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RESEARCH ARTICLE

PREVALENCE OF DYSLIPIDEMIA, VITAMIN B12 DEFICIENCY AND DEPRESSION IN PATIENTS WITH SUBCLINICAL, NEWLY DIAGNOSED AND ESTABLISHED HYPOTHYROIDISM

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Key words:-

Hypothyroidism, Dyslipidemia, Vitamin B12 Deficiency, Depression

Abstract

Objective: To find out prevalence of dyslipidemia, vitamin B12 deficiency and depression in hypothyroid patients.

Methodology: A cross sectional observational study was carried out in 2 hospitals to estimate the prevalence of dyslipidemia, vitamin B12 deficiency and depression in 60 patients of hypothyroidism. Data of demographic details, past medical history, current ongoing major illness, medications and past laboratory reports was collected from case record file of patients.

Results: Out of 60 hypothyroid patients, 90% of the patients were females and 10 % were males. The prevalence of hypothyroidism was highest in the age group of 31-40 (45 %) followed by the age group of 41-50 (35 %). According to BMI interpretation, 65 % of the patients were overweight. Out of 60 patients, 47 (78.3 %) patients had established hypothyroidism and 13 (21.7 %) patients were newly diagnosed. Out of 13 newly diagnosed patients, 6 (10.3 %) had subclinical hypothyroidism and 7 (11.7 %) had overt hypothyroidism. Percentage of patients with dyslipidemia, vitamin B12 deficiency and depression were 25, 16.7 and 10 respectively.

Conclusion: The prevalence of hypothyroidism was higher in patients having age of 31 to 40 years. Majority of the patients were females. Percentage of patients with established hypothyroidism were more than newly diagnosed patients. Majority of the patients were overweight. Prevalence of dyslipidemia was highest among hypothyroid patients followed by vitamin B12 deficiency and depression.

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Introduction:-

Thyroid diseases are the commonest endocrine disorders worldwide. The prevalence of thyroid diseases is increasing in India. According to a projection from various studies on thyroid diseases, it has been estimated in 2002 that about 42 million people in India suffered from thyroid diseases (Unnikrishnan & Menon, 2011). According to Bagcchi, the prevalence of hypothyroidism in India is 11 % as compared to only 2% in the UK and 4.6 % in the USA. The highest prevalence of hypothyroidism (13.1 %) was noted in people of age 46 to 54 years and less in people of age between 18 to 35 years (7.5 %) (Bagcchi, 2014). Prevalence of hypothyroidism was higher in older women than in men (Liberopoulos & Elisaf, 2002). Iodine deficiency is the most common cause of hypothyroidism worldwide (Vanderpump & Tunbridge, 2002). Subclinical hypothyroidism can be defined as a high serum TSH

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concentration and normal serum total or free T4 and T3 concentrations associated with a few or no symptoms and signs of hypothyroidism (Ayala et. al. 2000). It is referred to as a state of mild thyroid failure. Subclinical hypothyroidism is far more common disorder than overt hypothyroidism (Cooper, 2001). As per the study conducted in 2018, the prevalence of overt hypothyroidism in the general population ranges between 0.2% and 5.3% in Europe; between 0.3% and 3.7% in the USA, depending on the definition used and population studied (Taylor et. al. 2018). Hypothyroidism involves metabolic, nutritional and mental derangements. Hypothyroid patients often present with symptoms of paresthesia, numbness, weakness and poor memory, despite being on adequate replacement doses of thyroxine (El-Shafie, 2003). Thyroid disorders are known to influence lipid metabolism and are common in dyslipidemia patients. Levels of total cholesterol and LDL tend to increase as the thyroid function declines. Therefore, hypothyroidism constitutes a significant cause of secondary dyslipidemia (Liberopoulos & Elisaf, 2002). The study conducted by Desai et. al 2015, concluded that triglyceride and total cholesterol were elevated in hypothyroid patients. Level of serum vitamin B12 in hypothyroidism patients were significantly lower than in normal subjects (Jabbar et. al. 2008). According to another study, approximately 64% of hypothyroidism people suffered from vitamin B12 deficiency (Khubchandani, 2015). Several thyroid abnormalities have been associated with mood disorders particularly depression. Symptoms of anxiety and depression were found in hypothyroid patients and higher prevalence of depression (Mohammad et. al. 2019; Bathla et. al. 2016). However, the vast majority of patients with depression do not have biochemical evidence of thyroid dysfunction (Loosen, 1986). So, in this study we tried to find out prevalence of dyslipidemia, vitamin B12 deficiency and depression in hypothyroid patients from Indian population.

Methodology:-

Preparation of documents:

Case record form (CRF), Participant Information Sheet (PIS) and Inform consent form (ICF) were designed.

Ethic committee approval:

Protocol titled "Prevalence of Dyslipidemia, Vitamin B12 deficiency and Depression in Patients with Subclinical, Newly Diagnosed and Established Hypothyroidism" was approved by Ethics Committee of K. B. Institute of Pharmaceutical Education and Research (KB-IEC, Gandhinagar) (Protocol no : KBIEC/2019/142). Site approval was taken from the doctors.

Study design:

It was a cross sectional, observational and prospective study conducted in 60 patients of hypothyroidism at 2 hospitals.

Collection of data :

All the patients of hypothyroidism fulfilling the inclusion criteria and none of the exclusion criteria (Table 1) were enrolled in the study.

Table 1:- Selection criteria.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> ➤ Age: 18 to 68 years inclusive of both ➤ Both male and female patients ➤ Patients with (subclinical hypothyroidism: TSH - 4.5 to 10 µg/dL, T4 >12 µg/dL-as per lab. standards T4 within normal range and TSH elevated) and/or ➤ Patients with established clinical hypothyroidism (based on previous laboratory reports/patients case files as past medical history (PMH) and already taking levothyroxin as hormone replacement therapy) ➤ Newly diagnosed hypothyroidism patients (as confirmed based on abnormal TFTs with symptomatology by physician) (TSH >10 µg/dL, T4 <4 µg/dL) 	<ul style="list-style-type: none"> ➤ Patient refusing to give informed consent for the study ➤ Pregnant and lactating women ➤ Patients having or had a history of gastric or ileal resection, or pancreatic insufficiency ➤ Any other medical condition which in purview of investigator affects the study results.

The study procedure was explained to them and if they agree to participate in this study, ICF was taken. Data of demographic details (age, gender, body weight, height), past medical history (PMH), current ongoing major illness, medications and past laboratory reports based on case record file of patients was collected. Patients who were

already taking levothyroxine tablet daily (as per PMH and case record file), were considered as established hypothyroidism. All the patients showing hypothyroidism symptomatology were recommended thyroid function tests (TFTs) as a part of routine procedure by physician. If abnormal TFTs as per laboratory manual and physician confirms hypothyroidism then considered as newly diagnosed hypothyroidism. For all the established hypothyroidism patients, PMH of dyslipidemia, vitamin B12 deficiency and depression was taken and data was collected retrospectively. For all newly and subclinical hypothyroid patients, lipid profile was done and vitamin B12 test was recommended based on symptoms (questions). If there is no history of dyslipidemia, then lipid profile was suggested to patients. If no history of vitamin B12 deficiency, questions to find out probable vitamin B12 deficiency were asked and if 3 answers out of 5 were "YES" then vitamin B12 test was recommended. If no history of depression, then questionnaire for depressive symptomatology (DSM V criteria) was asked, if 5 answers out of 9 were "YES", patients were referred to psychiatrist as per opinion of physician. Questions for symptomatology for vitamin B12 deficiency (as per National Institutes of Health) and depressive symptomatology (as per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) were asked to patients (Table 2). The data was recorded in the case report form.

Table 2:- Questions for symptomatology for vitamin B12 deficiency and depressive symptomatology.

Questions for symptomatology for vitamin B12 deficiency	Questions for depressive symptomatology
<ol style="list-style-type: none"> 1. Feeling of weakness and fatigue without doing any strenuous activity? 2. Feeling of pricking sensation in hands and feet? 3. Did your handwriting get deteriorated than previously ?/Poor hand coordination-grip and power? 4. Changes in mood/mood swings? 5. Do you have frequent Leg cramping and trouble walking? 	<ol style="list-style-type: none"> 1. Depressed mood or irritable mood. 2. Diminished interest or loss of pleasure in almost all activities 3. Significant weight change or appetite disturbance 4. Sleep disturbance (insomnia or hypersomnia) 5. Psychomotor agitation or retardation 6. Fatigue or loss of energy. 7. Feeling of worthlessness. 8. Diminished ability to think. 9. Recurrent thoughts of death, recurrent ideation without a specific plan, or a suicide attempt or specific plan of committing suicide. <p>*Point 9 should not be asked as far as possible if minimum 5 criteria are matched out of first 8 questions</p>

Statistical Analysis

Categorical variables were expressed as numbers and percentages.

Results:-

The prevalence of hypothyroidism was highest in age group 31-40 years (45%) followed by the age group of 41-50 years (35 %) with mean age 42.3 ± 7.72 (Fig1). Out of 60 hypothyroid patients, 90 % of the patients were females and 10 % were males (Fig 2).

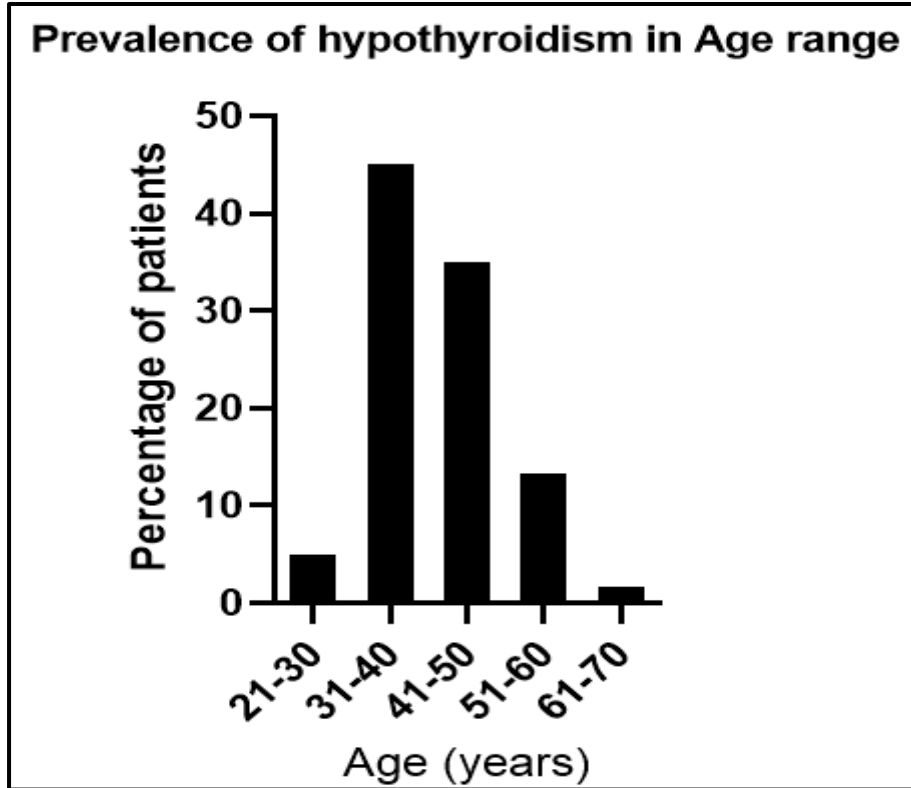


Figure 1:- Age wise prevalence of hypothyroidism.

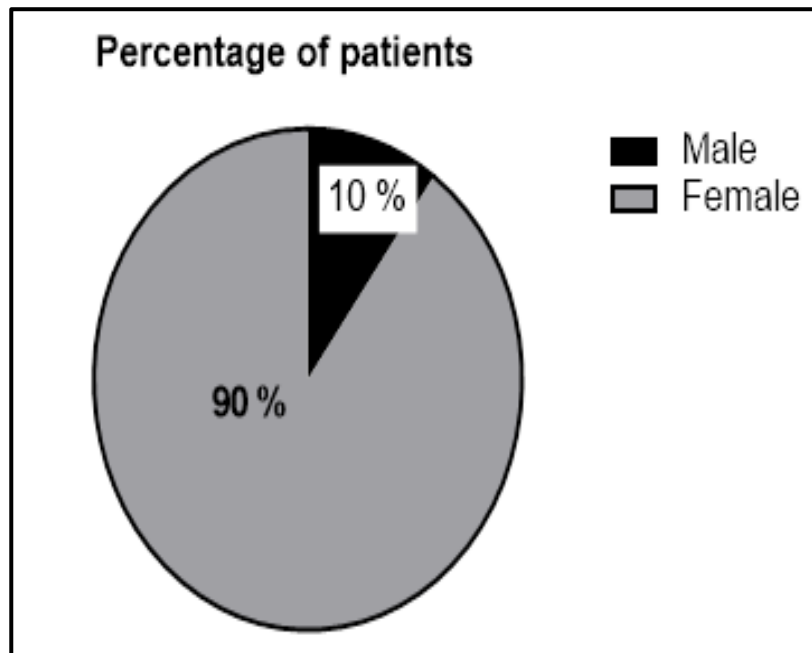


Figure 2:- Gender wise prevalence

Out of 60, 39 (65 %) of the patients were overweight according to BMI interpretation. The mean BMI was $26.89 \pm 0.43 \text{ kg/cm}^2$ (Fig 3). Majority of the patients completed secondary education (40 %) followed by primary education (23 %) (Fig 4). As per data of occupation in hypothyroid patients, majority of the patients were housewives (39= 65 %) followed by office working people (13=12.7 %) (Fig 5). Majority of patients were married (83.3 %) (Table 3).

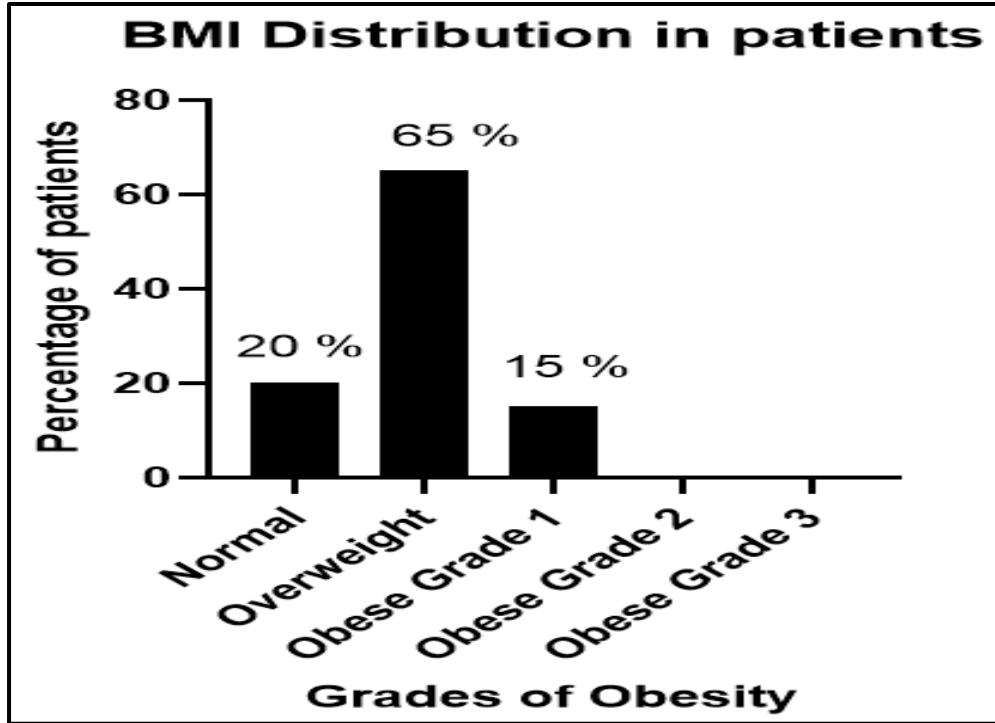


Figure 3:- BMI distribution.

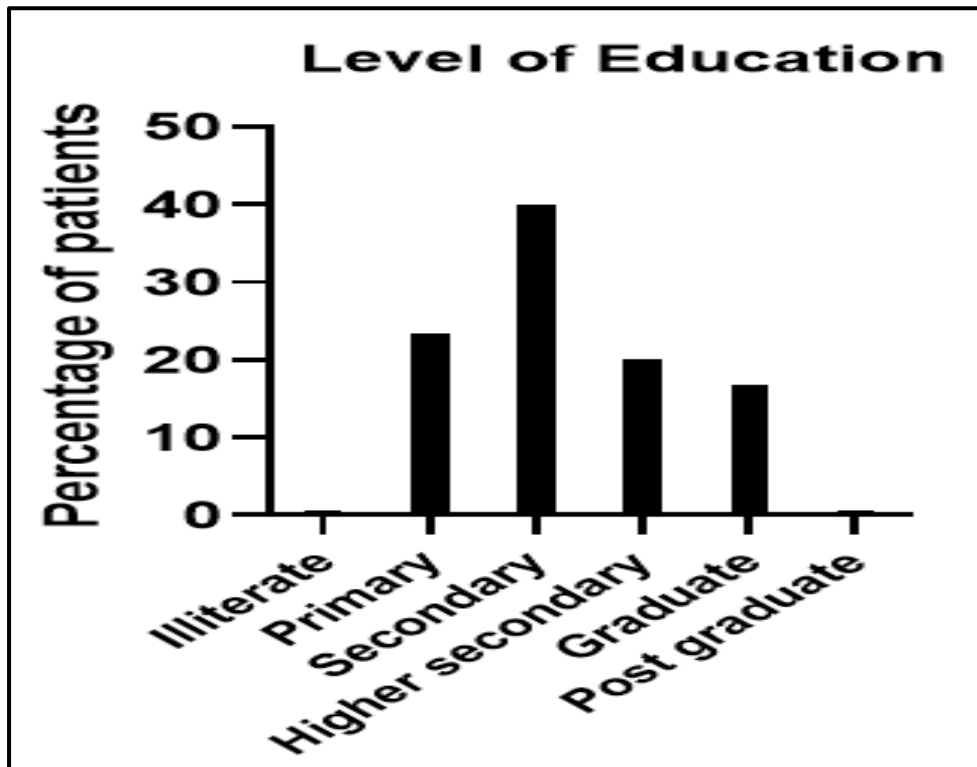


Figure 4:- Level of education.

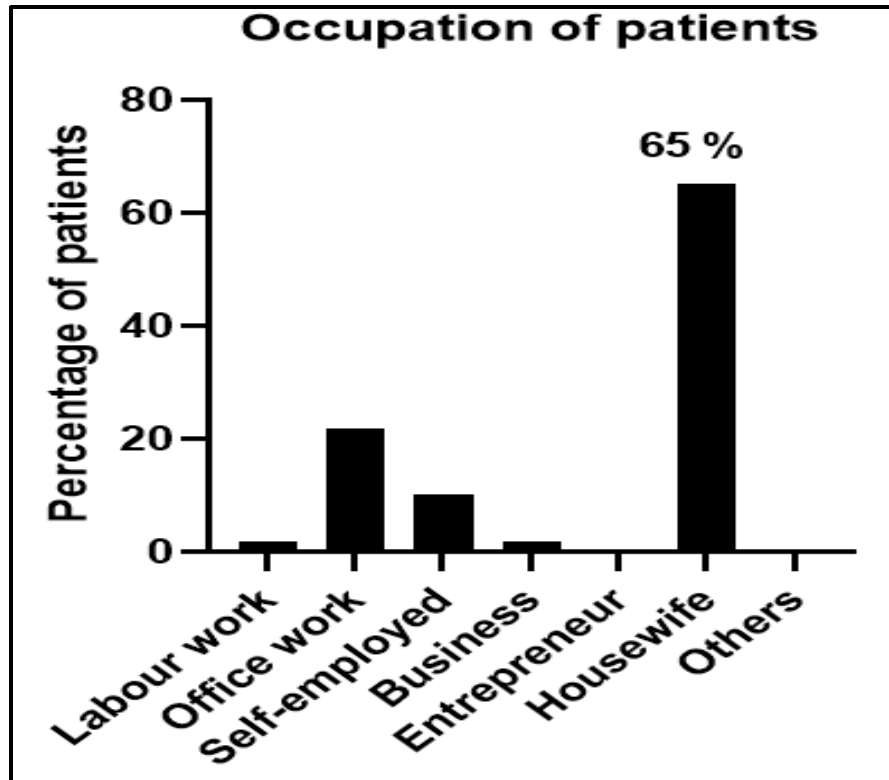


Figure 5:- Occupation of patients.

Out of 60 hypothyroid patients, patients with established hypothyroidism were 47 (78.33 %) and newly diagnosed were 13 (21.67 %). Out of 13 newly diagnosed patients, 6 (10.3 %) had subclinical disease and 7 (11.7 %) had overt disease (Table 4).

Table 3:- Marital status.

Marital status	Number	Percentage (%)
Married	50	83.33
Unmarried	1.67	1.67
Divorcee	4	6.67
Widow	4	6.67
Widower	1	1.67
Total	60	100

Table 4:- Status of hypothyroid patients.

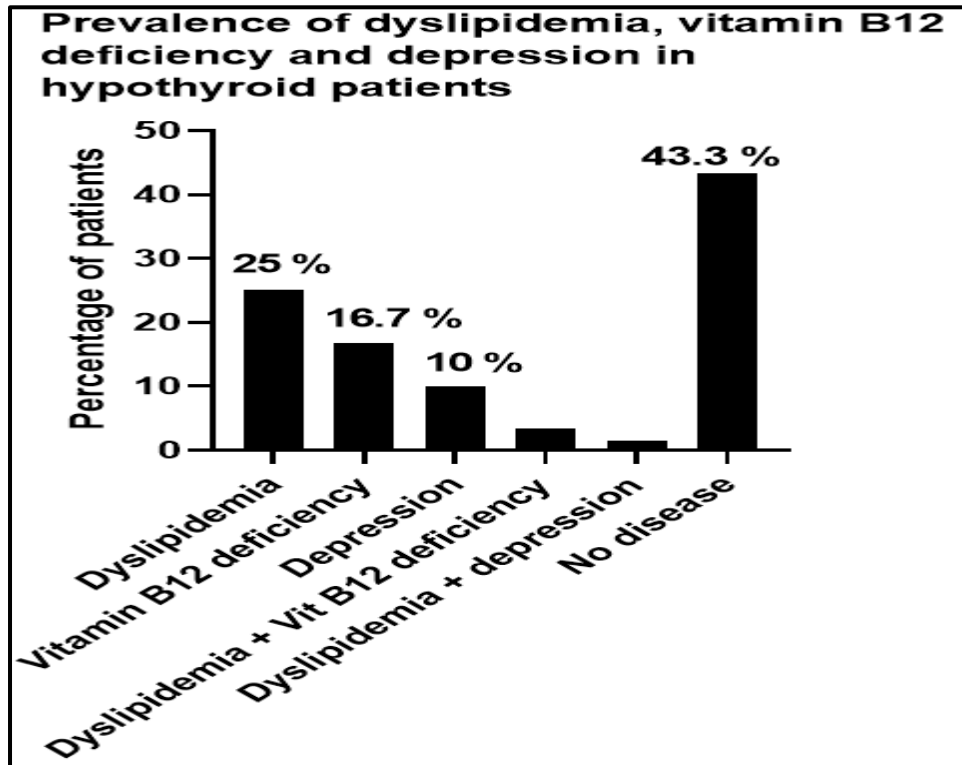
	N=47	Newly diagnosed (N=13)	
	Established hypothyroidism	Subclinical Hypothyroidism (SCH)	Overt hypothyroidism
No. of patients	47	6	7
Percentage (%)	78.33	10.3	11.7

The mean TSH levels in overt hypothyroid patients was 12.7 mIU/ml which is high compared to established and subclinical. Mean T3 and T4 levels were low in established and newly diagnosed(overt) patients respectively (Table 5).

Table 5:-Thyroid profile.

TFT	N=47	Newly diagnosed (N=13)	
	Established hypothyroidism	Subclinical Hypothyroidism (SCH)	Overt hypothyroidism
T3 (pg/ml)	1.51 ± 0.08	1.6 ± 0.17	1.69 ± 0.15
T4 (ng/dl)	0.94 ± 0.16	1.05 ± 0.31	0.35 ± 0.11
TSH (mIU/ml)	9.77 ± 0.32	8.83 ± 0.45	12.7 ± 1.89

Out of 60 patients, prevalence of dyslipidemia was highest (25%) followed by vitamin B12 deficiency (16.7 %) and depression (10%) (**Fig 6**). The mean LDL levels was higher than the normal range in established hypothyroid patients compared newly diagnosed patients whereas the mean VLDL and TG levels was higher than the normal range in newly diagnosed (overt) patients. Mean HDL levels were higher in established hypothyroid patients (**Table 6**).

**Figure 6:-** Prevalence of dyslipidemia, vitamin b12 deficiency and depression in hypothyroid patients.**Table 6:-** Lipid profile.

Lipid profile(mg/dl)	N=47	Newly diagnosed (N=13)	
	Established hypothyroidism	Subclinical hypothyroidism	Overt hypothyroidism
LDL	106.6 ± 3.56	92.33 ± 5.27	97.14 ± 7.38
VLDL	32.26 ± 1.17	31.17 ± 1.47	33.91 ± 5.41
HDL	54.38 ± 2.94	52.83 ± 3.84	40.71 ± 4.19
TG	150.8 ± 7.56	124.3 ± 9.83	161.4 ± 28.71

Discussion:-

Patients with hypothyroidism often have multiple co-morbidities, which may also impact on their QoL (Shivaprasad. et. al. 2018). In this study, we collected demographic data and PMH of patients. Out of 60 hypothyroid patients, majority i.e 54 (90 %) of the patients were females and 6 (10 %) were males. This was similar to findings of Dunn and Turner, 2016., which concluded that hypothyroidism as second most endocrine disorder in US women. Majority

of the patients belonged to the age group of 31-40 years (45 %) followed by the age group 41-50 years (35 %). Hypothyroidism is usually late to middle age disorder. Out of 60, 39 (65%) of the patients were overweight according to BMI interpretation which explains effect of metabolic derangements due to deficiency of thyroid hormones. Patients with established and newly diagnosed hypothyroidism were 47 (78.33 %) and 13 (21.67 %) respectively. Out of 13 newly diagnosed patients, 10 % were SCH and 11.67 % were overt. This was different from previous study reported by Hueston et.al. (2004) which showed subclinical was more disorder than clinical hypothyroidism. This may be due to large sample size around 8000 taken by them in their study. Another study showed that subclinical hypothyroidism is the most frequently undiagnosed thyroid dysfunction (Rashad and Samir, 2019). Prevalence of dyslipidaemia (25 %) was highest among hypothyroid patients followed by vitamin B12 deficiency (16.7 %) and depression (10 %). The mean VLDL and TG levels was higher than the normal range in newly diagnosed (overt) patients. Thyroid disorders are associated with vitamin B12 and vitamin D deficiency (Aktaş, 2020). Hypothyroidism patients commonly manifest the symptoms of depression and there may be connection between these two (Hage and Azar. 2012).

Conclusion:-

Higher prevalence of hypothyroidism was found in females. Prevalence of dyslipidaemia was highest followed by vitamin B12 deficiency and depression. This suggests that lipid profile tests should be carried out in recently diagnosed hypothyroid patients. Physicians should suggest vitamin B12 test and counsel the patients regarding symptoms of depression.

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