International Journal of Medical Science and Clinical Invention 10(5): 6716-6728, 2023
DOI:10.18535/ijmsci/v10i5.04
https://valleyinternational.net/index.php/ijmsci

Research Article,

Lipid Profile Abnormalities in Newly Diagnosed Hypothyroidism in Janakpur, Nepal

Dr. Sidhi Datri Jha[1], Dr. Digbijay Kumar Thakur[1*], Dr. Rameshwar Mahaseth[2]

[1]Head of Department of Internal Medicine at Provincial Hospital Janakpur, Nepal
[1]Consultant Physician at Department of Internal Medicine; Provincial Hospital Janakpur and Madanta Research Clinic Private Limited Janakpur
[2]Consultant Physician, Department of Internal Medicine, Provincial Hospital, Janakpur, Nepal
Email Address: drdigbijay.thakur@gmail.com

Abstract:

Objective: Thyroid disorders are known to influence lipid metabolism and are common in dyslipidemic patients. Overt and subclinical hypothyroidism have an adverse effect on the serum lipid profile that may predispose to the development of atherosclerotic disease. Our objective to conduct this study is to find out prevalence of lipid profile abnormalities in newly diagnosed case of hypothyroidism in Janakpur, Nepal.

Methods:

This study was conducted at provincial hospital Janakpur and Madanta Research Clinic Pvt.Ltd. Janakpur from December 2020-2021. This was a cross-sectional study of patients presented with symptoms and signs suggestive of hypothyroidism. Diagnostic algorithms were based on 2013 guidelines from European Thyroid Association. Subclinical hypothyroidism was defined as an elevated thyrotropin (TSH) concentration with normal serum level of thyroxine(fT4). Patients below 85 years old presented with symptoms and signs of hypothyroidism, who had given written consent were included in study. Those with current prescription of levothyroxine, anti-thyroid drugs, amiodarone and who had history of thyroid surgery or receipt of radioactive iodine within previous 12 month or having history of recent hospital admission for myocardial infarction and other terminal illness were excluded from study. Data were analyzed using IBM SPSS 25.

Results:

A total of 697 patients were enrolled in this study out of which 582(84.94%) were female and 105(15.1%) were male. Among them 58.97% of cases were from age group between 20 to 40 years. Symptoms like constipation (86.4%), tingling/numbness (85.5%), weight gain (85.5%), edema (85.5%), palpitation (85.5%), lethargy (85.5%) and easy fatigability (85.5%) were overall common clinical presentation documented. Overall mean TSH value(29.5mU/L) was significantly higher among age group 70 to 80 year followed by mean TSH value of 12.03021mU/L among age group 30 to 40 year. Symptoms like lethargy, easy fatigability, edema, tingling/numbness, weight gain, palpitation and constipation showing relatively high mean TSH value of around 7mU/L. TSH was normal in 529(75.9%) of cases, mildly increase in 121(17.4%) of cases and severely increased in 47(6.7%) of cases. Overall, 24.1% of cased were having TSH more than 4mU/L. Prevalence of subclinical hypothyroidism as calculated in this study was 12.3 percent whereas prevalence among group with TSH value more than 4mU/L was 45.83 percent. Overall, 6.7 percent of cases were having THS value more than 10mU/L. Mean cholesterol levels among group with TSH value less than 4, 4-10 and more than 10 were 180.35mg/dl, 241.22mg/dl and 355.32mg/dl respectively. Likewise, mean HDL level among groups with TSH value less than 4, 4-10 and more than 10 were 48.25mg/dl, 43.21mg/dl and 36.79mg/dl respectively. Mean LDL level among same TSH groups were 109.60mg/dl, 137.53mg/dl and 178.34mg/dl respectively. Mean TG level among same groups found to be 175.66mg/dl, 332.89mg/dl and 682.35mg/dl respectively. Mean cholesterol, LDL and TG were significantly higher among those with relatively higher TSH value ($p < 0.0001$). When calculating mean among patients with TSH more and less than 10mIU/L, mean cholesterol, mean HDL, mean LDL and mean TG values in group with TSH less than 10mIU/L were 191.68mg/dl, 47.31mg/dl, 114.8mg/dl and 204.95mg/dl respectively where in

groups with TSH more than 10mU/L were 335.32mg/dl, 36.19mg/dl, 178.34mg/dl and 682.55mg/dl respectively ($p < 0.0001$).

Conclusions: Hypothyroidism is associated with dyslipidemia, so biochemical screening for thyroid dysfunction is recommended in all patients with dyslipidemia and regular lipid screening is mandatory in patient with hypothyroidism.

Categories: Endocrinology, Internal Medicine, MD general practice KEYWORDS: subclinical hypothyroidism, high TSH, thyroid disorder, dyslipidemia, LDL, Lipid disorders

Introduction:

Dyslipidaemia often occurs in a spectrum of endocrine disorders. It can be caused by pathologies of the thyroid, the pituitary, the adrenals, or the gonads. Nearly 30% of patients with lipid profile abnormalities suffer from secondary dyslipidaemias, including type 2 dia- betes mellitus, alcohol abuse, and several endocrine disorders(1).

Table 1. The most common endocrinopathies and their influence on lipid profile

Endocrinopathy	TC	LDL-C	HDL-C	TG
Hyperthyroidism	Decreased	Decreased	Normal	Decreased
Hypothyroidism	Increased	Increased	Normal/increased	Increased
Cushing's syndrome	Increased	Increased	Normal/increased	Increased
Testosterone deficiency	Increased	Increased	Decreased	Increased
Oestrogen deficiency	Normal	Increased	Normal/decreased	Normal
Polycystic ovary syndrome	Increased	Increased	Decreased	Increased

Table: 01 (TC — total cholesterol; LDL-C — low-density lipoprotein cholesterol; HDL-C — high-density lipoprotein cholesterol; TG — triglycerides)

A relationship among hypothyroidism, lipid disorders, and coronary artery disease was first suggested in the 1960s. This was at a time when the diagnosis of hypothyroidism was based upon symptoms and signs, and sometimes serum cholesterol measurements, rather than measurements of serum thyroxine (T4) and thyroid-stimulating hormone (TSH). In some cases, a high serum cholesterol concentration was regarded as evidence for "premyxoedema" in the absence of symptoms of hypothyroidism.

Subclinical hypothyroidism

The diagnosis of subclinical hypothyroidism is based upon biochemical testing alone.
Subclinical hypothyroidism is defined as(2) :

- Normal serum free T4
- Elevated TSH

It may occur in the presence or absence of mild symptoms of hypothyroidism.

Definition of elevated TSH

For nonpregnant adults, an elevated serum TSH is defined as a TSH concentration above the upper limit of the normal TSH reference range, which is typically 4 to 5 mU/L in most laboratories. However, some experts suggest that the true upper limit is only 2.5 or 3 mU/L in healthy individuals without thyroid disease(3,4), while others argue that the serum TSH distribution shifts towards higher values with age, independent of the presence of antithyroid antibodies. In this case, the upper limit of normal could be as high as 6 to 8 mU/L in healthy octogenarians. For women trying to conceive who have ovulatory dysfunction or infertility, elevations in TSH can be defined using first trimester-specific TSH reference ranges. For pregnant women, elevations in TSH should be defined using population and trimester-specific TSH reference ranges.

Central hypothyroidism

The diagnosis of central hypothyroidism is based upon clinical manifestations and thyroid function tests. The majority of patients with central hypothyroidism have coexisting deficiencies in other pituitary

hormones, although isolated TSH deficiency may also occur. Central hypothyroidism should be suspected in the following circumstances(5):

- There is known hypothalamic or pituitary disease
- A mass lesion is present in the pituitary
- When symptoms and signs of hypothyroidism are associated with other hormonal deficiencies

In hypothyroidism caused by hypothalamic or pituitary disease, TSH secretion does not increase appropriately as T4 secretion falls. Thus, we measure both serum TSH and free T4 if pituitary or hypothalamic disease is suspected. We also measure free T4 if the patient has convincing symptoms of hypothyroidism despite a normal TSH result. In patients being monitored for central hypothyroidism (eg, irradiated childhood brain tumor survivors), a progressive decline in free T4 during surveillance is suggestive of central hypothyroidism.

Serum TSH	Serum free T4	Serum T3	Assessment
Normal hypothalamic-pituitary function			
Normal	Normal	Normal	Euthyroid
Normal	Normal or high	Normal or high	Euthyroid hyperthyroxinemia
Normal	Normal or low	Normal or low	Euthyroid hypothyroxinema
Normal	Low	Normal or high	Euthyroid: T3 therapy
Normal	Low-normal or low	Normal or high	Euthyroid: thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism
Low	High or normal	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
Abnormal hypothalamic-pituitary function			
Normal or high	High	High	TSH-mediated hyperthyroidism
Normal or low*	Low or low-normal	Low or normal	Central hypothyroidism

Table:-2 (T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone. * In central hypothyroidism, serum TSH may be low, normal, or slightly high.)

Overt Hypothyroidism

Overt primary hypothyroidism is characterized biochemically by a high serum thyroid-stimulating hormone (TSH) concentration and a low serum free thyroxine (T4) concentration. The clinical manifestations are highly variable, depending upon the age at onset and the duration and severity of thyroid hormone deficiency.

The terms dyslipidemia, lipid disorder, lipoprotein disorder, hyperlipidemia, and hypercholesterolemia are sometimes used interchangeably. However, they have different meanings(6):

- Lipid disorders – Includes disorders of lipoprotein metabolism but also lipodystrophies and some lipid storage disorders. In many clinical discussions, this term has been used to mean clinical disorders associated with abnormal levels of total, HDL, and LDL cholesterol, as well as triglycerides.
- Lipoprotein disorder – Specifically refers to clinical disorders of the lipoproteins that carry cholesterol and triglyceride.
- Dyslipidemia – Used for lipid values that are associated with disease or increased risk of disease and for which lipid-altering therapy might be of value.
- Hyperlipidemia – Elevation of serum total or LDL cholesterol or triglyceride

Dyslipidemias are disorders of lipoprotein metabolism that result in the following abnormalities(7–9):

- High total cholesterol (TC)
- High low-density lipoprotein cholesterol (LDL-C)
- High non-high-density lipoprotein cholesterol (non-HDL-C)
- High triglycerides
- Low HDL-C

In adults, dyslipidemia is an established risk factor for atherosclerotic cardiovascular disease (ASCVD), and correcting dyslipidemia reduces the risk of ASCVD.
We classify fasting serum (or plasma) TG levels according to the following criteria (to convert from mg/dL to mmol/L, divide by 88.5):

- **Normal** – <150 mg/dL (<1.7 mmol/L)
- **Moderate hypertriglyceridemia** – 150 to 499 mg/dL (1.7 to 5.6 mmol/L)
- **Moderate to severe hypertriglyceridemia** – 500 to 999 mg/dL (5.65 to 11.3 mmol/L)
- **Severe hypertriglyceridemia** – >1000 mg/dL (>11.3 mmol/L)

Guidelines and expert committees have used a variety of classification systems for hypertriglyceridemia. While the consensus of these committees is that a normal level is <150 mg/dL (1.7 mmol/L), committees have used differing terminology and criteria to classify severity of hypertriglyceridemia(9–12).

Methods:

Study design

This was a cross-sectional study of patients presented with features suggestive of hypothyroidism. conducted at provincial hospital Janakpur and Madanta research clinic private limited from December 2020 to December 2021. Provincial hospital Janakpur is the only referral center in province-2 of Nepal.

Inclusion Criteria

- Patient with definite history suggestive of thyroid disorders like those with history suggestive of lethargy, easy fatigability, tingling and numbness, palpitation, cold and hot intolerance, constipation and hoarseness of voice. Also, those having facial puffiness, pedal edema and dry lusterless skin.
- Patient with age below 85-year-old.
- Those with goiter.
- Patient or relatives who gave written consent.

Exclusion Criteria

The main exclusion criteria for the trial were

- Current prescription for levothyroxine, antithyroid drugs, amiodarone, or lithium.
- Thyroid surgery or receipt of radioactive iodine within the previous 12 months.
- Those with features suggestive of dementia.
- History of hospitalization for a major illness or an elective surgery within the previous 4 weeks.
- History suggestive of an acute coronary syndrome (including myocardial infarction or unstable angina) within the previous 4 weeks; and terminal illness(13).

Data Collection

All data from suspected patients were collected and documented. Parameters like age, sex, address, blood pressure, underlying comorbidities were documented. Clinical features like lethargy, easy fatigability, weight gain, cold intolerance, hoarseness of voices, dry lusterless skin, palpitation, constipation, tingling/numbness, facial puffiness, edema and goiter were noted. Laboratory test like TSH, T3 and T4 were sent and reports were collected. Age was classified into different age class interval for simplicity of analysis as <10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80 and >80. TSH was categorized into different severity level as those having normal TSH, mildly increased and severely increased TSH level. TSH value less than 4mU/L was told as having normal TSH, value between 4-10mU/L were told as having mildly

increased and value above 10mU/L were told as having severely increased(14). Diagnostic algorithms were based on 2013 guidelines from European Thyroid Association(15–17). Measurement of TSH, T3 and T4 were done in all patients, whereas anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies could not be done due to economic issues and non-availability of funds. These tests were performed on automated immunoassay analyzers with standard prescribed procedures.

Statistical methods

Data were analyzed using IBM SPSS statistic 25. Descriptive data were summarized using standard technique and reported as percentage with 95% confidence interval. Continuous data were presented as mean +/- SD and categorized data as absolute number and percentage. The student t-test and chi-square tests were used for comparison of continuous and categorical variables between groups respectively. Fisher's exact test used for analyzing difference between two groups when there were cells < 5. Correlation between continuous variable were assessed using Pearson's correlation. Predictive values of subclinical hypothyroidism were assessed by logistic regression.

Observations and Results:

A total of 697 patients were included in this study out of which 582(84.94%) were female and 105(15.1%) were male. Among them, 58.97% of them were lying in age group 20-40 while 12.20% were teens and around 18.37% were lying in age group 40-60. Only few around 9.04% of them were with age more than 60 year. Patients presented with varied symptoms and signs more common being constipation (86.4%), edema (85.5%), easy fatigability (85.5%), tingling/numbness (85.5%), weight gain (85.5%), palpitation (85.5%) on the other hand less common being dry lusterless skin (15.8%), goiter (15.6%), hoarseness of voice (14.1%), cold intolerance (16.5%) and facial puffiness (16.4%).

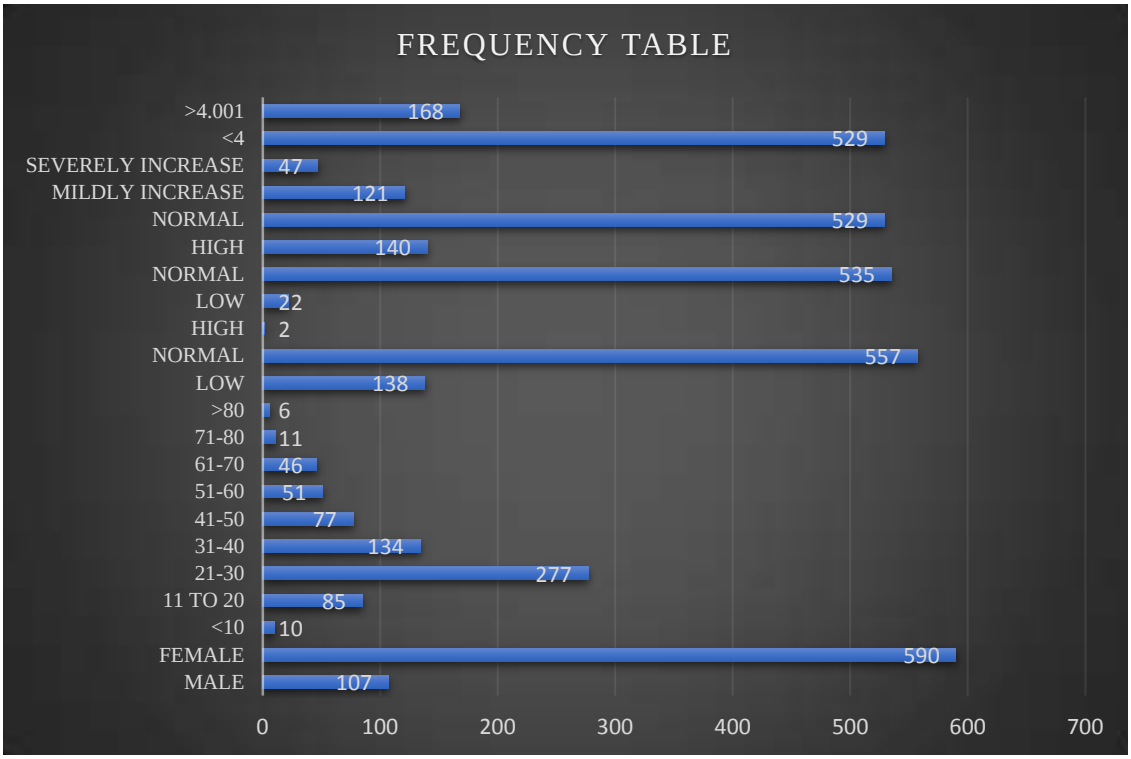
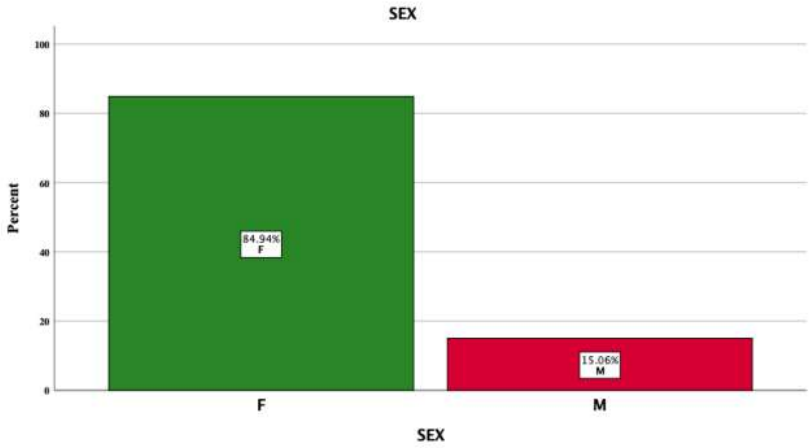


Figure 01-frequency of TSH > 4.001 & < 4, TSH levels, T3/T4 levels, age class interval and sex

Mean TSH among age group 30-40 year was 12.03021mU/L, that among age group 20-30 year was 5.64mU/L and that among 10-20 year was around 3mU/L. However mean TSH among age group 40-70 was around 5mU/L while that among 70-80 was significantly high around 29.5mU/L(figure-04).



FFigure-04 (showing frequency (%) of male and female enrolled in this study.
ootnote

MEAN TSH ACROSS DIFFERENT AGE GROUPS					
THS					
AGE CLASS INTERVAL	Mean	N	Std. Deviation	Minimum	Maximum
<10	3.3896	10	3.308733	0.156	12
11-20	3.44927	85	7.138031	0.22	63.4
21-30	5.64002	277	31.160075	0.01	493.53
31-40	12.03021	134	45.469054	0.015	389.15
41-50	5.60009	77	12.781072	0.04	100
51-60	5.11204	51	13.276708	0.03	94.06
61-70	5.78193	46	15.117425	0.05	100
71-80	29.51	11	57.873121	0.14	154.4
>80	1.85333	6	1.004682	0.53	3.32
Total	6.87954	697	29.932124	0.01	493.53

Table-3-(showing mean TSH levels across different age class interval)

Normal TSH was found in 529(75.9%) of cases while TSH was mildly increase in 121(17.4%) of cases and was severely increased in 47(6.7%) of cases. So overall 24.1% of all cases having TSH more than 4mU/L. When all the samples were taken into consideration as a population with signs and symptoms suggestive of thyroid disorders specially hypothyroidism, then overall prevalence of hypothyroidism come to be around 24.1% if 4mU/L is considered as upper limit of TSH. As only 12.3% of case were having normal fT4 level, so overall prevalence of subclinical hypothyroidism will be around 12.3%. However, when taking cases with TSH level more than 4mU/L into calculation then among this group, overall prevalence of subclinical hypothyroidism will come around N=77(45.83%).

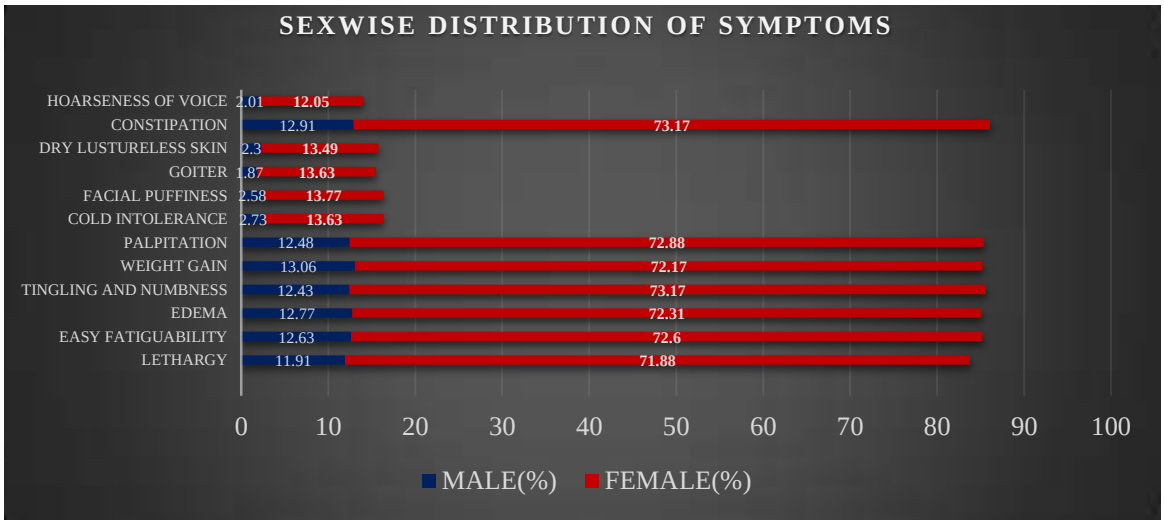


Figure 03: Histogram showing distribution of different symptoms across male and female.

TSH SEVERITY GRADING		TOTAL CHOLESTEROL	HDL LEVEL	LDL LEVEL	TRIGLYCERIDE LEVEL
<4	Mean	180.35	48.25	109.6	175.66
	N	529	529	529	529
	Std. Deviation	70.154	6.166	26.602	144.041
4 to 10	Mean	241.22	43.21	137.53	332.98
	N	121	121	121	121
	Std. Deviation	87.467	8.29	34.648	246.25
>10	Mean	355.32	36.79	178.34	682.55
	N	47	47	47	47
	Std. Deviation	67.65	3.961	23.968	197.426
Total	Mean	202.71	46.6	119.08	237.15
	N	697	697	697	697
	Std. Deviation	86.981	7.233	33.859	215.958

Figure 04- Table showing mean cholesterol, mean HDL, mean LDL and mean TG level across different TSH severity grading.

Overall, 239(34.3%) of patients found to have LDL level less than 100, 312(44.8%) had LDL level between 100-129mg/dl, 23(3.3%) had LDL level between 130-159mg/dl, 75(10.8%) of them had LDL level between 160-189mg/dl and 48(6.9%) among them found to have LDL
level above 190mg/dl. Similarly, 20.8% among them having their HDL level under 40mg/dl and around 18.5% (129) having their TG level between 500-999mg/dl.

Mean cholesterol levels among group with TSH value less than 4, 4-10 and more than 10 were 180.35mg/dl, 241.22mg/dl and 355.32mg/dl respectively. Likewise, mean HDL level among groups with TSH value less than 4, 4-10 and more than 10 were 48.25mg/dl, 43.21mg/dl and 36.79mg/dl respectively. Mean LDL level among same TSH groups were 109.60mg/dl, 137.53mg/dl and 178.34mg/dl respectively. Mean TG level among same groups found to be 175.66mg/dl, 332.89mg/dl and 682.35mg/dl respectively.

TSH GRADING<10>10		**TOTAL CHOLESTEROL**	**HDL LEVEL**	**LDL LEVEL**	**TRIGLYCERIDE LEVEL**
Less than 10	Mean	191.68	47.31	114.8	204.95
	N	650	650	650	650
	Std. Deviation	77.336	6.892	30.266	178.458
More than 10	Mean	355.32	36.79	178.34	682.55
	N	47	47	47	47
	Std. Deviation	67.65	3.961	23.968	197.426
Total	Mean	202.71	46.6	119.08	237.15
	N	697	697	697	697
	Std. Deviation	86.981	7.233	33.859	215.958

Table 5: Mean cholesterol, HDL, LDL and TG level among condidates with TSH value <10 and >10 U/L

ANOVA Table							
TOTAL CHOLESTEROL * TSH GRADING<10>10			Sum of Squares	df	Mean Square	F	Sig.
	Between Groups	(Combined)	1173688.531	1	1173688.531	199.339	0.000
	Within Groups		4092087.653	695	5887.896		
	Total		5265776.184	696			
HDL LEVEL * TSH GRADING<10>10	Between Groups	(Combined)	4855.441	1	4855.441	106.946	0.000
	Within		31553.474	69	45.401		

	Groups			5			
	Total		36408.915	696			
LDL LEVEL * TSH GRADING<10>10	Between Groups	(Combined)	176970.022	1	176970.022	198.078	0.000
	Within Groups		620939.152	695	893.438		
	Total		797909.174	696			
TRIGLYCERIDE LEVEL * TSH GRADING<10>10	Between Groups	(Combined)	9998155.147	1	9998155.147	309.357	0.000
	Within Groups		22461832.73	695	32319.184		
	Total		32459987.88	696			

Table 6: Anova table showing difference in mean cholesterol, mean HDL, mean LDL and mean TG level while comparing among group with TSH more and less than 10 mIU/L.

Mean cholesterol, LDL and TG were significantly higher among those with relatively higher TSH value ($p < 0.0001$). When calculating mean among patients with TSH more and less than 10mIU/L, mean cholesterol, mean HDL, mean LDL and mean TG values in group with TSH less than 10mIU/L were 191.68mg/dl, 47.31mg/dl, 114.8mg/dl and 204.95mg/dl respectively where in groups with TSH more than 10mU/L were 335.32mg/dl, 36.19mg/dl, 178.34mg/dl and 682.55mg/dl respectively ($p < 0.0001$).

LDL GRADING		**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	less than 100	239	34.3	34.3	34.3
	100-129	312	44.8	44.8	79.1
	130-159	23	3.3	3.3	82.4
	160-189	75	10.8	10.8	93.1
	190 and more	48	6.9	6.9	100
HDL GRADING					
Valid	under 40	145	20.8	20.8	20.8
	40-59	552	79.2	79.2	100
TG GRADING					
Valid	under 150	561	80.5	80.5	80.5
	150-499	7	1	1	81.5
	500-999	129	18.5	18.5	100

Table 7: frequencies of patients in different categories of lipid gradings

Discussion:

In a study conducted by Edip unal et al(18), the patient group was divided into two subgroups based on their serum TSH level: (I) patients with mildly elevated TSH (TSH=4.2±10 mIU/L) (n=33) and (II) patients with high TSH (TSH≥10 mIU/L) (n=5). However, no significant difference was found between the patients with mild and severe SH with regard to TC, LDL-C, HDL-C, triglyceride level and CIMT levels (p=0.635, p=0.424, p=0.310, p=0.342, and 0.610, respectively). However, in this study, TSH value less than 4mU/L was told as having normal TSH, value between 4-10mU/L were told as having mildly increased and value above 10mU/L were told as having severely increased. In our study, normal TSH was found in 529(75.9%) of cases while TSH was mildly increase in 121(17.4%) of cases and was severely increased in 47(6.7%) of cases. So overall 24.1% of all cases having TSH more than 4mU/L. When all the samples were taken into consideration as a population with signs and symptoms suggestive of thyroid disorders specially hypothyroidism, then overall prevalence of hypothyroidism come to be around 24.1% if 4mU/L is

considered as upper limit of TSH. As only 12.3% of case were having normal fT4 level, so overall prevalence of subclinical hypothyroidism will be around 12.3%.

ANOVA Table							
TOTAL CHOLESTEROL * TSH SEVERITY GRADING			Sum of Squares	df	Mean Square	F	Sig.
	Between Groups	(Combined)	1538618.996	2	769309.498	143.25	0
	Within Groups		3727157.188	694	5370.543		
	Total		5265776.184	696			
HDL LEVEL * TSH SEVERITY GRADING	Between Groups	(Combined)	7361.647	2	3680.823	87.943	0
	Within Groups		29047.268	694	41.855		
	Total		36408.915	696			
LDL LEVEL * TSH SEVERITY GRADING	Between Groups	(Combined)	253787.432	2	126893.716	161.85	0
	Within Groups		544121.742	694	784.037		
	Total		797909.174	696			
TRIGLYCERIDE LEVEL * TSH SEVERITY GRADING	Between Groups	(Combined)	12435495.54	2	6217747.772	215.49	0
	Within Groups		20024492.34	694	28853.735		
	Total		32459987.88	696			

Table 8- Table showing difference in mean HDL, LDL, TG and Cholesterol level while comparing among different TSH severity gradings.

However, when taking cases with TSH level more than 4mU/L into calculation then among this group, overall prevalence of subclinical hypothyroidism will come around N=77(45.83%). However, there was statistically significant difference between the patients with TSH value less than 10 mIU/L and more than 10 mIU/L with regard to TC, LDL, HDL and TG levels ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$ and $p < 0.0001$).

In another study conducted by Mishal Ejaz et al(19), Total cholesterol (TC) and low-density lipoprotein (LDL) was significantly higher in participants with SCH compared to participants without SCH (228.41 ± 35.21 mg/dL vs. 171.21 ± 30.21 mg/dL; p-value: <0.00001) and (131.65 ± 28.22 mg/dL vs. 89.26 ± 18.52 mg/dL; p-value: <0.0001), respectively. Similar findings were found in our study. We found mean TG (176mg/dl vs 333mg/dl vs 682mg/dl; p<0.0001), LDL (110mg/dl vs 137mg/dl vs 178mg/dl; p<0.0001) and TC (180mg/dl vs 241mg/dl vs 355mg/dl; p<0.0001) were significantly higher among patients with normal TSH, mildly elevated TSH and high TSH

In another study conducted by M. Gao et al(20), they found that the detection rate of subclinical hypothyroidism was 13.03%. Similar to findings of our study, they found Patients with subclinical hypothyroidism showed significantly higher levels of triglyceride (1.69±1.9 vs. 1.45±1.4) and the risk of hyper triglyceridemia in women with thyroid stimulating hormone (TSH) levels ≥10mIU/L was 4.96-fold higher compared with that in the normal population (P<0.01).

In another study conducted by Alireza Rastgooye Haghi et al(21), regardless of age groups and gender, there were no significant correlations between SCH and increased levels of TG and TCHOL (P-value <0.05). The prevalence of dyslipidemia and SCH was significant in females (P-value =0.009), but not in males (P-value =0.02). Totally, there was a significant correlation between the prevalence of dyslipidemia and SCH regardless of gender (P- value =0.04). In our study, we found as TSH severity increases from less than 4 mIU/L to mildly elevated(4-10mIU/L) to high TSH value above 10mIU/L; mean TG (175mg/dl vs 333mg/dl vs 682mg/dl), mean LDL (109mg/dl vs 137mg/dl vs 178mg/dl) and mean TC (180mg/dl vs 241mg/dl vs 355mg/dl) increases progressively as well ($p < 0.0001$ for all). We found there is statistically significant correlation between TSH severity grading and serum lipid levels like TC, TG and LDL levels ($p < 0.0001$).

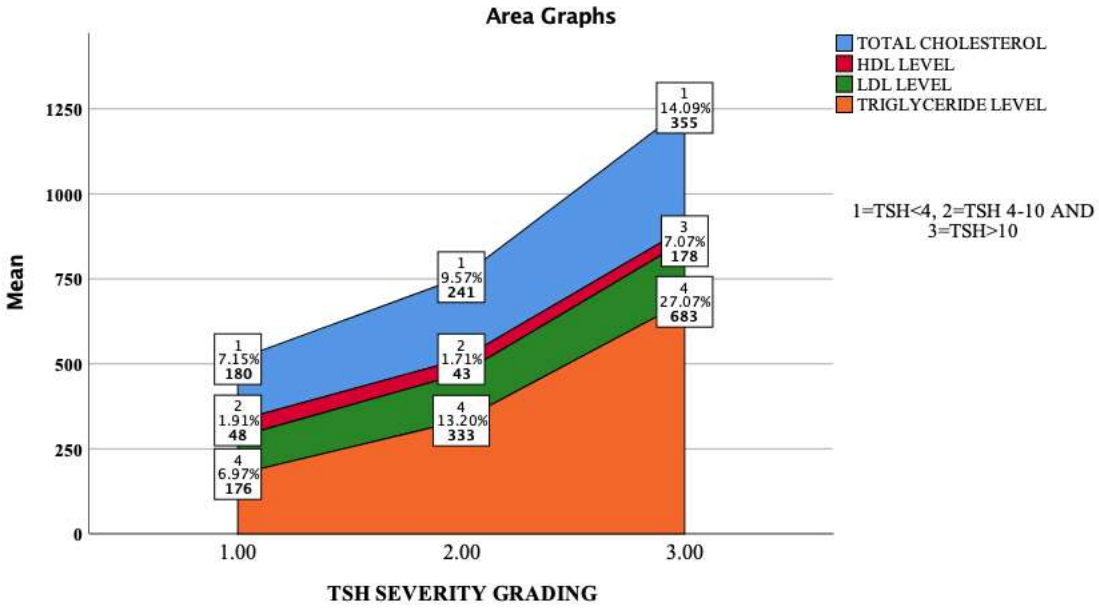
Correlations		TOTAL CHOLESTEROL	HDL LEVEL	LDL LEVEL	TRIGLYCERIDE LEVEL	TSH SEVERITY GRADING
TOTAL CHOLESTEROL	Pearson Correlation	1	-.597**	.741**	.801**	.532**
	Sig. (2-tailed)		0.000	0.000	0.000	0.000
	Sum of Squares and Cross-products	5265776.184	-261538	2E+06	10468482.26	19004.385
	Covariance	7565.77	-375.77	2181.1	15040.923	27.305
	N	697	697	697	697	697
HDL LEVEL	Pearson Correlation	-.597**	1	-.623**	-.707**	-.449**
	Sig. (2-tailed)	0.000		0.000	0.000	0.000
	Sum of Squares and Cross-products	-261538.086	36409	-1E+05	-768996.874	-1333.555
	Covariance	-375.773	52.312	-152.6	-1104.881	-1.916
LDL LEVEL	Pearson Correlation	.741**	-.623**	1	.876**	.561**
	Sig. (2-tailed)	0.000	0.000		0.000	0.000
	Sum of Squares and Cross-products	1518021.56	-106230	797909	4456155.179	7802.109
	Covariance	2181.065	-152.63	1146.4	6402.522	11.21
TRIGLYCERIDE LEVEL	Pearson Correlation	.801**	-.707**	.876**	1	.602**
	Sig. (2-tailed)	0.000	0.000	0.000		0.000
	Sum of Squares and Cross-products	10468482.26	-768997	4E+06	32459987.88	53463.303
	Covariance	15040.923	-1104.9	6402.5	46637.914	76.815
TSH SEVERITY GRADING	Pearson Correlation	.532**	-.449**	.561**	.602**	1
	Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000
	Sum of Squares and Cross-products	19004.385	-1333.6	7802.1	53463.303	242.68
	Covariance	27.305	-1.916	11.21	76.815	0.349

Table 9: ** Correlation is significant at the 0.01 level (2-tailed).

In a study conducted by N. Karthick et al(22), there were significant dyslipidaemic changes in SH women as compared to euthyroid controls. Serum total cholesterol and triglyceride levels were significantly higher as compared to those in controls. LDL levels were higher is SH women, but did not reach statistical significance and lower levels of HDL were noticed in SH subjects as compared to those in euthyroid women. A positive association was also reported between serum TSH and lipid parameters in our study group. In this study, there is no significant difference in mean values of TC ($p = 0.139$), TG ($p = 0.929$), LDL ($p = 0.600$) and HDL ($p = 0.596$) when comparing between male and female.

In another study conducted by Tetsuya Tagami et al(23), the primary hypothyroidism was seen in 27 cases (11 men and 16 women) with 17 cases of subclinical hypothyroidism (2.4%) and 10 cases of overt hypothyroidism (1.4%). The central hypothyroidism was seen in 4 cases (0.6%). The thyroid dysfunction other than hypothyroidism, such as thyrotoxicosis or inappropri- ate secretion of TSH, was seen in 22 patients and the others were euthyroid (Fig. 2). In consequence, total prevalence of hypothyroidism was 4.3 % in cases of hypercholesterolemia, with 3.8% of primary hypo- thyroidism and 0.6% of central hypothyroidism. In our

study, in patient with TG level more than 500mg/dl, we found 6.89% of them having TSH more than 4mIU/L and more than 6.03% among them having TSH more than 10mIU/L ($p < 0.0001$). Among patient with HDL under 40mg/dl, we found 7.75% of them having TSH more than 4mIU/L and 6.31% among them having TSH more than 10mIU/L ($p < 0.0001$).



Area graph showing relation between TSH severity grading and lipid levels

In a review article published by Xin Su et al(24), they mentioned that among multiple concomitant symptoms of hypothyroid- ism, dyslipidemia, as increased serum levels of low-density lipoprotein cholesterol (LDL-C), very LDL-C (VLDL-C), and triglyceride (TG), is recently suggested to be strongly cor- related with the occurrence of hypothyroidism. Consistent with this notion, increasing evidence has demonstrated that hypothyroidism could promote the risk and the pathologi- cal development of dyslipidemia. As reported, patients with increased serum concentrations of total cholesterol (TC) presented a relatively higher prevalence of both clinical hypo- thyroidism and subclinical hypothyroidism compared to that within healthy individuals. By contrast, the hypothyroidism patients with the serum concentrations of thyroid-stimulating hormone >10 mIU/L were confirmed to be correlated with a higher risk of cardiovascular diseases, suggesting that dysfunctional metabolism of thyroid hormones could be identified as the essential risk factor of lipid metabolic disorder.

Conclusion:

Subclinical hypothyroidism is common in Janakpur around half among those with hypothyroidism and so in other part of Nepal significantly higher in female with most patients complaining of constipation, lethargy, easy fatiguability, palpitation, edema and weight gain as main complain. Mean cholesterol, LDL and TG were significantly higher among those with relatively higher TSH value.

Recommendation:

Hypothyroidism is associated with dyslipidemia, so biochemical screening for thyroid dysfunction is recommended in all patients with dyslipidemia and regular lipid screening is mandatory in patient with hypothyroidism.

References:

[1] Szczepanek-Parulska E, Sokolowski J, Dmowska D, Klimek J, Stasikowski T, Zdebski P, et al. Lipid profile abnormalities associated with endocrine disorders. Endokrynol Pol. 2022 Oct 21;73(5):863–71.

[2] Biondi B, Cappola AR, Cooper DS. Subclinical Hypothyroidism: A Review. JAMA. 2019 Jul 9;322(2):153–60.

[3] Valdés S, Maldonado-Araque C, Lago-Sampedro A, Lillo-Muñoz JA, Garcia-Fuentes E, Perez-Valero V, et al. Reference values for TSH may be inadequate to define hypothyroidism in persons with morbid obesity: Di@bet.es study. Obes Silver Spring Md. 2017 Apr;25(4):788–93.

[4] Surks MI, Hollowell JG. Age-specific distribution of serum thyrotropin and antithyroid antibodies in the US population: implications for the prevalence of subclinical hypothyroidism. J Clin Endocrinol Metab. 2007 Dec;92(12):4575–82.

[5] Samuels MH, Ridgway EC. Central hypothyroidism. Endocrinol Metab Clin North Am. 1992 Dec;21(4):903–19.

[6] Musunuru K. Atherogenic dyslipidemia: cardiovascular risk and dietary intervention. Lipids. 2010 Oct;45(10):907–14.

[7] de Ferranti SD, Steinberger J, Ameduri R, Baker A, Gooding H, Kelly AS, et al. Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement from the American Heart Association. Circulation. 2019 Mar 26;139(13): e603–34.

[8] Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011 Dec;128 Suppl 5(Suppl 5): S213-256.

[9] Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019 Jun 18;139(25): e1082–143.

[10] Virani SS, Morris PB, Agarwala A, Ballantyne CM, Birtcher KK, Kris-Etherton PM, et al. 2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients with Persistent Hypertriglyceridemia: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021 Aug 31;78(9):960–93.

[11] Berglund L, Brunzell JD, Goldberg AC, Goldberg IJ, Sacks F, Murad MH, et al. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012 Sep;97(9):2969–89.

[12] Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, et al. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. Eur Heart J. 2016 Oct 14;37(39):2999–3058.

[13] Stott DJ, Rodondi N, Kearney PM, Ford I, Westendorp RGJ, Mooijaart SP, et al. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. N Engl J Med. 2017 Jun 29;376(26):2534–44.

[14] Pearce SHS, Brabant G, Duntas LH, Monzani F, Peeters RP, Razvi S, et al. 2013 ETA Guideline: Management of Subclinical Hypothyroidism. Eur Thyroid J. 2013 Dec;2(4):215–28.

[15] Pearce SHS, Brabant G, Duntas LH, Monzani F, Peeters RP, Razvi S, et al. 2013 ETA Guideline: Management of Subclinical Hypothyroidism. Eur Thyroid J. 2013 Dec;2(4):215–28.

[16] Lazarus J, Brown RS, Daumerie C, Hubalewska-Dydejczyk A, Negro R, Vaidya B. 2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children. Eur Thyroid J. 2014 Jun;3(2):76.

[17] Wiersinga WM. Guidance in Subclinical Hyperthyroidism and Subclinical Hypothyroidism: Are We Making Progress? Eur Thyroid J. 2015 Sep;4(3):143–8.

[18] Unal E, Akın A, Yıldırım R, Demir V, Yildiz İ, Haspolat YK. Association of Subclinical Hypothyroidism with Dyslipidemia and Increased Carotid Intima-Media Thickness in Children. J Clin Res Pediatr Endocrinol. 2017 Jun 1;9(2):144–9.

[19] Ejaz M, Kumar P, Thakur M, Bachani P, Naz S, Lal K, et al. Comparison of Lipid Profile in Patients with and Without Subclinical Hypothyroidism. Cureus [Internet]. 2021 Aug 19 [cited 2023 Mar 29]; Available from: https://www.cureus.com/articles/66654-comparison-of-lipid-profile-in-patients-with-and-without-subclinical-hypothyroidism

[20] Gao M. Correlation between Subclinical Hypothyroidism and Dyslipidemia in Women in Northeast China. Acta Endocrinol Buchar. 2021;17(2):282–5.

[21] Rastgooye Haghi A, Solhjoo M, Tavakoli MH. Correlation Between Subclinical Hypothyroidism and Dyslipidemia. Iran J Pathol. 2017 Apr 1;12(2):106–11.

[22] Karthick N. Dyslipidaemic Changes in Women with Subclinical Hypothyroidism. J Clin Diagn Res [Internet]. 2013 [cited 2023 Mar 29]; Available from:

http://www.jcdr.net/article_fulltext.asp?issn=0973-709x&year=2013&volume=7&issue=10&page=2122&issn=0973-709x&id=3448

[23] Tagami T, Kimura H, Ohtani S, Tanaka T, Tanaka T, Hata S, et al. multi-center study on the prevalence of hypothyroidism in patients with hypercholesterolemia. Endocr J. 2011;58(6):449–57.

[24] Su X, Chen X, Peng H, Song J, Wang B, Wu X. New insights into the pathological development of dyslipidemia in patients with hypothyroidism. Bosn J Basic Med Sci [Internet]. 2021 Nov 15 [cited 2023 Mar 29]; Available from: https://www.bjbms.org/ojs/index.php/bjbms/article/view/6606