Clinical Outcomes of Hypothyroidism during Pregnancy in Arar, Saudi Arabia

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Abstract

Hypothyroidism is a disorder characterized by reduced thyroid gland activity, which can manifest during pregnancy. If left untreated, maternal hypothyroidism may lead to impaired fetal growth, neuro-cognitive deficits, or congenital iodine deficiency syndrome due to inadequate thyroid hormone availability. This study aimed to identify the clinical outcomes of hypothyroidism in pregnant females. This cross-sectional study included 53 female patients diagnosed with hypothyroidism who attended the outpatient clinics at Central Hospital and Prince Abdul Aziz bin Musa'ad Hospital in Arar, Saudi Arabia, between January 2023 and June 2023. Blood samples were collected to assess thyroid hormone levels, lipid profile, hemoglobin, serum calcium, serum phosphate and vitamin D. The obtained laboratory parameters were analyzed for their correlation with thyroid hormone levels.

Hypocalcemia, hypophosphatemia, hypovitaminosis D and elevated lipid levels (TAG, cholesterol and LDL-C) were observed in all the female subjects. The prevalence of anemia among the hypothyroid patients was 58.49%. The correlation analysis demonstrated a significant positive correlation of TSH with cholesterol (r=0.318, p=0.02) and LDL-C (r=0.346, p=0.011) and a significant negative correlation with hemoglobin (r= -0.273, p=0.047). FT4 was found to have a significant negative correlation with cholesterol (r= -0.348, p=0.01) and significant positive correlation with hemoglobin (r=0.282, p=0.04). The study found a high prevalence of hypothyroidism among pregnant women in Arar (mean age: 41.62 years). Common symptoms included fatigue, weight gain, constipation and abdominal pain along with edema, dry skin, pallor, bradycardia and anemia. Hypothyroidism was linked to dyslipidemia, with elevated total cholesterol, LDL-C and triglycerides and reduced HDL-C, posing a risk for atherosclerosis and coronary artery disease.

Keywords: Hypothyroidism, Pregnancy, Lipid Profile.

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Introduction

Hypothyroidism presents a challenging diagnostic issue due to its often modest symptoms, which can be easily ignored. These symptoms, present throughout the pregnancy, are typically reversible after childbirth but they may pose challenges for clinical interpretation. The prevalence of hypothyroidism in pregnancy is estimated at approximately 0.3–0.5% for overt hypothyroidism and 2–3% for subclinical hypothyroidism[13]. If left untreated, maternal hypothyroidism can lead to impaired fetal growth, cognitive developmental deficits, or congenital iodine deficiency syndrome.

The most frequent cause of hypothyroidism during pregnancy is autoimmune thyroiditis[13]. There have been reports of increased miscarriage rates among euthyroid women undergoing *in vitro* fertilization (IVF) who have positive thyroid peroxidase (TPO) antibodies. Thyroid antibody positivity has been linked to premature delivery in euthyroid women and may also be associated with infant respiratory distress, according to a study by Negro et al[17]. An investigation conducted by Mannisto et al[16] discovered that antibodies and thyroid dysfunction during pregnancy appear to be indicators of thyroid disease in the future. Furthermore, overt hypothyroidism can increase the risk of developing diabetes later in life.

Numerous studies have demonstrated that children born to mothers with hypothyroidism exhibit a significantly higher risk of reduced IQ levels, impaired neuropsychological development and compromised learning abilities[12,15,20,24]. In addition to reduced fertility, women with hypothyroidism are at an increased risk of postpartum hemorrhage, gestational hypertension, anemia, placental abruption and miscarriage[1]. The likelihood of these complications is significantly higher in women with overt hypothyroidism compared to those with subclinical hypothyroidism.

Pregnancy is a phase that imposes substantial metabolic and hormonal demands on both the mother and the fetus, even under optimal conditions. However, the presence of endocrine disorders such as hypothyroidism can significantly increase the risk of adverse maternal and fetal outcomes. This study aimed to investigate the clinical impact of hypothyroidism in pregnant females.

Material and Methods

This cross-sectional study was carried out on pregnant hypothyroid females visiting Central Hospital and Prince

Abdul Aziz bin Musa'ad Hospital, Arar, Saudi Arabia between January 2023 to June 2023. All the female patients arriving for consultation were screened for thyroid disorder by laboratory tests. The common symptoms of hypothyroidism were found to be fatigue, weight gain, constipation and abdominal pain. The other common symptoms were edema, dry coarse skin, a change in skin pallor, bradycardia and anemia. All participants completed a questionnaire detailing their medical history and the primary reason for their visit to the medical center. Five milliliter of blood sample was collected from 53 hypothyroid pregnant females (age range between 18- 52 years) for estimation of thyroid hormones, lipid profile, hemoglobin, serum calcium, serum phosphate and vitamin D levels.

Inclusion criteria: Pregnant female subjects of more than 18 years of age, diagnosed with hypothyroidism, not receiving hormone therapy or oral contraceptive pills, not taking vitamins or mineral supplements and, with no history of autoimmune or chronic diseases were included in the study.

Exclusion criteria: Male participants, females under 18 years of age, individuals on hormonal therapy or contraceptive pills, as well as patients with a pre-existing diagnosis of infections, thyroid or other malignancies, or systemic conditions such as diabetes mellitus, cardiac, renal, or liver failure, were excluded from the study.

Measurement of thyroid profile: Thyroid hormone levels including free triiodothyronine (FT3), free thyroxine (FT4) and thyroid-stimulating hormone (TSH) were measured using immunoassay methods with Elisa kits. The normal reference ranges provided by the kits for thyroid hormones were as follows: FT3 (2.80-7.10 pmol/L), FT4 (12-22 pmol/L) and TSH (0.27-4.20 µIU/L). The diagnosis and classification of thyroid abnormalities were based on the guidelines of the National Academy of Clinical Biochemistry (NACB) for the laboratory diagnosis and monitoring of thyroid diseases[8]. Hypothyroidism was diagnosed when TSH levels exceeded 4.2 µIU/mL and FT4 levels were below 12 pmol/L.

Measurement of Hemoglobin: Whole blood samples (2.5 mL) were collected in EDTA-containing tubes and processed using the Sysmex XS 500 with a five-parameter differential (Sysmex, Lincolnshire, IL, USA) to measure hemoglobin concentration. Anemia was defined as a hemoglobin (Hb) level of less than 12 g/dL in women[23].

Lipid Profile: Serum total cholesterol and triglycerides concentrations were measured using standard enzymatic methods with Ortho-clinical diagnostics reagents on the fully automated analyzer (Vitros 950 dry chemistry system; Johnson and Johnson, Rochester, NY, USA). Low-density lipoprotein cholesterol (LDL-C) was estimated with the Friedewald et al's equation[11].

Estimation of serum Calcium, Phosphate and Vitamin D levels: Serum calcium, phosphate and vitamin D levels were analyzed using a Beckman Coulter DXC autoanalyzer using commercially available kits.

Data analyses: Data entry and analysis were performed using Statistical Package for Social Sciences (SPSS) version 22. Descriptive statistics was presented as mean ±SD for continuous variables. Pearson correlation coefficient was used for determining the degree of association between different parameters. A p value of <0.05 was considered to be statistically significant.

Results

Table 1 outlines the demographic and some biochemical parameters of the pregnant female hypothyroid patients. The mean age was 41.62 years with an age range of 18-52 years. All the patients exhibited hypocalcemia, hypophosphatemia and hypovitaminosis D. Thyroid hormones profile of the studied population is shown in table 2. Elevated lipid levels (TAG, cholesterol and LDL-C) were observed in all the females (table 3). The prevalence of anemia among the hypothyroid patients was 58.49% (figure 1).

Correlation analysis of thyroid hormones (TSH and T4) with various lipids (TAG, cholesterol and LDL-C) and Hemoglobin is shown in table 4. A significant positive correlation of TSH was observed with cholesterol (r=0.318, p=0.02) and LDL-C (r=0.346, p=0.011) whereas TSH was found to have a significant negative correlation with hemoglobin (r= -0.273, p=0.047).

Table 1
Clinical and demographic characteristics of the patients

	Hypothyroid patients (n=53) (Mean ± SD)	**Reference Range**
Age (years)	41.62 ± 14.17	Min age- 15 Max age- 77
BMI (kg/m^2)	33.15 ± 6.86	18.50-24.90
Hb (g/dL)	11.61± 1.51	11.60-15.00
Serum calcium (mmol/L)	2.10±0.13	2.2 - 2.7
Serum phosphorus (mg/dL)	1.86±0.33	2.5 - 4.5
Vitamin D (ng/mL)	16.31 ± 6.84	30 - 80

Table 2
Thyroid hormones profile of the studied population

	Hypothyroid Patients (n=53) Mean ± SD	Reference Range
TSH (µIU/mL)	10.52±3.50	0.27-4.20
FT3 (pmol/L)	4.29 ± 0.67	2.80-7.10
FT4 (pmol/L)	10.10± 1.48	12-22

Table 3
Lipid profile of the studied population

	Hypothyroid Patients (n=53) Mean ± SD	Normal Value
Triglycerides (mmol/L)	1.82± 0.46	< 1.7
Cholesterol (mmol/L)	5.56± 0.89	< 5.2
LDL-C (mmol/L)	3.39 ± 0.74	< 2.59

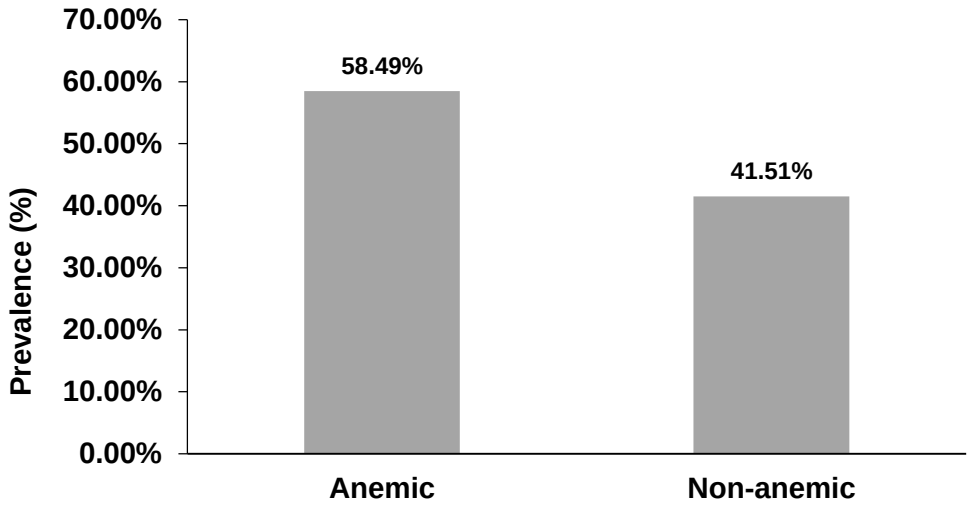

Figure 1: Prevalence of anemia in pregnant female hypothyroid patients

Table 4
Correlation of some biochemical parameterswith TSH and FT4 (*N*=53).

	TSH		FT4	
Parameters	**r**	**p**	**r**	**p**
Triglycerides	0.198	0.155	-0.216	0.120
Cholesterol	0.318	0.020	-0.348	0.010
LDL-C	0.346	0.011	-0.252	0.068
Hb	-0.273	0.047	0.282	0.040

On the other hand, FT4 was found to have a significant negative correlation with cholesterol (r= -0.348, p=0.01) and significant positive correlation (r=0.282, p=0.04) with hemoglobin.

Discussion

Hypothyroidism is a prevalent global health concern with a higher susceptibility observed in females compared to males. Thyroid function abnormalities encompass a broad spectrum of clinical manifestations and represent a prevalent medical concern. Many patients exhibit subclinical thyroid dysfunction, often identified through thyroid hormone assessments or incidental findings from other diagnostic evaluations. These may include alterations in blood parameters, lipid profile abnormalities, cardiovascular dysfunction, atherosclerosis and various other clinical conditions[4,10,21].

Patients with hypothyroidism frequently experience vitamin D deficiency which may be accompanied by hypocalcemia, as demonstrated in the present study. In hypothyroid patients, there may be an increased production of calcitonin coupled with reduced intracellular availability of thyroxine. This condition can lead to increased tubular excretion of calcium and decreased release of extracellular calcium, ultimately resulting in a lower concentration of serum

calcium[26]. There are two proposed causes for the decline in serum vitamin D levels among hypothyroid patients. First, there could be inadequate absorption of vitamin D within the intestine. Secondly, these patients may experience impaired activation of vitamin D within their systems.

Vitamin D exerts its biological effects by binding to the Vitamin D receptor (VDR), which then triggers the activation of specific genes in target tissues that are responsive to VDR[28]. Individuals diagnosed with hypothyroidism or in its initial stages are more likely to have reduced vitamin D levels than those with normal thyroid function. Vitamin D has been shown to exhibit a bidirectional relationship with inflammation in obese individuals, which may influence the severity and frequency of hypothyroidism[22]. Patients with thyroid abnormalities often present with low levels of iron, can impact hemoglobin concentrations.

Additionally, deficiencies in both folate and vitamin B12 have been observed in up to 25% of these patients, further influencing blood parameters such as hemoglobin and red blood cell (RBC) counts. Other potential causes of anemia in these patients may encompass bone marrow suppression and various related comorbid conditions[9]. Patients with thyroid abnormalities may exhibit various types of anemia with iron deficiency anemia being the most prevalent.

Microcytic and macrocytic anemias occur less frequently in this population[27]. Anemia in thyroid dysfunction is caused not only by nutritional deficiencies but also by reduced thyroid hormone levels, which impair erythrocyte precursor stimulation, decrease oxygen supply to tissues and lower erythropoietin levels[6,25].

Hypothyroidism is known to have an unfavorable impact on lipid profiles. The study demonstrated elevated levels of triglycerides, cholesterol and LDL-C among all participants. Thyroid hormones stimulate HMG-CoA reductase, the enzyme responsible for the first step in cholesterol biosynthesis. Additionally, triiodothyronine (T3) enhances LDL receptor activity by promoting the activation of the LDL receptor gene. This T3-mediated gene activation occurs through the direct binding of T3 to specific thyroid hormone responsive elements (TREs)[7]. Despite a decrease in thyroid function leading to reduced HMG-CoA reductase activity, total cholesterol and LDL-C levels remain elevated in patients with overt hypothyroidism[2,5,19]. This is attributed to decreased LDL receptor activity, which results in reduced catabolism of LDL and intermediate-density lipoproteins (IDL)[3,29].

Furthermore, reduced lipoprotein lipase (LPL) activity in overt hypothyroidism leads to impaired clearance of triglyceride-rich lipoproteins[18]. As a result, patients with overt hypothyroidism may also exhibit elevated triglyceride levels, often associated with increased VLDL and in some cases, fasting chylomicronemia[3,5,14]. The primary limitation of this study is the need for a larger sample size to enhance the accuracy of the findings.

Conclusion and Recommendations

This study found a high prevalence of hypothyroidism among pregnant women in Arar (mean age: 41.62 years), with common symptoms including fatigue, weight gain, constipation, edema, dry skin, pallor, bradycardia and anemia. Hypothyroidism was associated with dyslipidemia, characterized by elevated total cholesterol, LDL-C and triglycerides and reduced HDL-C, increasing the risk of atherosclerosis and coronary artery disease. Additionally, hypothyroidism during pregnancy is linked to adverse maternal and fetal outcomes, necessitating early diagnosis and timely intervention to minimize complications.

Effective management requires prompt detection, appropriate treatment, continuous monitoring and comprehensive education for both healthcare providers and patients. Raising awareness about the importance of early intervention is crucial for improving clinical outcomes. Further research is warranted to assess whether early intervention in hypothyroidism can mitigate dyslipidemia and reduce the risk of associated comorbidities.

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