

Relationship of Hypothyroidism in the Causation of Developing Mastalgia

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Abstract

Original Research Article

Background: Mastalgia and fibroadenomas are common among the women in reproductive age group. Thyroid dysfunction has been implicated as the etiology. **Objective:** To identify the relationship of Hypothyroidism in the causation of developing Mastalgia. **Methods:** This case-control study was carried out in the Department of General Surgery, BSMMU, Dhaka, between January 2019 to June 2019. A total of 90 patients with mastalgia due to nonadherence to antithyroid therapy, out of which 60 patients with Hypothyroidism were considered as a group I and 30 without Hypothyroidism were considered as group II. For statistical analyses of the results generation, using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-23). **Results:** The majority 96.7% of patients were married in group I and 85.0% in group II. Nearly three fourth 73.3% of patients had not a history of oral contraceptives in group I and 15.0% in group II. The mean TSH was 9.23 ± 8.84 mlu/l in group I and 3.25 ± 1.15 mlu/l in group II. The mean FT3 was 1.96 ± 0.68 (pg/ml) in group I and 3.10 ± 1.1 (pg/ml) in group II. More than half 53.3% of patients had mastalgia occurring within a year in group I. Mastalgia only found 55.3% and 30.0% in group I and group II respectively. More than half 52.2% of patients had taken fatty food, fast food, red meat daily in group I and 15.0% in group II. Physical exercise performed frequently found 8.3% and 50.0% in group I and group II respectively. The difference was statistically significant ($p < 0.05$) between the two groups. **Conclusion:** No history of oral contraceptive, consumption of fatty food, fast food, red meat, and never engagement in physical exercise were significantly more common in mastalgia patients with hypothyroidism. There was an association of thyroid dysfunction in patients with mastalgia.

Keywords: Breast, Hypothyroidism, Mastalgia.

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INTRODUCTION

Mastalgia is two types - cyclical and noncyclical. Cyclical is related to a women's monthly menstrual cycle minimum tenderness during this period thought to be typical. Non- Cyclical mastalgia is unaltered during the menstrual cycle. This type is not common. It has different causes and is difficult to diagnose. It occurred due to hormonal changes in adolescence, pregnancy, and menopause [1]. Hypothyroidism is a condition in which the body lacks

a sufficient level of thyroid hormone. Since the main purpose of the thyroid hormone is to maintain the body's metabolism. People with this condition typically see their metabolic rate drop sharply and experience a cluster of symptoms that can commonly include breast tenderness. Minimum tenderness during the menstrual cycle is thought to be typical. It is generally caused by a variety of other factors like fibrocystic disease, lumpiness, and mastalgia. Women going through menopause can experience breast tenderness. The mean

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age of the patient was 34+8 years[2]. It occurs due to hormonal changes in adolescence, pregnancy, and menopause. Hypothyroidism is a condition in which the body lacks sufficient levels of thyroid hormone. Since the main purpose of the thyroid hormone is to direct the body's metabolism. The main function of the thyroid gland can be caused by metabolic imbalance. Hypothyroidism is an important health problem worldwide. Prevention, detection, treatment, and control of this condition receive high priority. Mastalgia is breast pain in menopausal transition or reproductive life. Due to experiencing urbanization and modernization which cause changes in diet and physical activity. Particularly in the cities like many other developing countries. For hypothyroidism such as a sedentary lifestyle, obesity, consumption of fatty foods and resultant dyslipidemia are highly prevalent in the population. The complication often results from non-adherence to the anti-thyroid drugs. Non-adherence to prescribed drugs schedule has been and continues to be a major problem in the world. Long-term therapy severely compromises the effectiveness of treatment making this a critical issue in population health both from the perspective of quality of life and health. Poor adherence to long-term therapies severely compromises the effectiveness of treatment, making this a critical issue is me in population health both from the perspective of the quantity of life and of health. Compliance will help prevent the complication of hypothyroidism which are debilitating and if not present can increase the burden of a disease that is already on the increase.

II.OBJECTIVES

General Objective

To identify the relationship of hypothyroidism in the causation of developing mastalgia

Specific Objective

- To assess serum TSH, FT₃, FT₄ level in mastalgia patient
- To identify social demographic factors that affect the hypothyroid patient in study participants

III. MATERIALS AND METHODS

This case-control study was carried out in the Department of General Surgery, BSMMU, Dhaka, between January 2019 to June 2019. A total of 90 patients with mastalgia due to nonadherence to antithyroid therapy, out of which 60 patients with Hypothyroidism were considered as a group I and 30 without Hypothyroidism were considered as group II.

Inclusion Criteria

- Patient with noncyclical primary mastalgia
- Female age range 15 - 45 years.

Exclusion criteria

- The patient has secondary causes of other endocrine disorders.
- History of taking OCP, HRT
- Diagnosed case of breast abscess/malignancy and previous breast surgery.
- Patients were unwilling to take participants to the study.

Data were processed and analyzed using computer software SPSS version 23.0. The outcome variable was presented in frequencies and percentages. A hypothesis test was conducted using the chi-squared test.

IV. RESULTS

Table-1: Demographics & others information of participants (N= 90)

Particulars of the patients	Group I (n=60)		Group II (n=30)		p-value
	n	%	n	%	
Age(years)					
≤20	4	6.7	4	13.3	
21-29	20	33.3	8	26.7	
30-39	22	36.7	13	43.3	
≥40	14	23.3	5	16.7	
Mean ±SD	32.13±8.14		30.35±7.17		0.386 ^{ns}
Range (min-max)	20-48		18-40		
BMI					
Underweight (<18.5 Kg/m ²)	8	13.3	4	13.3	
Normal range (18.5-22.9 kg/m ²)	28	46.7	15	50.0	
Overweight (23-24.9 kg/m ²)	10	16.7	7	23.4	
Obesity (≥25 kg/m ²)	14	23.3	4	13.3	
Mean ±SD	22.90±6.46		21.60±2.96		
Range (min-max)	17-54		17-26		0.388 ^{ns}

In Table 1 it was observed that more than one-third (36.8%) of patients belonged to age 30-39 (years)

in group I and 13(40.0%) in group II. The mean age was 32.13±8.14 years in group I and 30.35±7.17 years

in group II. Almost half (46.7%) patients belonged to the BMI normal range of 18.5-22.9 kg/m² in group I and 15(50.0%) in group II. The mean BMI was

22.9±6.46 in group I and 21.6±2.96 in group II. The difference was statistically not significant (p>0.05) between the two groups.

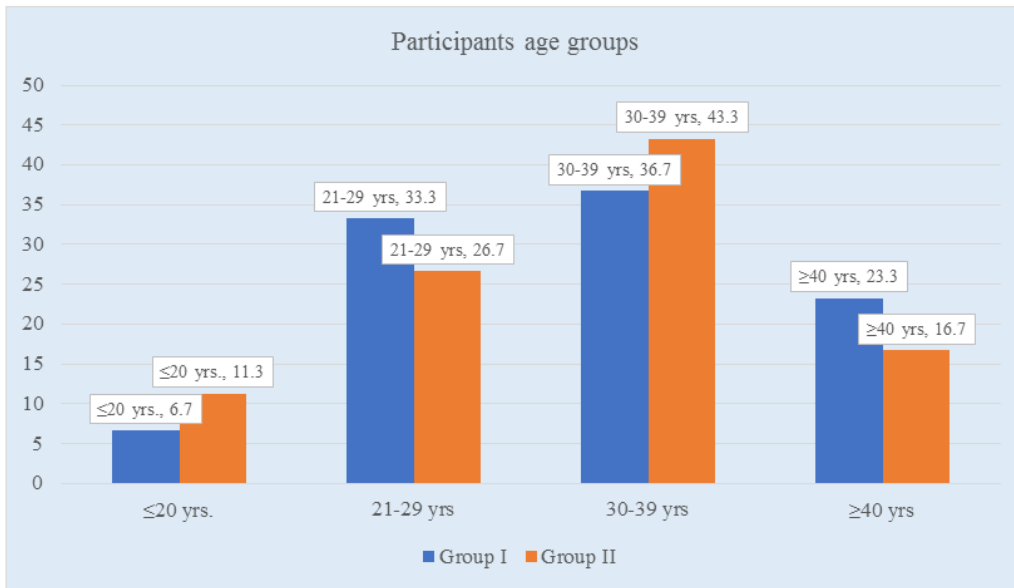


Fig-I: Participants According to age groups (N=90)

Table-2: Marital status of the participant (N= 90)

Marital status	Group I (n=60)		Group II (n=30)		p-value
	n	%	n	%	
Unmarried	0	0.0	6	20.0	0.001 ^s
Married	58	96.7	24	80.0	
Divorced	2	3.3	0	0.0	

Table 2 showed the marital status of the participants, it was observed that (96.7%) patients were married in group I and 24(85.0%) in group II. The

difference was statistically significant (p<0.05) between the two groups.

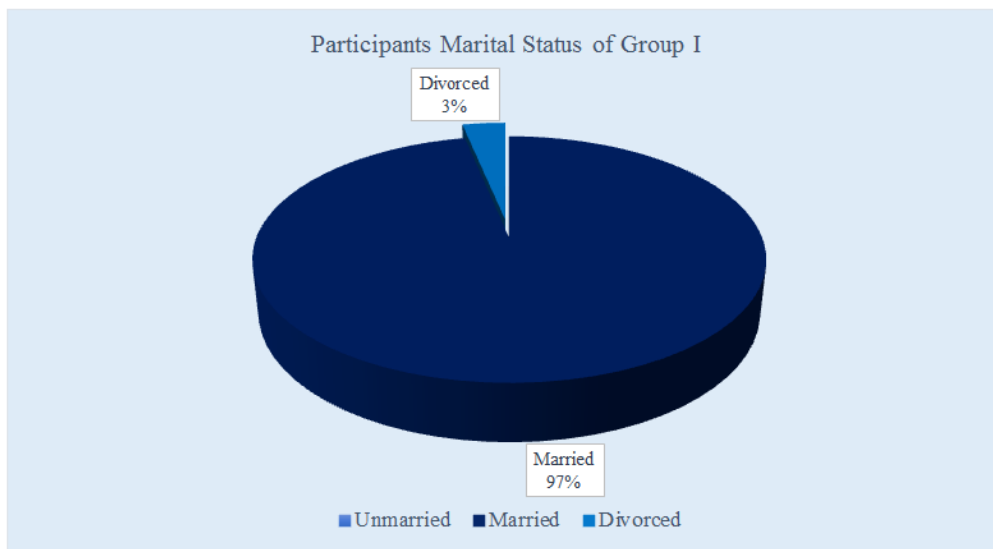


Fig-II: Participant’s Marital Status in group I (n=60)

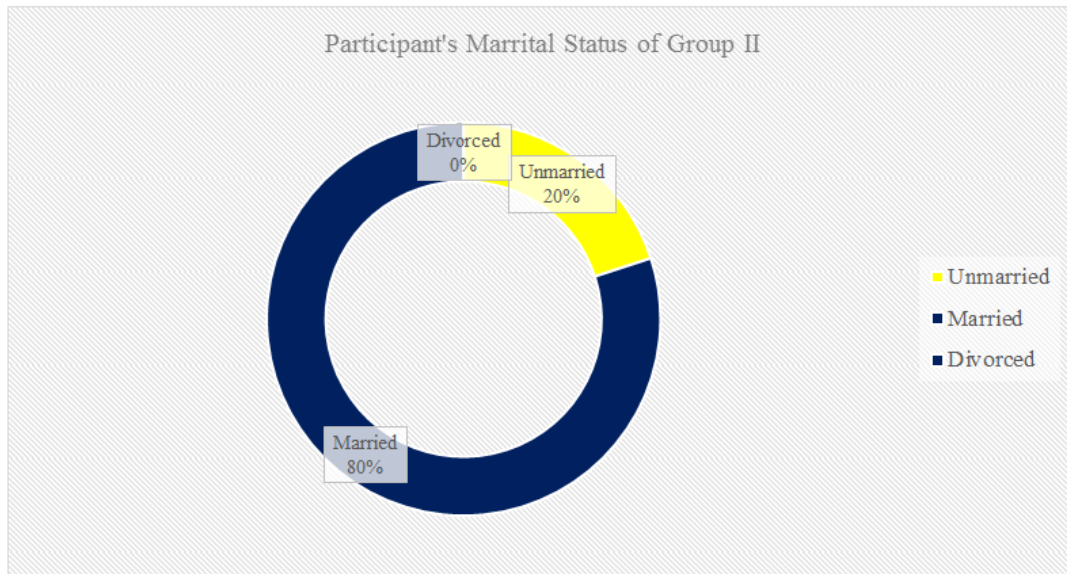


Fig-III: Participant’s Marital Status in group II (n=30)

Table-3: Participants by their age of menarche, breastfeeding history, and history of oral contraceptive (N= 90)

Age of menarche, history breastfeeding, and oral contraceptive	Group I (n=60)		Group II (n=30)		P-value
	n	%	n	%	
Age of menarche					
10-12 years	12	20.0	10	33.3	0.165 ^{ns}
13-14 years	48	80.0	20	66.7	
History of breastfeeding					
Yes	48	80.0	22	73.3	0.473 ^{ns}
No	12	20.0	8	26.7	
History of oral contraceptive					
Yes	16	26.7	25	83.3	0.001 ^s
No	44	73.3	5	16.7	

Table 3 showed participants by age of menarche, breastfeeding history, and history of oral contraceptive, it was observed that the majority (80.0%) of participants belonged to the age of menarche 13-14 years in groups I and 20(65.0%) in group II. The majority (80.0%) of patients had a history of

breastfeeding in group I and 22(70.0%) patients in group II. One-fourth (26.7%) of patients had a history of oral contraceptives in group I and 25(85.0%) in group II. The difference was statistically significant (p<0.05) between the two groups.

Table-4: Participant’s disease and drug-related factors (N=90)

Disease and drug-related factors	Group I (n=60)	Group II (n=30)	P-value
TSH (mlu/l)			
Mean ±SD	9.23±8.84	3.25±1.15	0.003 ^s
Range (min-max)	0.41-43	1.3-4-5	
FT3 (pg/ml)			
Mean ±SD	1.96±0.68	3.10±1.1	0.001 ^s
Range (min-max)	0.83-2.8	0.9-6.12	
FT4 (hg/dl)			
Mean ±SD	5.03±5.46	7.44±1.78	0.056 ^{ns}
Range (min-max)	0.3-19.87	5.37-10	

Table 4 showed the mean TSH was 9.23±8.84 (mlu/l) in group I and 3.25±1.15 in group II. The mean FT3 was 1.96±0.68 (pg/ml) in group I and 3.10±1.1 (pg/ml) in group II. The mean FT4 was 5.03±5.46

(hg/dl) in group I and 7.44±1.78 (hg/dl) in group II. The difference was statistically significant (p<0.05) between the two groups.

Table-5: Participant’s duration of diagnosis of hypothyroidism (n= 60)

Duration of diagnosis of hypothyroidism	Frequency (n)	Percentage (%)
Month	28	46.7
Years	32	53.3

Table 5 showed the participants by the duration of diagnosis of hypothyroidism, it was

observed that more than half (53.3%) patients had hypothyroidism was diagnosed within a year.

Table-6: Participant’s duration of mastalgia (N= 90)

Duration of mastalgia	Group I (n=60)		Group II (n=30)		p-value
	n	%	n	%	
Days	10	16.7	21	70.0	0.001 ^s
Month	18	30.0	9	30.0	
Years	32	53.3	0	0.0	

Table 6 showed the participant’s duration of mastalgia. It was observed that more than half (53.3%) patients had mastalgia occurring within a year in group

I. The difference was statistically significant (p<0.05) between the two groups.

Table-7: Participants by breast symptom (N= 90)

Breast symptom	Group I (n=60)		Group II (n=30)		p-value
	n	%	n	%	
Mastalgia only	33	55.0	8	26.7	0.001 ^s
Lumpiness	23	38.3	22	73.3	
Nipple discharge	4	6.7	0	0.0	

Table 7 showed the participants breast symptoms. It was observed that more than half (55.3%) patients had mastalgia only in group I and 8(30.0%) in

group II. The difference was statistically significant (p<0.05) between the two groups.

Table-8: Distribution of the study patients by treatment of hypothyroidism (n=60)

Treatment of hypothyroidism	Frequency (n)	Percentage (%)
Yes	34	56.7
No	26	43.3

Table 8 showed participants treatment of hypothyroidism. It was observed that more than half

(56.7%) patients had taken treatment for hypothyroidism.

Table-9: Distribution of the study patients by the history of taking thyroxin replacement therapy (n= 60)

History of taking thyroxin replacement therapy	Frequency (n)	Percentage (%)
Yes	34	56.7
No	26	43.3

Table 9 showed participants’ history of taking thyroxin replacement therapy. It was observed that

more than half (56.7%) patients had taken thyroxin replacement therapy.

Table-10: Participants by duration of medicine (n= 60)

Duration of medicine	Frequency (n)	Percentage (%)
Days	12	20.0
Months	20	35.0
Years	26	45.0

Table 10 showed participants by the duration of medicine. It was observed that almost half (44.8%) patients had taken medicine within a year.

Table-11: Participants by consumption of fatty food, fast food, red meat (N= 90)

Consumption of Fatty food, Fast food, red meat	Group I (n=60)		Group II (n=30)		p-value
	n	%	n	%	
Daily	31	51.7	5	16.7	0.002 ^s
Frequently	19	31.6	15	50.0	
Rarely	9	15.0	4	13.3	
Never	1	1.7	6	20.0	

Table 11 showed participants consumption of fatty food, fast food, red meat. It was observed that more than half (52.2%) patients had taken fatty food,

fast food, red meat daily in group I and 3(15.0%) in group II. The difference was statistically significant ($p<0.05$) between the two groups.

Table-12: Participants by frequency of physical exercise (N= 90)

Frequency of physical exercise	Group I (n=60)		Group II (n=30)		p-value
	n	%	n	%	
Daily	12	20.0	6	20.0	0.001 ^s
Frequently	5	8.3	15	50.0	
Rarely	14	23.3	9	30.0	
Never	29	48.4	0	0.0	

Table 12 showed participants' frequency of physical exercise. It was observed that one-fourth of 29(48.3%) patients had never engaged in physical exercise in group I and half (50.0%) had frequent physical activity. The difference was statistically significant ($p<0.05$) between the two groups.

V. DISCUSSION

In this present study, it was observed that 36.8% of participants belonged to age 30-39 (years) in group I and 40.0% in group II. The mean age was 32.13 ± 8.14 years in group I and 30.35 ± 7.17 years in group II. In Rajswaroob *et al.* [1] study most of the participants were in the age group of 26-35 years, 70.6% followed by age group of <25 years, 15.7%, and the age group of 36-45 years, 11.8%. Kumar *et al.* and Bansal *et al.* [3, 4] observed the mean age was 33.7 ± 7.45 years and 32.8 ± 8.35 years respectively, which supports the present study. Mastalgia is the most common symptom in women, who has gone under breast imaging. 70.0% of women face mastalgia at least once in their lifetime [5]. Though overtly not as clinically significant as breast cancer, BBD is a significant cause of concern in almost half of the female population [6]. Hypothyroidism is associated with decreased thermogenesis, decreased metabolic rate, and has also been shown to correlate with a higher body mass index (BMI) and a higher prevalence of obesity. TSH levels are at the upper limit of the normal range or slightly increased in obese children, adolescents, and adults and are positively correlated with BMI. The mean BMI was 22.9 ± 6.46 in group I and 21.6 ± 2.96 in group II. The difference was statistically not significant ($p>0.05$) between the two groups. In Raval *et al.* [7] study suggested that association of relatively higher BMI with "moderate to severe PMS" and "PMDD" group than "no/mild PMS" group ($p<0.05$), where the

authors found the mean body mass index (BMI) was 18.2 ± 3.5 kg/m² in No/mild PMS, 19.9 ± 3.6 kg/m² in Moderate to severe PMS and 19 ± 3.4 kg/m² in PMDD. The difference was statistically significant ($p<0.05$) between the two groups. The main function of the thyroid gland is to make thyroxine (T4) and triiodothyronine (T3) hormones. These hormones are important for the growth and normal function of the body, as well as for breastfeeding. Thyroid diseases include hypothyroidism hyperthyroidism and thyroid cancer. Some breastfeeding mothers with hypothyroidism struggle to make a full milk supply. Women who have been properly treated for hypothyroidism report they have had no problems with their milk supply. After a woman gives birth, it is important that hyperthyroidism due to Graves' disease is not confused with the hyperthyroid phase of post-partum thyroiditis [8]. In this present study, it was observed that 26.7% of participants had a history of oral contraceptives in group I and 85.0% in group II. No history of oral contraceptives was significantly ($p<0.05$) higher in group I. In this current study, it was observed that the mean TSH was 9.23 ± 8.84 mIU/l in group I and 3.25 ± 1.15 mIU/l in group II. The mean TSH was significantly higher in group I patients. Bhargav *et al.* [9] study found the rate of hypothyroidism and the mean serum TSH concentration were significantly higher among patients with nipple discharge than among those with mastalgia or a lump ($p<0.05$). In all, 39.0% of hypothyroid women had TSH concentrations >10 mIU/l [10]. The study observed among the BBD group serum TSH and triiodothyronine (T3) values were reported to be outside the normal range in 13 and 23% patients, respectively; of these patients, 63.0% had higher TSH and 71.0% had lower T3 values, indicating hypothyroidism. Most authorities recommend treatment for patients with a TSH concentration of >10 mIU/l and high-risk patients even if their TSH concentration is

between 4.5 and 10/0 mIU/l. For patients with TSH<10 mIU/l, it is suggested that treatment may be tried and should be continued if there is a clear symptomatic benefit to the patient [11-13]. In this present study, it was observed that the mean FT3 was 1.96 ± 0.68 (pg/ml) in group I and 3.10 ± 1.1 (pg/ml) in group II. The mean FT3 was significantly ($p<0.05$) higher in group II patients. Ditsch *et al.* [14] evaluated the thyroid status in 143 women with different benign and malignant breast disorders and they showed higher levels of FT3 in patients with BBD than in the control group. Also, their study found a higher rate of hypothyroidism in patients with BBD compared to controls (18.5% vs. 7.9%), without significant difference. In this current study, it was observed that the mean FT4 was 5.03 ± 5.46 hg/dl in group I and 7.44 ± 1.78 hg/dl in group II. The mean FT3 was higher in group II patients but the difference was not statistically significant. In this present study, it was observed that 53.3% of patients who had hypothyroidism were diagnosed within years. The prevalence of hypothyroidism in Bhargav *et al.* [15] study was 23.2%, which is significantly high compared to that of the cohort of patients who underwent thyroidectomy during the same study period. This is despite the fact that thyroid dysfunction is more likely in patients with goiter, although they accept that this group of the patients does not constitute the ideal control for the study. In this current study, it was observed that 53.3% of patients had mastalgia occurring within a year in group I. The difference was statistically significant ($p<0.05$) between the two groups. Jain *et al.* [16] reported that Gradual improvement in mastalgia with the passage of time up to 12 weeks. Following cessation of treatment at 12 weeks, partial relapse of pain was observed at 24 weeks. Plu-Bureau *et al.* and Kataria *et al.* [17, 18] have reported that cyclical mastalgia might be an independent risk factor for developing malignancy based on their finding that 22 of 247 cyclical mastalgia cases on 16-year follow-up developed breast cancer. In this present study, it was observed that 55.3% of patients had mastalgia in group I and 30.0% in group II. Breast lump found 37.7% and 70.0% in group I and group II respectively. Nipple discharge found 7.0% only in group I. Mastalgia was significantly ($p<0.05$) higher in group I. Tanwar *et al.* [19] study observed prevalence of hypothyroidism was 30.0%, out of these 74.5% cases were having subclinical hypothyroidism. The association of hypothyroidism was greater with a higher age group and nipple discharge than mastalgia or breast nodularity. Hypothyroid patients presenting with nipple discharge and mastalgia responded better to thyroxine replacement therapy than those with breast nodularity. Hypothyroid patients with nipple discharge and mastalgia were significantly better than their euthyroid counterparts. Salzmann *et al.* [20] in their study noted that 42% of women suffering from BBD had breast lumps and 66.0% of them had mastalgia either cyclical or non-cyclical. In this current study, it was observed that 56.7% of patients had taken treatment for

hypothyroidism. In this present study, it was observed that 56.7% of patients had taken thyroxine replacement therapy. In this current study, it was observed that 44.8% of patients had taken medicine within a year. In this current study, it was observed that physical exercise was performed daily 20.0% in group I and 20.0% in group II. Frequently performed found 8.3% and 50.0% in group I and group II respectively. Rarely performed physical exercise was found 23.3% in group I and 30.0% in group II. Nearly half (48.3%) of the patients had never engaged in physical exercise in group I but not found in group II. The difference was statistically significant ($p<0.05$) between the two groups. Raval *et al.* [21] studies found 24.1% had regular exercise in No/mild PMS, 18.1% in Moderate to severe PMS, and 5.6% in PMDD. Their study found no statistically significant association between groups with regards to physical activities such as regular exercise and games. The evidence for the effect of exercise on PMDD symptoms is largely anecdotal. However, regular exercise can be advised as part of a healthy lifestyle regimen [22]. Small trials have suggested aerobic exercise to be beneficial for PMS sufferers, and one trial found high-intensity aerobic exercise to be superior to low-intensity one for PMS treatment [23]. Fewer premenstrual complaints have been found in women participating in sports than in non-athletic women.

VI. CONCLUSION

This study was undertaken to identify the relationship of hypothyroidism in the causation of developing mastalgia. Most of the patients were in the 4th decade in both groups. Married, no history of oral contraceptive use, consumption of fatty food, fast food, red meat, and never engaged in physical exercise were significantly more common in mastalgia patients with hypothyroidism. TSH and FT3 were significantly higher in mastalgia patients with hypothyroidism. There was an association of thyroid dysfunction in patients with mastalgia.

VII. LIMITATIONS OF THE STUDY

The study population was selected from one selected hospital in Dhaka city, so the results of the study may not reflect the exact picture of the country. The present study was conducted in a very short period of time. Since the clinical examination is an observer-based investigative tool, this needs to be substantiated with radiological and pathological investigations. The small sample size was also a limitation of the present study.

VIII. RECOMMENDATIONS

All patients with mastalgia should be screened for hypothyroidism because a simple correction of hypothyroidism results in significant clinical improvement of the patients in most hypothyroid patients. Further studies can be undertaken by including a large number of patients.

REFERENCES

1. Rajswaroob, U., Kannan, R., Kannan, N.S., & Tirouaroul, T. (2016). Effectiveness of centchroman on regression of fibroadenomas and mastalgia. *Journal of clinical and diagnostic research: JCDR*, 10(10), PC10.
2. Bhargav, P.R., Mishra, A., Agarwal, G., Agarwal, A., Verma, A.K., & Mishra, S.K. (2009). Prevalence of hypothyroidism in benign breast disorders and effect of thyroxine replacement on the clinical outcome. *World journal of surgery*, 33(10), 2087-2093.
3. Kumar, S., Rai, R., Agarwal, G.G., Dwivedi, V., Kumar, S., & Das, V. (2013) A randomized, double-blind, placebo-controlled trial of ormeloxifene in breast pain and nodularity. *Natl Med J India*, 26(2), 69-74.
4. Bansal, V., Bansal, A., & Bansal, A.K. (2015). Efficacy of Sevista (Ormeloxifene) in treatment of mastalgia and fibrocystic breast disease. *Int J Reprod Contracept Obstetr Gynecology*, 4(4), 1057-1060.
5. Engin, Ö., Güliz, Y. (2013). Mastodynia: is imaging necessary in young patients? 29(1); 011-016, DOI: 10.5152/UCD.2013.03
6. Goehring, C., & Morabia, A. (1997). Epidemiology of benign breast disease, with special attention to histologic types. *Epidemiologic reviews*, 19(2), 310-327.
7. Raval, C.M., Panchal, B.N., Tiwari, D.S., Vala, A.U., & Bhatt, R.B. (2016). Prevalence of premenstrual syndrome and premenstrual dysphoric disorder among college students of Bhavnagar, Gujarat. *Indian Journal of psychiatry*, 58(2), 164.
8. Speller, E., & Brodrigg, W. (2012). Breastfeeding and thyroid disease: A literature review. *Breastfeeding Review*, 20(2), 41-47. <https://search.informit.org/doi/10.3316/informit.659261398291384>
9. Bhargav, P.R., Mishra, A., Agarwal, G., Agarwal, A., Verma, A.K. and Mishra, S.K. (2009). Prevalence of hypothyroidism in benign breast disorders and effect of thyroxine replacement on the clinical outcome. *World journal of surgery*, 33(10), 2087-2093.
10. Adamopoulos, D.A., Kapolla, N., Michalakis, A., Vassilaros, S., Papadiamantis, J., & Georgiakodis, F. (1986). Thyroid disease in patients with benign and malignant mastopathy. *Cancer*, 57(1), 125-128.
11. Vanderpump, M.P.J., Tunbridge, W.M.G., French, J., Appleton, D., Bates, D., Clark, F., Evans, J.G., Hasan, D.M., Rodgers, H., Tunbridge, F. and Young, E.T. (1995). The incidence of thyroid disorders in the community: a twenty-year follow-up of the Wickham Survey. *Clinical endocrinology*, 43(1), 55-68.
12. Wilson, G.R., & Curry, Jr, R. (2005). Subclinical thyroid disease. *American family physician*, 72(8).
13. Arrigo, T., Wasniewska, M., Crisafulli, G., Lombardo, F., Messina, M.F., Rulli, I., Salzano, G., Valenzise, M., Zirilli, G., & De Luca, F. (2008). Subclinical hypothyroidism: the state of the art. *Journal of endocrinological investigation*, 31(1), 79-84.
14. Ditsch, N., Liebhardt, S., Von Koch, F., Lenhard, M., Vogeser, M., Spitzweg, C., Gallwas, J., & Toth, B. (2010). Thyroid function in breast cancer patients. *Anticancer research*, 30(5), 1713-1717.
15. JOUR Bhargava, Atul Shukla, Sudhir Kumar, Rakesh Ohri, Deepak 2009/01/01, Metroglyph Analysis of Morphological Variation in *Chenopodium* spp 5, World J. Agric. Sci
16. Jain, B.K., Bansal, A., Choudhary, D., Garg, P.K., & Mohanty, D. (2015). Centchroman vs tamoxifen for regression of mastalgia: a randomized controlled trial. *International Journal of Surgery*, 15, 11-16.
17. Plu-Bureau, G., Lê, M.G., Sitruk-Ware, R., & Thalabard, J.C. (2006). Cyclical mastalgia and breast cancer risk: results of a French cohort study. *Cancer Epidemiology and Prevention Biomarkers*, 15(6), 1229-1231.
18. Kataria, K., Dhar, A., Srivastava, A., Kumar, S., & Goyal, A. (2014). A systematic review of current understanding and management of mastalgia. *Indian Journal of Surgery*, 76(3), 217-222.
19. Tanwar, P., Gupta, S., Bharti, D., Kalra, D., Kumar, N., & Sodha, V.S. (2018). Magnitude of Hypothyroidism in Benign Breast Disorders and Effect of Thyroxin Replacement on Clinical Outcome of Benign Breast Disorders with Hypothyroidism as Comorbidity.
20. Salzman, B., Fleege, S., & Tully, A.S. (2012). Common breast problems. *American family physician*, 86(4).
21. Raval, C.M., Panchal, B.N., Tiwari, D.S., Vala, A.U. and Bhatt, R.B. (2016). Prevalence of premenstrual syndrome and premenstrual dysphoric disorder among college students of Bhavnagar, Gujarat. *Indian Journal of psychiatry*, 58(2), 164.
22. Vigod, S.N., Ross, L.E., & Steiner, M. (2009). Understanding and treating premenstrual dysphoric disorder: an update for the women's health practitioner. *Obstetrics and Gynecology Clinics*, 36(4), 907-924.
23. Mendiratta, V., & Lentz, G.M. (2017). Primary and secondary dysmenorrhea, premenstrual syndrome, and premenstrual dysphoric disorder: etiology, diagnosis, management. *Comprehensive Gynecology*. 7th ed. Philadelphia, PA: Elsevier.