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DYSLIPIDEMIA AND ITS CORRELATION WITH HEPATIC ENZYMES IN HYPOTHYROID PATIENTS: A PUBLIC HEALTH PERSPECTIVE

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ABSTRACT:

Background: Underactive thyroid is an endocrine system disorder defined by inadequate thyroid hormone synthesis by the thyroid gland. Hypothyroidism affects lipid profiles is via thyroid hormone and thyroid hormone receptor, which is mostly expressed in the liver, may bind to thyroid hormone to control the expression of downstream target genes. The objectives of this study aimed to determine lipid parameters and liver function in hypothyroid patients and correlate dyslipidemia and deranged Liver functions with the thyroid profile.

Methodology: This Descriptive Cross-Sectional study was conducted in the Medical department at PMC Hospital and NORIN Hospital Nawabshah, SBA for the period of 06 months from July 2023 to Dec 2023. After taking approval from Ethical review committee of the Institute, 200 males and females diagnosed patients of hypothyroidism fulfilling the inclusion Criteria were selected. Non probability purposive sampling technique was used. A written consent was taken and required laboratory reports were collected for information. Demographic information, history of the patient and physical examination were collected using a structured questionnaire. To analyze the pattern of dyslipidemia, a lipid profile and routine tests were performed.

Results: Mean age of the participants was 38.46 ± 2.68 years and majority of the participants were belonging to lower and middle socioeconomic class. There was statistical significant association **(p-value <0.05)** between poor class and middle class. There was significant association between obesity and deranged liver function **(p-value 0.037)** and with deranged lipid parameters **(p-value 0.010)**. Pearson correlation (2 tailed) test was applied to measure the correlation between deranged lipid profiles and deranged liver enzyme. There was positive correlation **(0.169)** between deranged lipids profile and deranged liver enzyme.

Conclusion: Results of this study reveal that hypothyroidism is directly linked with deranged liver enzymes and lipid parameters because in hypothyroidism there is low metabolism especially in liver. Dyslipidemia and abnormal liver enzymes make the condition worse and have an impact on

the prognosis and course of the disease. To lessen the severity, it is advised that dyslipidemia should also be treated in these patients.

Key Words: Hypothyroidism, Deranged liver enzymes, Deranged lipid enzymes

INTRODUCTION:

Hypothyroidism: Underactive thyroid or hypothyreosis is an endocrine system disorder that is defined by inadequate thyroid hormone synthesis by the thyroid gland. It may cause a variety of symptoms, such as a decreased ability to tolerate cold, tiredness, constipation, a slow pulse, depression, and weight gain. Swelling at the front of the neck may sometimes be brought on by goiter [1]. Changes in thyroid hormone levels may have an impact on the overall metabolism since they control the basal metabolic rate of all cells [2]. Due to iodine shortage and other causes; the body prevalence of thyroid-related illnesses is quickly rising across the world. Thyroid dysfunction prevalence rates have increased in Pakistan during the last 20 years. In Pakistan, there are 4.1 and 5.4% more people with hypothyroidism and subclinical hypothyroidism, respectively [3].

It is estimated that one billion people suffer from iodine shortage globally; however it is unclear how often this results in hypothyroidism. Age is important factor associated with hypothyroidism and its prevalence increases with age. This disease is more common over the age of sixty years [4]. Primary hypothyroidism affects around a thousand times more persons than central hypothyroidism. There are three main causes of hypothyroidism; Primary hypothyroidism (Insufficient thyroid gland activity), Secondary hypothyroidism (Insufficient pituitary stimulation), and Insufficient thyrotropin [5].

Dyslipidemia in hypothyroidism: Different effects of hypothyroidism are shown in blood lipid levels. Patients with TSH >10 mlU/L had more ApoB-containing lipoprotein cholesterols than those with TSH 4.0–10.0 mlU/L. Regardless of thyroid function, levels of lipoprotein cholesterols containing ApoB are always positively associated with circulating TSH levels. Therefore, the risk of dyslipidemia increases as TSH levels rise. Blood lipids even become better over time if there is not a major impairment of thyroid function caused by a low TSH level. As a result, we would first assume that TSH, in addition to TH, is crucial for controlling lipid metabolism [6].

Mechanism of action of dyslipidemia in hypothyroidism: The major way that hypothyroidism affects lipid profiles is via TH. The thyroid hormone receptor (THR), which is mostly expressed in the liver, may bind to thyroid hormone (TH) to control the expression of downstream target genes. Without the aid of TH, TSH alone has the ability to raise TC levels in CVD patients. According to studies, TSH regulates cholesterol metabolism via attaching to TSH receptors (TSHRs) on the surface of hepatocytes and adipocytes. According to the available data, TH and TSH both have an effect on how cholesterol is metabolized. These are a few of the regulatory elements that affect the metabolism of cholesterol [7]. When a person has hypothyroidism, their lipid metabolism is impacted by both high TSH and reduced TH. In the presence of hypothyroidism, the changed functions are identified. Actions of decreased TH are shown by red arrows, whereas raised TSH is indicated by blue arrows [8].

Even while increased HDL-C levels are cardio-protective and a biomarker of HDL functioning, they cannot always shield people from CVD and death [9]. TSH has also been shown to have a significant role in affecting lipid metabolism both in vitro and in vivo, in addition to established TH metabolic pathways [10]. Higher TSH levels may influence lipid metabolism via a distinct TSH signaling route even in those with appropriate thyroid function and subclinical hypothyroidism. From a medical standpoint, treating hypothyroidism seems to need maintaining TSH at a low normal level in order to reduce cholesterol levels [11]. In hypothyroidism patients, TH is the main cause of hormone physiological change, and TH negative feedback regulation may impact TSH levels [12].

***Correlation of thyroid hormones and liver function*:** Since the liver is the primary location for the metabolism of triglycerides and cholesterol, thyroid hormones are crucial for maintaining the equilibrium of hepatic lipids. Because thyroid hormones stimulate the production of LDL receptors on hepatocytes and the activity of liver enzymes that lower cholesterol, low-density lipoprotein levels are reduced. Thyroid hormones cause a higher expression of apolipoprotein A1, a vital component of HDL [13].

Thyroid hormones are essential for lifelong metabolic balance because of their close relationship with the liver. Normal thyroid function is required to maintain liver metabolism even though thyroid disorders may affect how clinically liver disease develops. Despite the fact that thyroxine(T4), free T4, and thyroid-stimulating hormone (TSH) may all effectively reflect the loss of thyroid function, TSH readings above the reference range frequently signify that the thyroid gland is underactive, as in poor thyroid function, such as subclinical hypothyroidism. According to reports, sub clinical hypothyroidism has a 4–20% incidence rate, elevated plasma TSH levels, and normal FT4 levels. A recent study found that patients with SCH and FLD who attended the clinic were bigger and more likely to have metabolic issues than those who just had SCH and a healthy liver [14].
The objectives of this study aimed to determine the status of lipid parameters in hypothyroid patients and deranged Liver functions in hypothyroid patients and correlate dyslipidemia and deranged Liver functions with the thyroid profile in hypothyroid patients.

Methodology:
This Descriptive Cross-Sectional study was conducted in the Medical department at PMC Hospital and NORIN Hospital Nawabshah, SBA for the period of 06 months from July 2023 to Dec 2023, after taking approval from Ethical review committee of the Institute (Vide letter No. PUMHS/SBA/PVC/165 dated: 12-10-2021). 200 males and females diagnosed patients of hypothyroidism fulfilling the inclusion Criteria were selected. Non probability Purposive sampling technique was used. **Data collection procedure:** Data was collected from the patients who were visiting Out-Patient Department and/or admitted in Medical ward of PMC Hospital, and NORIN Hospital, diagnosed and confirmed by Physicians. A written consent was taken and required laboratory reports were collected for information. Demographic information, history of the patient and physical examination were collected using a structured questionnaire. To analyze the pattern of dyslipidemia, a lipid profile and routine tests were performed. **Data analysis:** The data were analyzed using the Statistical Program for Social Sciences (SPSS), version 26.0. The variables with means and standard deviations were age, BMI, duration of liver disease, LFT, and Lipid Profile. Age, Gender, Socioeconomic status, Obesity, liver disease severity (Child-Pugh class), and dyslipidemia pattern were the categorical covariates with frequencies and percentages. Chi-square test was used for categorical variables, and Pearson correlation test for correlation and a p-value was set at < 0.05.

Results

Table No. 01 Sociodemographic information of the study participants (n=200)

Sr. No	Characteristics	Frequency	Relative Percentage
1	**Gender Distribution of Participants**		
	Male	**59**	29.5
	Female	**141**	100.0
2	**Age of Participants (in years)**		
	Less than 30 years	**26**	13.0
	31 to 45 years	**67**	46.5
	46 to 60 years	**73**	83.0
	60 years of more	**34**	100.0
3	**Residence of Participants**		

	Urban	**52**	26.0
	Rural	**148**	100.0
4	**Socioeconomic status of the participants**		
	Poor Class	**72**	36.0
	Middle Class	**128**	100.0
	Upper Class	**0**	100.0
5	**Literacy status of Participants**		
	Illiterate	**63**	31.5
	Primary	**101**	82.0
	Secondary	**30**	97.0
	Graduate	**6**	100.0

Data from the above table shows the brief socio-demographic information and characteristics of the study participants.

Table No. 02 Mean Thyroid Profile Parameters, Mean Lipid profile Parameters and Mean Liver Function Teat Parameters of the Participants (n=200)

Sr. No.		Mean & Standard Deviation	Minimum	Maximum
Thyroid Profile Parameters of the Participants				
1	TSH (mIU/L)	**6.88 ± 0.899**	5.10	8.50
2	T3 (mIU/L)	**0.89 ± 0.078**	0.60	0.98
3	T4 (mIU/L)	**3.99 ± 0.804**	2.50	5.20
Lipid profile Parameters of the Participants				
4	Cholesterol (mg/dL)	**177.52 ± 44.051**	136	295
5	TG (mg/dL)	**132.48 ± 41.373**	130	314
6	LDL (mg/dL)	**113.75 ± 20.599**	71	125
7	HDL(mg/dL)	**33.74 ± 2.854**	32	40
8	VLDL (mg.dL)	**42.74 ± 3.193**	30	62
Liver Function Teat Parameters of the Participants				
9	Bilirubin (mg/dL)	**1.37 ± 0.59**	0.65	6.75
10	SGPT (IU/L)	**46.65 ± 19.01**	29	118
11	SGOT (IU/L)	**38.92 ± 8.49**	30	60
12	ALP (IU/L)	**136.43 ± 17.14**	115	215

The above table shows mean value of thyroid parameters, mean lipid profile parameters, and mean liver function parameters.

Table No. 03 Distribution of Deranged Total Lipids and Liver Enzyme (ALT) in Hypothyroidism Cases (n=200)

		Hypothyroid Patients	Total
Total Lipids	Normal	**160**	160
	Deranged	**40**	40
Total		200	200
Liver Enzyme (ALT)	Normal	**132**	132
	Deranged	**68**	68
Total		200	200

The above table shows the number of cases of deranged lipid profile and deranged liver enzyme (ALT is mainly deranged when liver compromises) in our hypothyroid study participants. It was

noted that 40 (20.0%) out of 200 had deranged lipid profile and 68 (34.0%) out of 200 had deranged liver enzymes.

Table No. 04 Association between Socioeconomic status with Liver Enzymes and Total Lipids (n=200)

Count

		Liver Enzymes		Total	Total Lipids		Total	P-value
		Normal	Deranged		Normal	Deranged		
Socioeconomic Status	Poor Class	**50**	**22**	72	**57**	**15**	72	**0.03**
	Middle Class	**82**	**46**	128	**103**	**25**	128	
Total		132	68	200	160	40	200	

Socioeconomic status of the participants was also compared with dyslipidemia and deranged Liver enzymes in hypothyroid patients. There was no participant from the upper class this may be because the study was taken from government hospital where majority of the patients come from remote areas. There was statistical significant association (p-<0.05) between Poor Class and middle Class.

Table No. 05 Association between Body Mass Index of Participants and Liver Enzymes and Total Lipids

Count

		Body Mass Index of Participants			Total	p-value
		Under Weight	Normal Weight	Over Weight & Obese		
Liver Enzymes	Normal	**8**	**49**	75	132	**0.037**
	Deranged	**3**	**24**	41	68	
Total		11	53	116	200	
Total Lipids	Normal	9	55	96	160	**0.010**
	Deranged	2	18	20	40	
Total		11	73	116	200	

* Binomial logistic regression analysis was performed

The above table shows the status of obesity according to BMI in participants (both genders) and their association with deranged liver function and dyslipidemia in hypothyroid patients. Binomial regression analysis was performed and there was significant association between obesity and deranged liver function **(p-value 0.037)** and with deranged lipid parameters **(p-value 0.009)**

Table No. 06 Correlations between Deranged total lipids and Liver enzymes in hypothyroid patients (n=200)

		Total Lipids	Liver Enzymes
Total Lipids	Pearson Correlation	1	**0.169***
	Sig. (2-tailed)		0.017
	N	200	200
Liver Enzymes	Pearson Correlation	**0.169***	1
	Sig. (2-tailed)	0.017	
	N	200	200

*Correlation is significant at the 0.05 level (2-tailed).

Pearson correlation (2 tailed) test was applied to measure the correlation between deranged lipid profiles and deranged liver enzyme (ALT is mainly deranged when liver compromises) in

hypothyroid patients and it was seen that there was significant positive correlation **(0.169)** between deranged lipids profile and deranged liver enzyme**.**

Discussion: Hypothyroidism is a condition that can be caused by several thyroid gland disorders. Dyslipidemia and hypothyroidism usually go along. The development of hepatic insulin resistance is brought on by intrahepatic fat buildup brought on by hypothyroidism-associated dyslipidemia, which in turn causes nonalcoholic fatty liver disease (NAFLD) [15]. Subclinical hypothyroidism (SH), which is much more prevalent and asymptomatic than overt hypothyroidism, is described as the clinical condition of modestly increased blood TSH levels (up to 10 uIU/ml) with normal levels of FT4 and FT3. Hypothyroidism is diagnosed in 1% to 10% of adult population where hypothyroidism is endemic. It appears to be more common in older and female participants. Subclinical hypothyroidism, which is characterized by changes in lipid metabolism, cardiovascular, and neuromuscular functioning, may be the initial stage or start of a degenerative illness state. Both overt and subclinical hypothyroidisms have negative effects on the blood lipid profile, which may make atherosclerotic disease more likely to occur. Serum total and LDL cholesterol levels are often higher in SH patients. In our study altered lipid profile was seen in 20% hospitalized hypothyroid cases [16].

Deranged lipid function is an important systemic consequence of deranged liver enzymes. The body's attempt to repair liver injury results in the development of hepatic fibrosis. Protein anabolism, bilirubin excretion, and lipid metabolism are all affected by liver illness [17]. Recent studies have demonstrated that lipid profiles change with the severity of the illness and are an important element in the management of such patients, despite the fact that at our facility lipid profile monitoring is not part of the standard of care for such patients. Depending on the severity of the disease, dyslipidaemia was present in a sizable majority of individuals with chronic liver disease, also seen in our study data [18].

The age of the patients is very important in the management of chronic liver disease because increasing age has many complications it was noted in our study that age more than sixty years has been linked with increased risk of lipid profile disturbance as seen in our study. It was concealed that the male to female ratio was 2.4:1. A cross-sectional research by Farooque U. et al included 171 individuals with chronic liver disease who had a severe form of the illness and were all between the ages of 18 and 60 [19]. According to the study's findings, the average age of the participants was 51.2±7.3 years and 7.3 years, and the male female ratio was 1.5:1 in the study which is in accordance with our study as well.

A disadvantageous risk factor for many diseases is socioeconomic status. Numerous studies have demonstrated that people with poor socioeconomic status, particularly in developing nations, have higher rates of morbidity and disability. We also looked at the socioeconomic status of the participants in order to investigate the relationship between socioeconomic status and temporal sequences in the development or worsening of deranged liver enzymes. Deranged liver enzyme (ALT) was seen in 22 participants out of 72 from lower class and in 46 participants out of 128 from middle class. Dyslipidemia was observed in 15 participants out of 59 from poor class and 25 participants out of 141 from middle class with p-value of 0.05 that shows statistical significant association between Poor Class, middle Class and Dyslipidemia. A study conducted by Kivimaki M, et al to determine low socioeconomic status as a risk factor for a range of hospital-treated diseases. In many diseases or health disorders, low socioeconomic status was strongly correlated, 32% of them are closely associated and correlated this status [20]. In another study conducted by Giammarino AM, et al. also concluded that in patients with liver illnesses and deranged lipid profile the socioeconomic status has a double-edged impact on the patients' prognosis for health. The study's results revealed that the groups were divided based on the median values of socioeconomic characteristics, and this finding was statistically significant (P 0.0001) [21]. This is also in accordance with our study as well.

Obesity has a number of harmful impacts on one's health, and it is closely related to hypertension, insulin resistance DM, and dyslipidemia. Obesity and the metabolic syndrome are the two main causes of non-alcoholic fatty liver disease, which develops from a modest triglyceride buildup to hepatic inflammation and cirrhosis. Obesity increases the likelihood of primary liver malignancies, and body mass index (BMI) is a prognosticator of decompensated liver cirrhosis. In our study, 58% participants were overweight and 20% out of them had deranged liver enzyme mainly ALT. Lipid profile was also measured in this category there was deranged Lipids profile. The severity of the disease and outcome was also affected by the weight of the participants and it was noted that overweight participants were having more complications and poor outcome. According to a study by Schiavo L. et al. obesity is linked to a higher risk of liver disease severity. Their study data revealed that clinical decompensating of cirrhosis (ascites, encephalopathy, or jaundice) occurred in 14% of patients who were normal weight, 31% of overweight patients, and 43% of patients who were obese [22]. This is also consistent with our results.

A deficit or excess of thyroid hormones has a significant impact on the metabolism of lipids as well as on many other cardiovascular risk factors since thyroid hormones are an essential component in the normal metabolism of lipids. The composition and transit of lipoprotein are known to change as a result of changes in thyroid function. Hypothyroidism is associated with hypometabolism, which includes reduced resting energy expenditure, weight gain, higher cholesterol levels, impaired lipolysis, and decreased gluconeogenesis. In a cross-sectional research by Gopalakrishnan M. et al. 165 people with newly diagnosed untreated hypothyroidism and hyperthyroidism were recruited. The mean blood levels of total cholesterol were all considerably higher in the hypothyroid group than they were in the control group ($P = 0.000$). The mean blood levels of total cholesterol, LDL, triglycerides, and VLDL in the hypothyroid group were significantly greater compared to the control patients ($P = 0.000$) [23]. This is also in accordance with our study as well.

Patients with liver diseases frequently also have abnormal lipid profiles. Recent research has demonstrated that lipid profiles vary with illness severity and should be taken into account while managing and treating such patients in order to lessen the disease's severity. In our study deranged serum cholesterol was found in in 97 (48.5%) cases and 103 (51.5%) cases shown normal cholesterol level. Pearson Correlation test was applied and there was statistically significant association between deranged cholesterol levels and deranged liver enzymes with p-value of 0.017. Another study conducted by Badawi R, et al. to observe the association between lipid markers and severity of illness in Liver disease patients [24].

Although the link between dyslipidemia and a number of cancers is now well established, it is still unknown if hepatocellular carcinoma (HCC) and blood lipid levels with or without cirrhosis is connected. The results of a different study by Hou X, at al. examining the relationship between nonalcoholic fatty liver disease and serum triglyceride concentration showed that the participants with nonalcoholic fatty liver disease had higher fasting and postprandial TG concentrations than the healthy participants ($P < 0.05$) [25]. This is consistent with our research.

Conclusion: Results of this study reveal that hypothyroidism is directly linked with deranged liver enzymes and lipid parameters because in hypothyroidism there is low metabolism especially in liver. Liver is a vital organ for lipid metabolism that's why dyslipidemia and deranged liver enzymes correlatively found in these patients. Dyslipidemia and abnormal liver enzymes make the condition worse and have an impact on the prognosis and course of the disease. To lessen the severity, it is advised that dyslipidemia should also be treated in these patients. Additionally, there was a statistically significant correlation with socioeconomic level, advancing age, obesity, and severity of illness.

Limitations: This cross-sectional design limits the generalizability and averts causal inference.

Conflict of Interest: The author declares no conflicts of interest.

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