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Thyroid Dysfunction in Patients with Hepatocellular Carcinoma: A 60-Case Study at BSMMU, Dhaka, Bangladesh

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide, with increasing incidence in Bangladesh. Thyroid hormones play a key role in hepatic metabolism, and altered thyroid function has been reported in patients with chronic liver disease. However, data on the prevalence and impact of thyroid dysfunction in HCC patients are limited. ***Objectives:*** This study aimed to evaluate thyroid hormone abnormalities in patients with HCC and explore correlations with liver function parameters and tumor characteristics. ***Methods:*** This prospective observational study included 60 adult HCC patients attending the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from January 2021 to December 2021. Clinical, laboratory, and imaging data were collected. Thyroid function tests (TSH, free T4, free T3) were performed at diagnosis. HCC was diagnosed according to AASLD criteria. Thyroid dysfunction was classified as hypothyroidism, hyperthyroidism, or subclinical forms. Statistical analysis was conducted using SPSS v25. ***Results:*** Among 60 patients (mean age 56.8 ± 11.2 years; 45 males, 15 females), 26 patients (43.3%) exhibited thyroid dysfunction. Hypothyroidism was the most common (21.7%), followed by subclinical hypothyroidism (11.7%) and hyperthyroidism (10%). Patients with thyroid dysfunction had significantly higher serum bilirubin (3.1 ± 1.2 vs 2.2 ± 1.0 mg/dL, $p<0.05$) and lower albumin levels (3.1 ± 0.5 vs 3.5 ± 0.4 g/dL, $p<0.05$). Tumor size and Child-Pugh score were positively correlated with TSH levels ($r=0.42$, $p=0.002$). ***Conclusion:*** Thyroid dysfunction is prevalent in HCC patients and correlates with liver function impairment and tumor burden. Routine thyroid function assessment in HCC patients may help optimize clinical management and prognostication. Further studies are needed to clarify the underlying mechanisms and therapeutic implications.

Keywords: Hepatocellular Carcinoma, Thyroid Dysfunction, Hypothyroidism, Bangladesh, Liver Cancer.

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1. INTRODUCTION

Hepatocellular carcinoma (HCC) represents the most common primary liver malignancy and ranks among the leading causes of cancer-related death globally [1]. In Bangladesh, the incidence of HCC has been rising due to chronic hepatitis B and C infection, aflatoxin exposure, and non-alcoholic fatty liver disease [2,3]. Despite advances in diagnostic imaging and therapy, the prognosis remains poor, especially when diagnosed at advanced stages. The liver plays a central role in thyroid hormone metabolism. Thyroxine (T4) is converted to the biologically active triiodothyronine (T3) predominantly in the liver through deiodinase activity [4]. Chronic liver disease, including cirrhosis and HCC, can impair this conversion, leading to abnormal thyroid hormone profiles [5]. Conversely, thyroid hormone imbalance may influence hepatocyte proliferation, apoptosis, and tumor progression via thyroid hormone receptors expressed in hepatic tissue [6,7]. Several studies have demonstrated an association between hypothyroidism and increased risk of HCC, as well as altered thyroid hormone levels in patients with liver cirrhosis [8,9]. Low T3 syndrome, subclinical hypothyroidism, and overt hypothyroidism have been reported in cirrhotic and HCC patients, correlating with disease severity and liver function impairment [10]. However, data specific to Bangladeshi populations remain scarce, with few prospective studies examining thyroid dysfunction in HCC patients. Understanding thyroid dysfunction in HCC patients is clinically important because it may affect disease progression, response to therapy, and overall prognosis. Early identification of thyroid abnormalities could allow timely interventions, potentially improving metabolic balance, quality of life, and therapeutic outcomes [11]. This study aimed to investigate the prevalence and pattern of thyroid dysfunction in 60 HCC patients at BSMMU, Dhaka, Bangladesh, and to explore the relationship between thyroid hormone abnormalities and liver function parameters, tumor characteristics, and disease severity.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted at the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh between January 2021 and December 2021. Written informed consent was obtained from all participants.

Inclusion Criteria:

- Adults ≥18 years diagnosed with HCC according to the American Association for the Study of Liver Diseases (AASLD) criteria [12].
- Willingness to participate in the study and provide informed consent.

Exclusion Criteria:

- History of prior thyroid disease or treatment.
- Concurrent malignancies other than HCC.
- Severe systemic illness interfering with study assessment (e.g., sepsis, acute coronary syndrome).

Data Collection: Demographic data (age, sex), clinical history, and laboratory parameters were recorded. Liver function tests (AST, ALT, bilirubin, albumin, INR), complete blood count, viral markers (HBsAg, anti-HCV), and imaging findings (ultrasound, CT/MRI) were collected.

Thyroid Function Assessment: Fasting blood samples were collected at diagnosis. Thyroid function tests included:

- TSH (normal range: 0.4–4.0 mIU/L)
- Free T4 (normal range: 0.8–1.8 ng/dL)
- Free T3 (normal range: 2.3–4.2 pg/mL)

Classification of Thyroid Dysfunction:

- Hypothyroidism: TSH >4.0 mIU/L with low free T4
- Subclinical hypothyroidism: TSH >4.0 mIU/L with normal free T4
- Hyperthyroidism: TSH <0.4 mIU/L with high free T4
- Subclinical hyperthyroidism: TSH <0.4 mIU/L with normal free T4

Tumor Assessment: Tumor size, number of lesions, vascular invasion, and Child-Pugh score were documented.

Statistical Analysis: Data were analyzed using SPSS version 25. Continuous variables were presented as mean ± SD, categorical variables as frequency and percentage. Student's t-test and Chi-square test were used for comparison. Pearson correlation was applied to assess relationships between thyroid hormones and clinical parameters. $p < 0.05$ was considered statistically significant.

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RESULTS

Patient Demographics and Clinical Characteristics

A total of 60 patients with hepatocellular carcinoma (HCC) were included in this study. The mean age was 56.8 ± 11.2 years, with the majority being male (45 males, 15 females). The primary etiologies of HCC were hepatitis B virus (HBV) infection in 33 patients (55%), hepatitis C virus (HCV) infection in 15 patients (25%), and non-alcoholic fatty liver disease (NAFLD) in 12 patients (20%). Based on the Child-Pugh classification, 20 patients (33.3%) were classified as Child-Pugh A, 30 patients (50%) as Child-Pugh B, and 10 patients (16.7%) as Child-Pugh C. The mean tumor size was 5.2 ± 2.1 cm, and 18 patients (30%) had multifocal tumors, while the remaining had single lesions.

Table 1: Demographics and Clinical Characteristics of HCC Patients (n=60)

Parameter	Value
Age (years)	56.8 ± 11.2
Sex (M/F)	45/15
Etiology of HCC	HBV: 33 (55%), HCV: 15 (25%), NAFLD: 12 (20%)
Child-Pugh Score	A: 20 (33.3%), B: 30 (50%), C: 10 (16.7%)
Tumor size (cm)	5.2 ± 2.1
Multifocal tumor	18 (30%)

Thyroid Dysfunction Prevalence

Thyroid function assessment revealed that 34 patients (56.7%) were euthyroid, while 26 patients (43.3%) exhibited thyroid dysfunction. Among the dysfunctional group, hypothyroidism was the most common, found in 13 patients (21.7%), followed by subclinical hypothyroidism in 7 patients (11.7%) and hyperthyroidism in 6 patients (10%). The mean TSH among hypothyroid patients was 6.8 ± 1.5 mIU/L, with a mean free T4 of 0.7 ± 0.1 ng/dL. Subclinical hypothyroid patients had a mean TSH of 5.1 ± 0.9 mIU/L with normal free T4 levels, and hyperthyroid patients had a mean TSH of 0.2 ± 0.1 mIU/L with elevated free T4.

Table 2: Distribution of Thyroid Dysfunction in HCC Patients

Thyroid Status	Frequency (n)	Percentage
Euthyroid	34	56.7%
Hypothyroidism	13	21.7%
Subclinical Hypothyroidism	7	11.7%
Hyperthyroidism	6	10%

Correlation of Thyroid Dysfunction with Liver Function

Patients with thyroid dysfunction demonstrated significantly higher serum bilirubin (3.1 ± 1.2 mg/dL) compared to euthyroid patients (2.2 ± 1.0 mg/dL, p=0.03) and lower serum albumin (3.1 ± 0.5 g/dL vs 3.5 ± 0.4 g/dL, p=0.02). Liver enzymes (AST and ALT) were slightly elevated in thyroid dysfunction patients but did not reach statistical significance. TSH levels were positively correlated with tumor size (r=0.42, p=0.002), indicating that patients with higher TSH tended to have larger tumors. Additionally, thyroid dysfunction was more common among patients with higher Child-Pugh scores, suggesting a relationship between thyroid hormone abnormalities and the severity of liver disease.

Table 3: Liver Function Parameters in Relation to Thyroid Status

Parameter	Thyroid Dysfunction	Euthyroid	p-value
Bilirubin (mg/dL)	3.1 ± 1.2	2.2 ± 1.0	0.03*
Albumin (g/dL)	3.1 ± 0.5	3.5 ± 0.4	0.02*
ALT (IU/L)	78 ± 30	72 ± 28	0.45
AST (IU/L)	95 ± 40	88 ± 35	0.38

*Statistically significant

Tumor Characteristics and Thyroid Status

Analysis of tumor characteristics revealed that patients with hypothyroidism and subclinical hypothyroidism had a higher proportion of multifocal tumors (42%) compared to euthyroid patients (21%). Moreover, the mean tumor size was slightly larger in the thyroid dysfunction group (5.8 ± 2.3 cm) than in the euthyroid group (4.7 ± 1.9 cm), supporting a potential association between thyroid dysfunction and tumor burden.

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Table 4: Tumor Characteristics by Thyroid Status

Parameter	Thyroid Dysfunction	Euthyroid	p-value
Mean Tumor Size (cm)	5.8 ± 2.3	4.7 ± 1.9	0.04*
Multifocal Tumor (%)	42	21	0.05

*Statistically significant

Figure 1: Pie chart showing the distribution of thyroid status among HCC patients. Euthyroid patients constitute 56.7%, hypothyroid 21.7%, subclinical hypothyroid 11.7%, and hyperthyroid 10%. The figure visually highlights that nearly half of the HCC patients exhibited thyroid dysfunction, emphasizing the clinical relevance of thyroid assessment in this population.

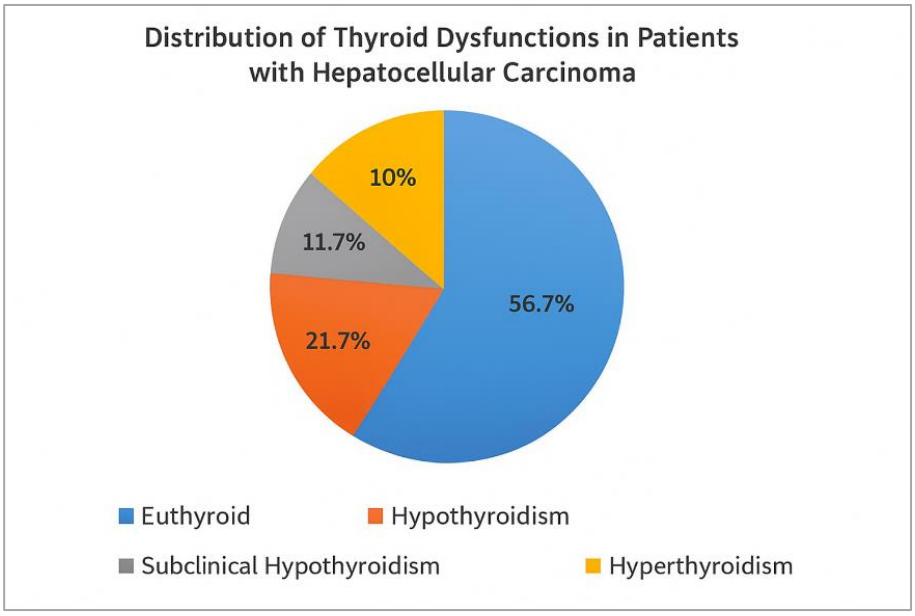

Figure 1. Distribution of thyroid dysfunction among hepatocellular carcinoma patients (n=60).

DISCUSSION

The present study demonstrates a notably high prevalence of thyroid dysfunction among patients with hepatocellular carcinoma (HCC) in Bangladesh, with 43.3% of the 60 cases exhibiting abnormal thyroid function. Hypothyroidism emerged as the most common abnormality, accounting for 21.7% of patients, followed by subclinical hypothyroidism and hyperthyroidism. These findings are consistent with prior studies in both cirrhotic and HCC populations, which report thyroid dysfunction rates ranging from 30% to 50%, with hypothyroidism being predominant [13,14,18]. The high prevalence observed in this study underscores the importance of assessing thyroid function as part of the routine evaluation of HCC patients, especially considering the potential clinical implications of thyroid hormone abnormalities on disease progression, metabolic status, and overall prognosis. The pathophysiology linking thyroid dysfunction and HCC is multifactorial. The liver is the principal site for the peripheral conversion of thyroxine (T4) to the biologically active triiodothyronine (T3) through deiodinase activity. In chronic liver disease, including HCC, this conversion is impaired due to reduced expression and activity of hepatic deiodinases, leading to the low T3 syndrome [15]. Moreover, liver dysfunction results in altered serum protein levels, particularly albumin and thyroid-binding globulin, which affect the total and free concentrations of circulating thyroid hormones [16]. In the present study, patients with thyroid dysfunction had significantly lower serum albumin levels and higher bilirubin levels, reflecting the association between impaired liver synthetic function and altered thyroid hormone metabolism. These observations corroborate previous findings that hypothyroidism and subclinical hypothyroidism are often markers of more severe liver disease and correlate with the Child-Pugh score [14,18]. Thyroid hormone receptors (TRs) expressed in hepatocytes play a role in regulating cell proliferation, differentiation, apoptosis, and metabolic activity [6,7]. Dysregulation of thyroid hormone signaling may therefore contribute to hepatocarcinogenesis and tumor progression. Experimental studies have demonstrated that thyroid hormone deprivation or hypothyroidism can enhance hepatic tumor growth, whereas euthyroid status or T3 supplementation may exert protective effects via modulation of hepatocyte proliferation and apoptosis pathways [17]. This mechanistic insight provides a biological basis for the clinical observation in this study that higher TSH levels correlated positively with tumor size ($r=0.42$, $p=0.002$), suggesting that thyroid dysfunction may not only reflect liver impairment but could also influence tumor burden. The observed sex distribution, with a predominance of males (75%), aligns with the known epidemiological pattern of HCC, which shows a higher incidence in males globally and in Bangladesh [1–3]. Etiologically, hepatitis B virus

(HBV) infection accounted for the majority of cases (55%), followed by hepatitis C virus (HCV) infection and non-alcoholic fatty liver disease (NAFLD). The interplay between viral hepatitis, liver inflammation, and thyroid hormone metabolism is complex. Chronic HBV and HCV infections can induce systemic inflammation and cytokine release, which may interfere with the hypothalamic-pituitary-thyroid axis, further predisposing to thyroid dysfunction [16,19]. Therefore, in regions with high HBV/HCV prevalence, thyroid abnormalities in HCC patients may be more common than in populations with a lower prevalence of viral hepatitis. Clinical implications of these findings are multifaceted. Thyroid dysfunction in HCC patients may exacerbate fatigue, weight changes, and metabolic disturbances, further impairing quality of life. Moreover, hypothyroidism can contribute to dyslipidemia, insulin resistance, and cardiovascular morbidity, potentially complicating the management of HCC patients who often have underlying metabolic comorbidities [11]. Recognizing and addressing thyroid dysfunction may therefore improve supportive care and overall patient outcomes. In addition, routine thyroid function assessment could serve as an adjunct prognostic tool, as suggested by the correlation between TSH levels and tumor size in this cohort. While causal inference cannot be established in this observational study, these associations highlight the potential relevance of thyroid status in the clinical trajectory of HCC. Comparisons with international literature reveal similar trends. Wong et al. reported thyroid hormone abnormalities in cirrhotic patients with HCC, noting a prevalence of 38% for low T3 syndrome, which was associated with more advanced disease and poorer prognosis [19]. Chen et al. found that hypothyroidism was an independent risk factor for HCC development in patients with chronic hepatitis [8]. These studies, together with the present findings, suggest a bidirectional relationship whereby liver disease alters thyroid function, and altered thyroid function may in turn influence hepatocarcinogenesis and tumor progression. The high prevalence of subclinical hypothyroidism observed in 11.7% of patients also merits attention. While often asymptomatic, subclinical hypothyroidism has been associated with cardiovascular risk, metabolic derangements, and subtle hepatic functional impairment [11]. In the context of HCC, even mild thyroid hormone perturbations may affect metabolic homeostasis, drug metabolism, and response to therapy. Therefore, identifying and monitoring subclinical thyroid abnormalities could be clinically relevant, particularly in patients undergoing systemic therapy or loco-regional interventions such as transarterial chemoembolization (TACE), where metabolic stability can influence treatment tolerance and outcomes. Limitations of the current study should be acknowledged. This was a single-center study with a relatively small sample size (n=60), which may limit generalizability. The cross-sectional assessment of thyroid function precludes longitudinal analysis of temporal changes during HCC progression or treatment. Additionally, potential confounders such as nutritional status, concurrent medications, and systemic illnesses were not exhaustively controlled, which could influence thyroid hormone levels. Despite these limitations, the study provides valuable preliminary evidence regarding the prevalence and clinical correlates of thyroid dysfunction in HCC patients in Bangladesh, where such data are scarce. Future research directions include larger, multi-center studies to validate these findings and to explore the prognostic significance of thyroid dysfunction in HCC. Longitudinal studies could elucidate the dynamics of thyroid hormone changes over the disease course and in response to therapy. Furthermore, mechanistic studies investigating the molecular interactions between thyroid hormones, TRs, and hepatic tumor pathways may reveal novel therapeutic targets. Interventional trials assessing the impact of correcting thyroid dysfunction on HCC progression, treatment tolerance, and survival outcomes could ultimately inform clinical practice guidelines.

CONCLUSION

In conclusion, the present study highlights that thyroid dysfunction is common in patients with HCC in Bangladesh, with hypothyroidism being the predominant abnormality. The findings demonstrate significant associations between thyroid hormone abnormalities, liver function impairment, and tumor burden. Routine assessment of thyroid function in HCC patients could provide valuable clinical information for prognosis, metabolic management, and supportive care optimization. Given the potential impact on disease trajectory and patient well-being, integrating thyroid evaluation into the standard HCC work-up appears warranted. Further prospective and mechanistic studies are needed to clarify the causative links and therapeutic implications of thyroid dysfunction in hepatocellular carcinoma.

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