less than five hours in the night; daytime naps meant those who found it difficult to stay awake in the day time while increased sleep latency meant those who find it difficult to fall asleep within 30 minutes of staying in bed. In Nigeria, the usual time for sleeping is between 20–21h and 05–06 hours.

Each subject was administered the PSQI questionnaire.[19, 21] This was a validated questionnaire that utilizes self reporting to assess sleep quality and disturbances during the preceding month. This study dealt with blind patients thus making self reporting impossible. It was however adapted for use by the pre-trained assisting nurse who read the statements to the patient and filled the response on the questionnaire.

Scoring of answers was based on a 0 to 3 scale, whereby 3 reflected the negative extreme on the Likert Scale. The sum of the seven component scores gives one global score that was used to categorize the sleep-wake disorder. For the purpose of this study, sleep was considered to be disturbed if the PSQI was greater than 5 as done in previous studies.[22] Sleep-wake disorder was classified as mild (PSQI score, 6–8), moderate (PSQI score 9-12) and severe (PSQI score >12).[22] However, for the purpose of this study, moderate and severe sleep-wake disorders were considered significant.

Statistical Analysis

The normality of the distribution of data was tested graphically and established before analysis. Analysis of data was done using SPSS version 15.0. Percentage frequency was used as measure of prevalence. Chi square statistical method and analysis of variance (ANOVA) were used to test associations between blindness and sleep-wake disorder. The relationship between duration and rapidity of blindness and degree of sleep-wake disorder (PSQI score) was assessed using ANOVA and Chi square respectively. Average values are expressed as mean (SD). Significance was drawn at $P< 0.05$.

The mean age difference in the categories of degree of sleep-wake disorder was examined by ANOVA while association between sex and degree of sleep-wake disorder was assessed by Chi square statistical method.

RESULTS

One hundred and seventy patients formed the study group and this consisted of 46 patients with no light perception and 124 patients with light perception or better.

Eighty-nine, 56, 10, 2 and 13 patients had cataract, glaucoma, optic atrophy (non-glaucomatous), uveitis and others as the cause of their blindness respectively. Both glaucoma and non-glaucomatous atrophy are optic nerve disease which was therefore found in 66 patients.

There were 93 males and 77 females (male: female ratio of 1.2:1) Table 1. The mean age was 60.4 ± 18.6years. The mean ages were 63.0 ± 14.7 and 59.4 ± 19.8 years for the NLP group and other blinds respectively ($p = 0.28$). All the people who had severe sleep disorders were older than 50 years. The mean age difference in the degree of sleep-wake disorder was not statistically significant ($F= 2.6$, $P= 0.053$). There was no significant association ($P=0.64$) between sex and degree of sleep-wake disorder.

The mean PSQI score was 8.4 ± 2.9. Of the 170 blind patients, 138 (81.2%) had some form of sleep-wake disorder being severe in 21(12.4%), moderate in 63(37.0%) and mild in 54 (31.8%) (Table 1). Significant sleep-wake disorder was therefore found in 84(49.4%) patients.

The commonest type of sleep-wake disorder was day time naps in 112(65.9%) patients followed by short sleep in 73(42.9%) patients, interrupted sleep in 57(33.5%) patients and increased sleep latency in 38(22.4%) patients (Table 1).

Degree of Blindness and Sleep-wake Disorder

Thirty-eight (82.6%) and 100 (80.7%) of the NLP group and other blinds respectively had sleep-wake disorders (Table 2). The other blinds were made up of the CF, HM and LP groups in which 43 (72.9%), 38 (82.6%) and 19 (100%) had sleep-wake disorders respectively.

Of the NLP group, 12(26.1%), 19 (41.3%) and 7(15.2) had severe, moderate and mild sleep-wake disorder respectively (Table 2) while 9(7.3%), 44(35.5%) and 47(37.9%) of other blinds had severe, moderate and mild sleep-wake disorder respectively. Therefore, significant sleep-wake disorder was found in 31(67.4%) and 53(42.7%) of the NLP group and other blinds respectively.

Table 1: Selected Characteristics of Study Sample

Characteristic	Frequency (%)
Age (years) (60.4 ± 18.6)	
PSQI (8.4 ± 2.9)	
Duration (months) (4.2 ± 4.9)	
Sex – Male	93 (54.7)
– Female	77 (45.3)
Degree of blindness	
– CF	59 (34.7)
– HM	46(27.1)
– LP	19(11.1)
– NLP	46(27.1)
NLP group	46 (27.1)
Other blinds	124(72.1)
Causes of blindness	
– Cataract	89(52.4)
– Glaucoma	56(32.9)
– Optic atrophy	10 (5.9)
– Uveitis	02(1.2)
– Others	13(7.6)
PSQI categories	
– ≤ 5	32(18.8)
– 6–8	54(31.8)
– 9–12	63(37.0)
– >12	21(12.4)
Types of sleep disorder	
– Daytime Naps	112(65.9)
– Short Sleep	73(42.9)
– Interrupted Sleep	57(33.5)
– ISL	38(22.4)

ISL – Increased Sleep Latency

The mean PSQI scores were 7.5 ± 2.7, 8.3 ± 2.7, 9.0 ± 2.2 and 9.6 ± 3.3 for the CF, HM, LP and NLP groups respectively (Table 3). The mean PSQI score ± SD for other blinds (CF, HM and LP) when grouped together was 8.0 ± 2.7.

The relationship between degree of blindness and prevalence/severity of sleep-wake disorder was very significant statistically ($p = 0.002/0.004$), Table 2.

There was no statistically significant association between degree of blindness and daytime naps ($p=0.54$), short sleep ($p = 0.23$) interrupted sleep ($p =0.07$) and increased sleep duration ($p=0.57$) (Table 4).

Causes of Blindness and Sleep-Wake Disorder

Of 89, 56, 10, 2 and 13 patients with cataract, glaucoma, optic atrophy (non-glaucomatous), uveitis and others respectively, 73 (82.0%), 44 (78.6%), 8(80.0%), 2 (100%) and 11(84.6%) had sleep-wake disorders (Table 2).

Table 2: Relationship between Blindness and Severity of Sleep-wake Disorder

	Sleep Disorder No (%)				
	Normal	Mild	Moderate	Severe	Total
Degree of Blindness					
CF	16(27.1)	23(39.0)	18(30.5)	2(3.4)	59(100)
HM	8(17.4)	16(34.8)	17(37.0)	5(10.9)	46(100)
LP	0(0.0)	8(42.1)	9(47.4)	2(10.5)	19(100)
NLP	8(17.4)	7(15.2)	19(41.3)	12(26.1)	46(100)
Total	32(18.8)	54(31.8)	63(37.1)	21(12.4)	170(100)
p = 0.004					
Cause of blindness					
Cataract	16(18.0)	32(36.0)	33(37.0)	08(9.0)	89(100.0)
Glaucoma	12(21.4)	11(19.6)	23(41.1)	10(17.9)	56(100.0)
Optic atrophy	02(20.0)	0(0.0)	06(60.0)	02(20.0)	10(100.0)
Uveitis	0(0.0)	0(0.0)	01(50.0)	01(50.0)	02(100)
Others	02(15.4)	11(84.6)	0(0.0)	0(0.00)	13(100)

p=0.001; % frequency and Pearson chi square were used in this Table.
CF, Count fingers; HM, Hard movement; LP, Light perception, NLP, No light perception.

Table 3: Relationship between Blindness and Sleep-wake Disorder

Degree of Blindness	N	Mean ± SD PSQI	F test	P
CF	59	7.5 ± 2.7		
HM	46	8.3 ± 2.7	5.2	0.002
LP	19	9.0 ± 2.2		
NLP	46	9.6 ± 3.3		
Cause of blindness				
Cataract	89	8.4 ± 2.8		
Glaucoma	56	8.6 ± 3.1	3.6	0.007
Optic atrophy	10	9.9 ± 3.4		
Uveitis	02	13.0 ± 1.4		
Others	13	6.5 ± 1.2		

N, Number of patients; ANOVA was used to test association in this Table.

Table 4: Relationship between Blindness and Type of Sleep-wake Disorder

Blindness	Type of Sleep-wake Disorder [No (%)]			
Degree of Blindness	**DN**	**SS**	**IS**	**ISL**
CF	37(33.0)	20(27.4)	17(29.8)	10(26.3)
HM	34(30.4)	19(26.0)	12(21.1)	13(34.2)
LP	13(11.6)	10(13.7)	11(19.3)	04(10.5)
NLP	28(25.0)	24(32.9)	17(29.8)	11(28.9)
Significance (P)	0.54	0.23	0.07	0.57
Cause of blindness				
Cataract	63(56.3)	36(49.3)	34(59.6)	24(63.2)
Glaucoma	35(31.3)	28(38.4)	17(29.8)	12(31.6)
Optic atrophy	05(4.5)	06(2.7)	02(3.5)	0(0.0)
Uveitis	02(1.8)	02(2.7)	01(1.8)	01(2.6)
Others	07(6.3)	01(1.4)	03(5.3)	01(2.6)
Significance (P)	0.38	0.02	0.59	0.17

CF, Count fingers; DN, daytime naps; HM, Hard movement; IS, Interrupted sleep; ISL, Increased sleep latency; LP, Light perception, NLP, No light perception; SS, Short sleep.
% frequency and Pearson chi square were used in this table.

Of the 89 patients who had cataract, 32(36.0%), 33(37.1%) and eight (9.0%) had mild, moderate and severe sleep-wake disorder respectively. Only two patients had uveitis as the cause of blindness. One of them had moderate sleep-wake disorder while the other one had severe sleep-wake disorder. Of 10 patients with optic atrophy (non-glaucomatous), six had moderate, two had severe and none had mild sleep-wake disorder.

However, of the 66 patients who had optic nerve disease (glaucomatous and non-glaucomatous), 11(16.7%), 29(43.9%) and 12(18.2%) had mild, moderate and severe sleep disorder respectively (Table 2).

Forty-one (62.1%), 41(46.1%), 2(100%) and 0(0.0%) of those who had optic nerve disease (glaucomatous and non-glaucomatous), cataract, uveitis and others respectively had significant sleep-wake disorder.

The mean PSQI scores for cataract, glaucoma, optic atrophy (non-glaucomatous), uveitis and others were 8.4 ± 2.8, 8.6 ± 3.1, 9.9 ± 3.4, 13 ± 1.4 and 6.5 ± 1.2 respectively (Table 3). When optic atrophy (non-glaucomatous) and glaucoma are combined as optic nerve disease, the mean PSQI score was 8.8 ± 3.1.

The relationship between causes of blindness and prevalence of sleep-wake disorder was statistically significant (p=0.007).

The relationship between causes of blindness and degree of sleep-wake disorder was found to be very significant statistically (p= 0.001) (Table 2).

Table 4 shows the pattern of the types of sleep-wake disorders within the various causes of blindness. There was no significant association between causes of blindness and increased sleep latency (p= 0.17), interrupted sleep (p= 0.59) and daytime naps (p=0.38). However, a significant association was found to exist between cause of blindness and short sleep (p=0.02).

Rapidity of Loss of Vision

One hundred and fifty two (89.4%) and 18(10.6%) out of 170 blind patients had progressive and sudden loss of vision respectively. Of the 152 patients with progressive loss of vision, 78(51.3%)

had significant sleep disorder while only 6 (33.3%) of the 18 patients with sudden loss of vision had significant sleep disorder. We did not find a significant association between rapidity of blindness and degree of sleep disorder (p = 0.19).

The association between duration of blindness and degree of sleep disorder was also not statistically significant (p = (0.60).

DISCUSSION

This study was embarked upon in order to determine the prevalence, types and severity of sleep disorders in the blind and their relationship to the degree and cause of blindness.

Most authors did not report on demographic factors.[22] In this study, majority (145[85.3%]) of the patients were older than 40 years and there was no significant statistical association between sleep-wake disorder and age or sex**.** However, Wee R *et al*[23] working on young adults aged 12 to 20 years also found that eye disease can be a risk factor for sleep disorders, and the health of the optic nerve strongly influences this risk. The prevalence of sleep-wake disorder found in this study is higher than was found by Tabandeh H. *et al* (48.7%)[22] and Skene D.J. *et al* (58.0%).[24] This difference may not be unconnected with the different socioeconomic and environmental factors prevailing in this country. It may also be due to the fact that there was no uniformity in the definition of blindness used by various authors. This study used the WHO definition of VA worse than 3/60 in the better eye with best correction while Tabandeh *et al*[22] used VA of less than 6/60 or visual field of less than 5 degrees. Skene D.J. *et al* however used a less stringent cut off of 5 and above while this study and Tabandeh H. *et al* used score of greater than 5.

In this study, if the moderate and severe sleep-wake disorders are considered significant, then only 84(49.4%) had sleep-wake disorder. The determination of the prevalence of significant sleep-wake disorder is necessary in order to recommend the use of medication that can safely regulate the sleep-wake cycle in the blind.

The finding of day time naps as the commonest type of sleep-wake disorder in this study is contrary to Tabandeh et al's[22] finding in which interrupted sleep was the commonest. However, as found in this study, Tabandeh *et al*[22] also found that various types of sleep disorders are common in the blind.

The reports of graded inhibition of melatonin levels by light of different intensity[12] suggest a reduction in the input of signals to the SCN and the pineal gland by any degree of visual loss. Therefore, subjects with severe loss of vision are expected to have a higher prevalence and greater severity of sleep disorders than others.

This findings of this view as it showed that the relationship between visual loss and prevalence of sleep disorder was very significant statistically (p = 0.002). It also showed that a highly significant association exists between degree of visual loss and severity of sleep-wake disorder. Also, the finding of a higher mean PSQI ± SD of 9.6 ± 3.3 in the NLP group as against 9.0 ± 2.2, 8.3 ± 2.7 and 7.5 ± 2.7 for the LP, HM and CF groups respectively (or 8.0 ± 2.7 in the remaining blind patients when grouped together) has shown that the worse the VA and thus light signals reaching the SCN and thus the pineal gland, the more the derangement of the circadian rhythm and thus a sleep-wake disorder. This is similar to what was found by Tabandeh *et al*.[22]

It may also be said that diseases of the retina and optic nerve may have more severe effects on light signals reaching the SCN and thus a derangement of the circadian rhythm than other diseases such as cataract. This was the situation in this study in which a significant association (P=0.001) between causes of visual loss and degree of sleep-wake disorder was found contrary to previous findings.[22] The prevalence of significant sleep-wake disorder was higher in patients with optic nerve disease and uveitis than cataract patients. This is very interesting as it appears that patients with uveitis and optic nerve disease (glaucomatous and non-glaucomatous) were found to have many more patients with significant sleep disorder than the patients with cataract. Also, the mean PSQI score was higher in the uveitis (13 ± 1.4) cases and the optic nerve disease (8.77 ± 3.1) cases than for cataract (8.4 ± 2.8) cases. A relationship has been found to exist between pinealocytes and photoreceptor elements as antigens and some metabolic pathways have been found to be common to both of them.[25–29] Also pinealitis has been demonstrated to accompany experimental uveo-retinitis and a syndrome involving uveitis and pinealitis has been reported in animals.[30–33] This may explain why the two patients with uveitis had significant sleep disorder. However, this number is too small to make a generalized conclusion. Another study comparing a large number of uveitic cases with normal ones will be highly desirable.

It has been found that those with optic nerve disease have highly variable wake-up times and also have trouble falling asleep, compared to blind ones without optic nerve damage. Those sleep problems led them to nap more frequently, and those with optic nerve disease napped, on average, about 28 minutes a day.[23]

However, a statistically significant association was found to exist only between causes of blindness and short sleep (p=0.02) in this study. The influence of duration and rapidity of blindness on degree of sleep disorder was not statistically significant as found in previous studies.[22] The importance of a case-control study comparing the findings in age and sex matched subjects in future cannot be over-emphasized.

Conclusion

This study has shown that the prevalence of sleep disorder in the blind is high and that a strong relationship exists between visual loss and the sleep–wake cycle in humans.

The recognition of disorders of the sleep-wake cycle in the blind or visually disabled by physicians and eye care professionals cannot be over-emphasized.

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