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ORIGINAL PAPER

A Study on Pineal Gland and Melatonin in relation to 'Severe Depressive Episode'

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ABSTRACT

The pineal gland or epiphysis cerebri is a small grey organ occupying a depression between the superior colliculi. The importance of the pineal gland lies in its function. The gland is a neuroendocrine gland and consists of parenchymal cells, called pinealocytes and neuroglial cells. The pinealocytes secrate a hormone called melatonin. Melatonin, 5methoxy-N-acetyltryptamin, is a neurohormone of the brain produced by pineal gland. The precursor to melatonin is serotonin, a neurotransmitter that itself is derived from the amino acid tryptophan. On the other hand 'severe depressive episode' is one of the commonest problems encountered by the doctors in the tropical countries like India, Pakistan and Bangladesh. Two particularly notable features of depression is diminished nighttime release of melatonin and abnormal sensitivity to melatonin suppression. Variation of the blood melatonin level, in the patients suffering from "severe depressive episode" with the normal individuals was seen in two groups: group "A" & group "B". In group "A" (control) subjects were selected from the medical and non medical voluntaries working at Gauhati Medical College & Hospital. In the other group "B" (case) patients attending the Psychiatry 'Out Patient Department' of Gauhati Medical College & Hospital with "severe depressive episode" were taken. The data recorded was analysed statistically using Student's T-test. P value ≤ 0.05 is considered as statistically significant. Such a study may be useful in establishing a database which may be useful in treating the patients suffering from 'severe depressive episode'.

***Keywords:** Pineal gland, Melatonin, Depression*

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INTRODUCTION

The pineal gland is innerveted by a nerve called nervus conarii which consists of postganglionic sympathetic fibers arising from superior cervical ganglion.[1] Melatonin,5methoxy-N-acetyltryptamin, is a neurohormone of the brain produced by pineal gland. Within the pineal gland, serotonin is acetylated to yield melatonin.[2] The main environmental control of the pineal melatonin synthesis is light intensity. Light perceived by the retina reaches the supra chiasmatic nucleus (SCN) through the retinohypothalamic tract. The SCN innervates the pineal gland via the dorsomedial hypothalamic nucleus, the upper thoracic intermediolateral cell columns of the spinal cord and the superior cervical ganglia, resulting in the rhythmic secretion of melatonin.[3] In humans, as in animals, the plasma melatonin level rises in darkness and falls during the day.[4] This has led researchers and clinicians to try melatonin as an experimental treatment for depression, with gratifying results.[5] Disruption of circadian rhythms produces amnesia by interfering with the circadian organization of memory processes.[6] Melatonin, by correcting circadian rhythms should, theoretically, improve mental performance.[7] Melatonin has also been shown to improve immunity and extend lifespan in some mammels.[8,9] In 'severe depressive episode', the sufferer usually shows considerable distress or agitation, unless retardation is a marked feature. Loss of self-esteem or feelings of uselessness or guilt are likely to be prominent, and suicide is a distinct danger in particularly severe cases.[10] Low nocturnal Melatonin has been proposed as a trait marker for major depressive disorders.[11] Melatonin has been suggested for the improvement of sleep patterns in patients with depression, although research is limited in this area.[12,13,14,15]

OBJECTIVES

To ascertain the variation of the blood melatonin level, in patients suffering from 'severe depressive episode' with normal individuals.

MATERIALS AND METHODS

The study has been done at Gauhati Medical College & Hospital

involving the Departments of Anatomy, Psychiatry and Biochemistry.

Selection of subjects: Two groups were made by selecting subjects of 10 years and above.

Selection of control (group "A"): Subjects were selected from the medical and non medical employees working at Gauhati Medical College & Hospital who volunteered themselves for the study. Subjects were screened free from severe depressive episode. Then they were taken as subjects after elimination of 'Severe Depressive Episode'.

Selection of cases (group "B"): Cases of 'severe depressive episode' are selected as per – The ICD-10 Classification of Mental and Behavioral Disorders, clinical descriptions and diagnostic guidelines, World Health Organization, Geneva, 2002.

Time for collection of sample: To minimize the diurnal variation of melatonin in circulation, samples were collected between 10.00 am to 2.00 pm.

Estimation of blood melatonin level: Estimation of the melatonin was carried by ELISA method using the reagent kit "Melatonin ELISA-RE54021" manufactured and marketed by IBL (Immunobiological Laboratories) D-22335 HAMBURG, GERMANY in the department of Biochemistry, Gauhati Medical College.

Statistical analysis: The data recorded were analysed statistically using Student's T-test. P value ≤ 0.05 is considered as statistically significant.

OBSERVATION & RESULTS

The results and observations of the present study is tabulated and graphed as follows:

Table 1 Number of subjects in different age group

Age groups of control	Number of cases	Number of controls
10 to 19 years	0	6
20 to 29 years	8	19
30 to 39 years	11	15
40 to 49 years	8	5
50 years & above	3	5
Total number(n)	**30**	**50**

Table 2 Number of normal subjects in 20 to 29 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	27	M	8.38
2	28	F	8.38
3	29	F	8.01
4	29	M	10.21
5	28	M	8.34
6	29	M	6.70
7	25	M	5.63
8	28	M	6.20
Mean			**7.73**
S.D			**±1.476**
S.E.M.			**±0.521**

In this group consisting of 8 normal subjects between the age group of 20 to 29 years the serum melatonin level ranges from 5.63 to 10.21 pg/ml with a mean value of 7.73, Standard Deviation ±1.476 and Standard Error of Mean ±0.521.

Table 3 Number of normal subjects in 30 to 39 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	35	M	6.90
2	38	F	8.33
3	38	M	4.60
4	30	M	4.94
5	37	M	8.36
6	35	F	8.37
7	39	M	8.40
8	34	M	8.34
9	37	M	8.07
10	33	M	5.44
11	37	M	4.62
Mean			**6.94**
S.D.			**± 1.687**
S.E.M			**±0.508**

In this group consisting of 11normal subjects between the age group of 30 to 39 years the serum melatonin level ranges from 4.60 to 8.40 pg/ml with a mean value of 6.94, Standard Deviation ± 1.687 and Standard Error of Mean ±0.508

Table 4 Number of normal subjects in 40 to 49 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	40	M	4.93
2	47	M	5.43
3	42	M	5.42
4	40	M	5.65
5	42	M	6.50
6	46	M	6.40
7	45	M	8.02
8	40	M	4.92
Mean			**5.91**
S.D.			**±1.036**
S.E.M			**±0.366**

In this group consisting of 8 normal subjects between the age group of 40 to 49 years the serum melatonin level ranges from 4.92 to 8.02 pg/ml with a mean value of 5.91, Standard Deviation ±1.036 and Standard Error of Mean ±0.366

Table 5 Number of normal subjects in 50 years and above

Sl. No.	Age in years	Sex	Value in pg/ml
1	50	M	6.40
2	55	M	8.06
3	55	M	8.36
	Mean		7.61
	S.D.		**±1.055**
	S.E.M		**±0.609**

In this group consisting of 3 normal subjects between the age group of 50 years and above the serum melatonin level ranges from 6.40 to 8.36 pg/ml with a mean value of 7.61, Standard Deviation ±1.055 and Standard Error of Mean ±0.609

Table 6 Number of cases in 10 to 19 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	19	F	9.60
2	15	F	281
3	18	F	9.58
4	17	F	6.80
5	18	M	9.62
6	18	M	286
	Mean		**100.43**
	S.D.		**±141.815**
	S.E.M		**±57.895**

In this group consisting of 6 no of patients suffering from 'severe depressive episode' between the age group of 10 to 19 years the serum melatonin level ranges from 6.80 to 286 pg/ml with a mean value of 100.43, Standard Deviation ±141.815 and Standard Error of Mean ±57.895.

Table 7 Number of cases in 20 to 29 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	20	M	285
2	27	M	4.86
3	26	M	6.58
4	25	M	8.09
5	28	F	4.87
6	25	M	5.04
7	23	F	6.83
8	25	F	284
9	22	F	5.02
10	21	M	9.57
11	27	F	280
12	24	M	267
13	21	F	6.84
14	25	M	4.88
15	21	F	8.05
16	22	F	280
17	29	M	8.06
18	22	F	7.46
19	25	M	7.48
	Mean		**78.40**
	S.D.		**±123.341**
	S.E.M		**±28.296**

In this group consisting of 19 no of patients suffering from 'severe depressive episode' between the age group of 20 to 29 years the serum melatonin level ranges from 4.86 to 285 pg/ml with a mean value of 78.40, Standard Deviation ±123.341 and Standard Error of Mean ±28.296

Table 8 Number of cases in 30 to 39 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	30	M	264
2	36	F	416
3	30	M	281
4	32	M	266
5	33	F	268
6	38	M	5.06
7	36	M	8.08
8	35	F	265
9	31	F	6.56
10	32	F	280
11	38	F	272
12	32	F	6.57
13	31	M	10.48
14	37	M	266
15	30	M	7.52
	Mean		**174.82**
	S.D.		**±146.289**
	S.E.M		**±37.769**

In this group consisting of 15 no of patients suffering from 'severe depressive episode' between the age group of 30 to 39 years the serum melatonin level ranges from 5.06 to 416 pg/ml with a mean value of 174.82, Standard Deviation ±146.289 and Standard Error of Mean ±37.769.

Table 9 Number of cases in 40 to 49 years

Sl. No.	Age in years	Sex	Value in pg/ml
1	42	M	10.50
2	43	F	6.57
3	40	M	281
4	45	M	4.89
5	40	F	6.82
	Mean		**61.96**
	S.D.		**±122.466**
	S.E.M		**±54.768**

In this group consisting of 5 no of patients suffering from 'severe depressive episode' between the age group of 40 to 49 years the serum melatonin level ranges from 4.89 to 281 pg/ml with a mean value of 61.96, Standard Deviation ±122.466 and Standard Error of Mean ±54.768.

Table 10 Number of cases in 50 years & above

Sl. No.	Age in years	Sex	Value in pg/ml
1	53	M	7.51
2	73	F	5.00
3	65	F	268
4	62	M	10.46
5	52	M	10.52
	Mean		**60.30**
	S.D.		**±116.131**
	S.E.M		**±51.935**

In this group consisting of 5 no of patients suffering from 'severe depressive episode' between the age group of 50 years and above the serum melatonin level ranges from 5.00 to 268 pg/ml with a mean value of 60.30, Standard Deviation ±116.131 and Standard Error of Mean ±51.935

The mean values of serum melatonin for both the groups are presented in **Table 2 to 10**. Mean values of serum melatonin for both groups are represented in **Figure 1.**

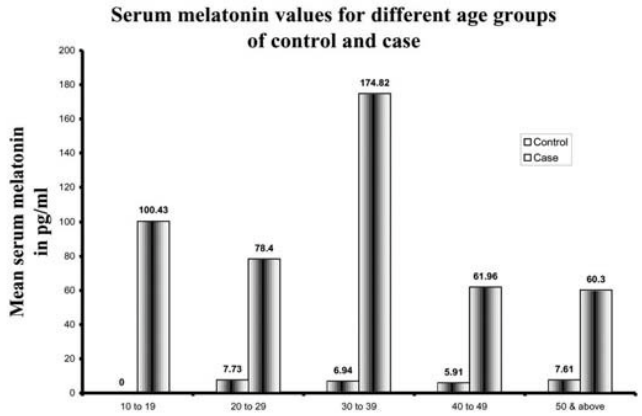

Table 11 Distribution of frequency, relative frequency and percentage of frequency

Class interval of melatonin in pg/ml	Normal			Patient		
	Simple frequency	Relative frequency	Percentage	Simple frequency	Relative frequency	Percentage
0 to 2	0	0.000	0.00	0	0.000	0.00
2 to 4	0	0.000	0.00	0	0.000	0.00
4 to 6	10	0.248	33.33	8	0.007	15.38
6 to 8	6	0.188	16.68	12	0.016	23.08
8 to 10	13	0.514	41.66	8	0.014	15.38
10 to 12	1	0.050	8.33	4	0.008	7.69
200 to 400	0	0.000	0.00	17	0.877	30.78
400 to 600	0	0.000	0.00	1	0.078	7.69
Above 600	0	0.000	0.00	0	0.000	0.00
n	**30**	**1.000**	**100.00**	**50**	**1.000**	**100.00**

Table 11 shows that for the normal group the highest number of subjects (maximum numbers of subject) in this group have total melatonin values in the class interval of 8 to 10 pg/ml with relative frequency of occurrence of 0.514. A secondary pick in serum melatonin value is present in the class interval of 4 to 6 pg/ml with a relative frequency of 0.248 as evident in **Figure 2**. In the patient group the distribution is more uniform and compact with highest relative frequency of occurrence 0.877 in the class interval of 200 to 400 pg/ml as evident in **Figure 2**.

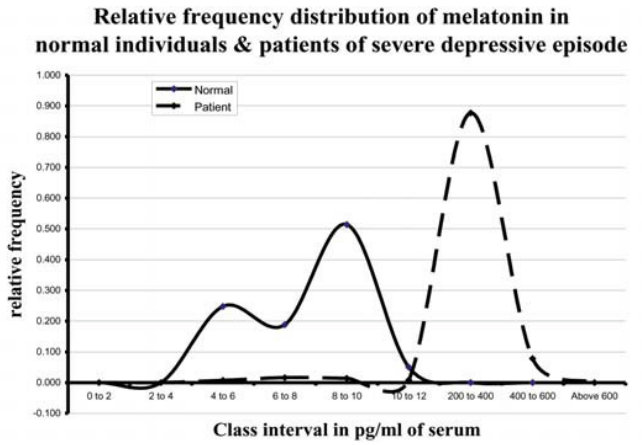

Figure 2 Distribution of 'Relative frequency'

Table 12 Showing values of melatonin for total number of control & cases

Sl. No.	Melatonin in pg/ml in normal	Melatonin in pg/ml In severe depression
1.	4.60	4.86
2.	4.62	4.87
3.	4.92	4.88
4.	4.93	4.89
5.	4.94	5.00
6.	5.42	5.02
7.	5.43	5.04
8.	5.44	5.06
9.	5.63	6.56
10.	5.65	6.57
11.	6.20	6.57
12.	6.40	6.58
13.	6.40	6.80
14.	6.50	6.82
15.	6.70	6.83
16.	6.90	6.84
17.	8.01	7.46
18.	8.02	7.48
19.	8.04	7.51
20.	8.06	7.52
21.	8.07	8.05
22.	8.33	8.06
23.	8.34	8.08
24.	8.34	8.09
25.	8.36	9.56
26.	8.36	9.58
27.	8.37	9.60
28.	8.38	9.62
29.	8.38	10.46
30.	10.21	10.48
31.		10.50
32.		10.52
33.		264.00
34.		265.00
35.		266.00
36.		266.00
37.		267.00
38.		268.00
39.		268.00
40.		272.00
41.		280.00
42.		280.00
43.		280.00
44.		281.00
45.		281.00
46.		281.00
47.		284.00
48.		285.00
49.		286.00
50.		416.00
Sum	**207.95**	**5325.76**
Mean	**6.932**	**106.52**
SD	**±1.525**	**±135.0543**
SEM	**±0.278**	**±19.1**

Table 13 Level of significance of differences

Sl. No.	Comparison of mean melatonin between	"t"	P
1	Patient of 30 to 39 years and 10 to 19 years	1.07	>0.05
2	Patient of 30 to 39 years and 20 to 29 years	1.04	>0.05
3	Patient of 30 to 39 years and 40 to 49 years	1.50	>0.05
4	Patient of 30 to 39 years and 50 years & above	1.27	>0.05
5	Control of 30 to 39 years and 20 to 29 years	0.07	>0.05
6	Control of 30 to 39 years and 40 to 49 years	0.09	>0.05
7	Control of 30 to 39 years and 50 years & above	0.02	>0.05

DISCUSSION

Considering the differential trends in melatonin secretion by pineal gland under the circadian rhythm and variations in exposure to darkness and light as reported by various workers on the allied subject,[16,17] in the present investigation the samples for evaluation of pineal function through serum melatonin estimation has been collected between midday and afternoon which is extensively reported as the period of generalized depletion for circulating melatonin levels. Mean serum melatonin concentration in subjects with 'severe depressive episode' is found to be significantly high than the control group of normal subjects which may appear as contradicting with reports of related works on serum melatonin concentration under different conditions, situations and experimental setup.[18,19] In most of these studies over serum melatonin concentrations with or without depressive episodes, the nocturnal serum melatonin status was reported which may be a factor for the discrepancy with the findings of the present study. However, with reference to the well established 'serotonin hypothesis '[20], it has been tried to explain here that in presence of conditions associated with 'severe depressive episode' if somehow the biosynthesis of melatonin is hampered then there will be increase in melatonin level even at day time without neuronal stimulus of darkness resulting in increase in day time basal melatonin in circulation as observed in the present study. One of the contrasting trends in serum melatonin level is in the distribution pattern between control and the group with 'severe depressive episode'. In the 'severe depressive episode' group the serum melatonin is found to be fluctuating under different age groups but in contrast to this there is no any fluctuation in the serum melatonin level in the control group.

CONCLUSION

In the control group 30 numbers of subjects were taken and in the 'severe depressive episode' group 50 number of subjects were taken. The mean serum melatonin in the control group is 6.932±0.278 pg/ml and the mean serum melatonin in the group with 'severe depressive episode' is 106.52±19.1 pg/ml which is significantly higher ($P<0.05$) than the control. The highest mean serum melatonin level in 'severe depressive episode' was observed as 174.82±37.769 pg/ml in the age group of 30 to 39 years but without any significant differences ($P>0.05$) from the other age groups.

Finally, it may be concluded that day time serum melatonin level is significantly elevated in subjects with 'severe depressive episode' under the limitations of the presented setup.

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Conflicts of interest: None declared.

Contribution of Authors: We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

Ethical clearance: Taken.

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