

# Thyroid Function Status of Female Nurses Working Night-shift at a Tertiary Care Hospital

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## ABSTRACT

**Background & objective:** Night shift work has well-known adverse effects on health like sleep disturbances and other medical conditions including thyroid diseases. Various studies have revealed that the effect of night shift work on health is mainly related to its interference with circadian rhythm, which can also influence thyroid hormone levels in accordance with sleep patterns. Therefore, night work can modify thyroid function and increase the risk of thyroid disorders. The present study was therefore conducted to evaluate the impact of the night shift work on the thyroid function status of female nurses in a tertiary care hospital.

**Methods:** This case-control study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka over a period of 1 year from January 2021 to December 2021. All female nurses (in the age range of 25-50 years) working at Dhaka Medical College in different shifts were the study population. Of them, the case group consisted of 90 female nurses who worked the night shift in different wards from 8.00 pm. to 8.00 am and the control group consisted of 90 female nurses who worked the morning shift in the Outpatient Department (OPD) from 8.00 am to 2.00 pm. However, nurses with a personal or family history of sleep disorder, taking medications that may interfere with sleep, history of diabetes mellitus, bronchial asthma, or diagnosed with any kind of thyroid disease, such as Hashimoto's thyroiditis, and pregnant nurses were excluded from the study. While the exposure variable was shift-work, the outcome variable was thyroid function status, evaluated in terms of serum FT<sub>4</sub>, FT<sub>3</sub>, and TSH and the presence of thyroid disorders.

**Results:** The cases and controls were almost alike in terms of age, BMI, and blood pressure. The mean age of the case and the control groups were between 34 and 35 years with no significant difference between the groups. While serum levels of free thyroxine (FT<sub>4</sub>) and free triiodothyronine (FT<sub>3</sub>) were somewhat reduced in the case group than those in the control group, the serum TSH was significantly elevated in the former group than that in the latter group – a picture typical of subclinical hypothyroidism. Overt hypothyroidism was also higher in the former group than that in the latter group. Subclinical and clinical hyperthyroidism was found in 2(2.2%) and 3(3.3%) subjects of the control group only. Overall, 60% of the cases had some form of thyroid disorders as opposed to 15% of the controls with the risk of having thyroid disorders in night shift nurses being > 8(95% CI = 4.1 – 17.5) times higher than that in morning shift nurses (p < 0.001).

**Conclusions:** The study concluded that night shift nurses may have a higher risk of developing subclinical hypothyroidism due to significantly higher levels of TSH and normal FT<sub>3</sub>, and FT<sub>4</sub> levels. About two-fifths of the nurses working night shifts are at increased risk of having thyroid disorders, primarily subclinical hypothyroidism.

**Keywords:** Serum free tri-iodothyronine (FT<sub>3</sub>), free thyroxine (FT<sub>4</sub>), TSH etc.

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## INTRODUCTION:

The thyroid gland produces hormones like tri-iodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ), which are essential for metabolism, heat production, proper development and differentiation of cells, and growth of the human body.<sup>1</sup> Thyroxine and tri-iodothyronine ( $T_3$ ) hormones are secreted in response to the pituitary thyroid stimulating hormone (TSH). TSH levels change with the alteration of circadian rhythms and sleep patterns.<sup>2</sup> The circadian system regulates all physiological processes which are controlled by changes in the external environment, such as light exposure, food intake time, etc.<sup>1</sup> Shift work (any work schedule different from the typical work time from 9 am to 5 pm per day) disorder is a circadian rhythm sleep disorder that occurs if a person's work schedule is planned during normal sleep time as happens in night shift workers. There are many adverse impacts of the night shift on physical & mental health, performance, and safety.<sup>3,4</sup>

Shift work specially night-work act as a stressor affecting the circadian rhythm of the human body. Night shift work interferes with the worker's normal physiological functions.<sup>5</sup> Alterations of the sleep/wake cycle can affect human biological functions, physical, and psychological conditions, quality of life, and also working efficiency.<sup>2</sup> It has been seen that the nurses working the night shift are at increased risk of subclinical hypothyroidism,<sup>5</sup> which may be associated with higher odds of coronary heart disease and heart failure.<sup>6</sup> The TSH level is a sensitive test for early diagnosis of thyroid disorder.<sup>7</sup> The TSH production peaks at its highest level between 2:00 and 4:00 am each morning and then drops reaching its lowest point between 4 and 8 pm in the evening.<sup>1</sup> The TSH released into the blood is normally inhibited during sleep and its release continues during sleep deprivation.<sup>8</sup> So, the morning plasma TSH is higher in subjects who had sleepless nights. Sleep can inhibit TSH secretion and opposes the circadian influence on this hormone.<sup>9</sup> In rotating shift workers, the level of TSH significantly decreases from the beginning to the end of a morning shift but  $T_4$  values significantly increase.<sup>2</sup> Sleep deprivation elevates TSH level and also significantly increase  $T_3$ ,  $T_4$  level.<sup>10</sup>

Nurses as shift workers play an important role in the health care system. In tertiary care hospitals they must work rotating shift duties including night shifts to provide 24-hour services to patients.<sup>11</sup> The schedules of night shift nurses vary from 8 hours to 12 hours.<sup>12</sup> It has also been observed that night-shift work can affect the immune system function, increasing the risk of autoimmune diseases including autoimmune thyroiditis.<sup>13</sup> In Korea, Moon and associates<sup>5</sup> conducted a study on shift workers and found that night-shift workers had higher levels of TSH values than non-night-shift workers. Similarly, Shaker and colleagues<sup>7</sup> observed an increase in TSH levels among night-shift workers in India. Hwang and Jeon<sup>14</sup> performed a study on shift workers and observed higher TSH levels in night-shift workers but normal  $FT_4$  levels—a feature of subclinical hypothyroidism, which may increase the risk of cardiovascular diseases.

Though many studies were conducted on the impact of shift work on  $FT_3$ ,  $FT_4$ , and TSH levels in female nurses, there are few studies on this topic in the setting of Bangladeshi nurses. The present study was conducted to evaluate the effect of night-shift on  $FT_3$ ,  $FT_4$ , and TSH levels of Bangladeshi female nurses. It will help in raising awareness regarding the thyroid health of night-shift workers and taking preventive and promotive approaches to overcome thyroid health hazards caused by night-shift work.

## METHODS:

This case-control study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka over a period of 1 year from January 2021 to December 2021. All female nurses (in the age range of 25-50 years) working at Dhaka Medical College, Dhaka in different shifts were the study population. Of them, the case group consisted of 90 female nurses who worked the night shift in different wards from 8.00 pm. to 8.00 am and the control group consisted of 90 female nurses who worked the morning shift in the Outpatient Department (OPD) from 8.00 am to 2.00 pm. However, nurses with a personal or family history of sleep disorder, taking medications that may interfere with sleep, history of

diabetes mellitus, bronchial asthma, or diagnosed with any kind of thyroid disease, history of autoimmune diseases that affect thyroid hormones, such as Hashimoto's thyroiditis, pregnant nurses and nurses doing more than one job were excluded from the study. While the exposure variable was shift work (night-shift and morning-shift), the outcome variable was thyroid function status, evaluated in terms of serum FT<sub>4</sub>, FT<sub>3</sub>, and TSH and the presence of thyroid disorders (subclinical and overt hypo or hyperthyroidism).

On obtaining ethical clearance from the Ethical Review Committee of Dhaka Medical College, Dhaka, data were collected on variables of interest using a semi-structured questionnaire. Collected data were processed and analyzed using SPSS (statistical package for social science Inc., Chicago, Illinois USA,) version 25.0. The test statistics used to analyze the data were Chi-square ( $\chi^2$ ) Test and the Student's t-Test. Data presented on a categorical scale were expressed as frequency & corresponding percentage and were compared between groups using Chi-square ( $\chi^2$ ) Test, while the data presented on a continuous scale were expressed as mean  $\pm$  SD and were compared between groups using Student's t-Test. The level of significance was set at 0.05 and a p-value < 0.05 was considered significant.

## RESULTS:

The cases and controls were almost alike in terms of age, BMI, and blood pressure. The mean age of the case and the control groups were between 34 and 35 years with no significant intergroup difference (p=0.421). The nurses of both groups maintained a healthy BMI and there was no difference between the groups in terms of BMI (p = 0.155). The mean systolic and diastolic blood pressures of both groups were almost identical and within the normal range (p=0.496 and p = 0.665 respectively) (Table I).

The serum levels of free thyroxine (FT<sub>4</sub>) and free triiodothyronine (FT<sub>3</sub>) were somewhat lower in the case group than those in the control group (p=0.103 and p=0.086 respectively). However, the serum TSH was found to be significantly elevated in the former group than that in the latter group (p<0.001) (Table II). Over half (53.3%) of the cases had subclinical

hypothyroidism as compared to 7.8% of the control group nurses (p < 0.001). Overt hypothyroidism was also considerably higher in the former group than that in the latter group. While none of the cases had subclinical and clinical hyperthyroidism, 2(2.2%) and 3(3.3%) controls had subclinical and clinical hyperthyroidism respectively (Table III). Nearly 60% of the cases had some form of thyroid disorders as opposed to 15% of the controls with the risk of having thyroid disorders in night shift nurses being 8.5(95% CI = 4.1 – 17.5) fold greater than that in morning shift nurses (p < 0.001) (Table IV).

**Table I : Distribution of general characteristics of the subjects between groups**

Baseline characteristics	Group		p-value
	Case (n=90)	Control (n=90)	
Age (years)	34.2 $\pm$ 4.8	34.8 $\pm$ 5.7	0.421
BMI (kg/m <sup>2</sup> )	22.5 $\pm$ 1.8	21.8 $\pm$ 1.7	0.155
Systolic Pressure (mmHg)	115.1 $\pm$ 6.3	115.7 $\pm$ 5.6	0.496
Diastolic Pressure (mmHg)	75.3 $\pm$ 4.9	74.9 $\pm$ 5.4	0.665

\*Data were analyzed using an Unpaired t-Test and were presented as mean  $\pm$  SD.

**Table II : Comparison of thyroid hormones and TSH between the study groups**

Thyroid function parameter*	Group		p-value
	Case (n=90)	Control (n=90)	
Serum FT <sub>4</sub> (pg/ml)	11.1 $\pm$ 1.6	11.7 $\pm$ 2.8	0.103
Serum FT <sub>3</sub> (pg/ml)	2.4 $\pm$ 0.5	2.6 $\pm$ 0.5	0.086
Serum TSH ( $\mu$ U/ml)	6.5 $\pm$ 2.7	2.7 $\pm$ 1.4	< 0.001

\*Data were analyzed using an Unpaired t-Test and were presented as mean  $\pm$  SD.

**Table III : Association between night shift work and types of thyroid disorders**

Thyroid status	Group		p-value
	Case (n=90)	Control (n=90)	
Euthyroid	37(41.1)	77(85.6)	
Sub-clinical hypothyroidism	48(53.3)	7(7.8)	
Hypothyroidism	5(5.6)	1(1.1)	< 0.001
Subclinical hyperthyroidism	0(0.0)	2(2.2)	
Hyperthyroidism	0(0.0)	3(3.3)	

\*Chi-squared Test ( $\chi^2$ ) was done to analyze the data; figures in the parentheses indicate corresponding %;

**Table IV : Association between night shift work and thyroid function status**

Thyroid disorder	Group		Odds Ratio (95% CI of OR)	p-value
	Case (n=90)	Control (n=90)		
Present	53(58.9)	13(14.4)	8.5(4.1 – 17.5)	< 0.001
Absent	37(41.1)	77(85.6)		

\*Chi-squared Test ( $\chi^2$ ) was done to analyze the data; figures in the parentheses indicate corresponding %;

## DISCUSSION:

The present study was undertaken to evaluate the impact of night shift work on the thyroid function status of female nurses. The cases and controls were almost identical with respect to age, BMI, and blood pressure. The mean age of the case and the control groups were approximately 35 years. Both groups of nurses maintained a healthy BMI of approximately 22 kg/m<sup>2</sup> and they did not differ by BMI. Their blood pressures (both systolic and diastolic blood pressures) were almost similar and also were within the normal range.

While the serum levels of free thyroxine (FT<sub>4</sub>) and free triiodothyronine (FT<sub>3</sub>) were somewhat reduced in the night-shift nurses than those in the morning-shift nurses, the serum TSH was significantly raised in the former group than that in the latter group. The changes in thyroid hormone levels that took place in the night shift workers were typical of subclinical hypothyroidism. Very few had overt hypothyroidism. Approximately 60% of the cases had some form of thyroid disorder as opposed to 15% of the controls. The night shift nurses carry more than 8-fold (95% CI = 4.1 – 17.5) higher risk of developing thyroid disorders than their morning shift counterparts. As all the baseline demographic and clinical characteristics were almost similarly distributed between the study groups, the outcome obtained could be attributed to night shift work (the exposure variable). Consistent with this finding, Moon and associates<sup>5</sup> reported a similar finding with the risk of having subclinical hypothyroidism in night shift workers being 1.4 times higher than that in day shift workers. Magrini and colleagues<sup>13</sup> also showed a significant increase in the prevalence of subclinical autoimmune hypothyroidism in night shift workers than that in day shift workers.

In the current study, the mean total FT<sub>3</sub> hormone level of both groups was although within the normal range, it was somewhat lower in the study group than that in the control group. Thyroid hormone synthesis is regulated by TSH, which changes with circadian rhythm and sleep pattern. In the early evening before sleep, the TSH begins to increase and declines during sleep at night. In night shift work due to sleep deprivation, the TSH continues to release due to the lack of inhibitory effect of sleep. On the other hand, in night shift duty circadian disruption causes a misaligned HPT-Axis and reduced negative feedback suppression of TRH and TSH. As a result, though TSH secretion increases, thyroid hormone synthesis remains normal, a condition known as subclinical hypothyroidism.<sup>15</sup> In the present study, thyroid disorders were mostly subclinical hypothyroidism thus supporting the mechanism of development of subclinical hypothyroidism among night-shift workers. Night shift duty also increases anti-TPO levels which may interrupt thyroid hormone synthesis.<sup>15</sup>

On the contrary, Rizza et al.<sup>16</sup> found similar FT<sub>3</sub> levels between night shift workers and day shift workers. This contrast in findings might have occurred due to variations in the duration of working hours. Gary and associates<sup>10</sup> although found higher FT<sub>3</sub> levels in the study group than that in the control group, the difference was not statistically significant. They concluded that FT<sub>3</sub> concentration might be increased due to noncircadian causes such as nutritional status, physical activity, and cognitive workload that influence the peripheral conversion of T<sub>4</sub> to T<sub>3</sub>. Yan and colleagues<sup>17</sup> showed that the mean FT<sub>3</sub> level of night shift workers increased significantly more than that of the morning shift workers. During night shift work, insufficient sleep might cause impairment of the HPT-Axis which again increases serum FT<sub>3</sub> level. This finding was in agreement with Kuetting et al.<sup>18</sup> In the current study, the mean FT<sub>4</sub> level of both groups was within the normal range but somewhat lower in the study group than that in the control group. A similar type of observation was also found by Radowicka et al.<sup>19</sup> They concluded that autoantibodies against thyroid peroxidase and thyroglobulin developed in night-shift workers decrease thyroid hormone synthesis. As a result, serum FT<sub>4</sub> levels decrease.

In the current study, the mean TSH level of study subjects was a little higher than the upper limit of the normal range but it was within the normal range in the control group. A similar type of observation was also found by other researchers.<sup>5,7,17,19</sup> In their study, it was found that the TSH level in night shift workers was significantly higher than that in the morning shift workers. The circadian system regulates all physiological processes that are modulated by changes in the external environment light exposure and food intake. Thyroid hormone synthesis and secretion are regulated by TSH. TSH production and secretion are regulated by thyrotropin-releasing hormone (TRH). TRH is produced in the paraventricular nucleus of the hypothalamus and secreted from the median eminence and transported to the pituitary gland via hypothalamic- hypophyseal portal system. TRH stimulates thyrotropes to synthesize TSH in the pars distalis of the pituitary gland. Then TSH stimulates the thyroid gland to produce thyroid hormone (mainly the prohormone T<sub>4</sub>) via TSH receptors on the cell membrane of the thyroid follicle. T<sub>3</sub> is derived from circulating T<sub>4</sub> which regulates the synthesis and release of TRH and TSH by a negative feedback loop mediated by the thyroid hormone receptor. This regulatory pathway is called the hypothalamic-pituitary thyroid axis. TSH secretion shows daily rhythmicity and the HPT axis is under the control of the circadian clock via the suprachiasmatic nucleus.

Night shift work causes disruption of circadian rhythm and induces changes in hormonal regulation. Melatonin acts as a primary output signal of the central circadian pacemaker. It maintains the internal hormonal environment to the light-dark cycle of the external environment. In a typical sleep-wake cycle melatonin concentrations are low during the day and high at night.<sup>20</sup> Melatonin involves in thyroid function directly by regulating thyroglobulin gene expression in follicular cells. It also has an inhibitory effect on cell proliferation and thyroid hormone synthesis. Night shift duty decreases melatonin secretion causing a reduced negative feedback loop and increase TSH.<sup>21</sup> Some studies also found night shift work to induce stress which may affect the immune system. Night shift duty increases the release of corticotropin-releasing

factor, a 41-aminoacid peptide that affects the hypothalamic-pituitary-adrenal axis, the sympathetic nervous system, and the immune system. Shift work also increases the risk for the development of autoimmune thyroid disorder by increasing the prevalence of both subclinical auto-immune hypothyroidism and isolated increases of anti-TPO antibodies.<sup>13</sup> In contrast, several investigators<sup>15,22</sup> found a significantly decreased TSH in the night shift than in morning shift workers. However, some researchers<sup>9,16</sup> found no difference in TSH levels between night shift and day shift workers. Like any other scientific study, the present study is not without limitations. Before concluding the findings of the study, the following limitations deserve mention.

#### LIMITATIONS:

- The sample was taken purposively. So, there is every chance of sampling bias that can influence the result.
- The sample was collected from Dhaka Medical College Hospital only which does not represent the entire study population. Only female nurses were included in this study, who were again not representative of the whole study population. So, caution should be exercised to generalize the findings to the reference population.
- Thyroid peroxidase antibody (TPO-Ab) and Thyroglobulin antibody (TG-Ab) levels were not measured due to financial constraints.

#### CONCLUSIONS:

The study concluded that the changes in thyroid hormone levels that took place in the night shift female nurses are typical of subclinical hypothyroidism. While serum levels of free thyroxine (FT<sub>4</sub>) and free triiodothyronine (FT<sub>3</sub>) are somewhat decreased in the night-shift nurses than those in the morning-shift nurses, the serum TSH is significantly increased in the former group than that in the latter group. About two-fifths of the nurses working night shifts are at increased risk of having thyroid disorders, primarily subclinical hypothyroidism. The findings derived from the study may be helpful for clinicians to bring awareness among night shift nurses to prevent thyroid disease-related morbidity.

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