

Association of feto-maternal outcomes in pregnant women with thyroid dysfunction

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ABSTRACT

Objective: To determine the frequency of thyroid disorders in pregnant women and its association with adverse pregnancy outcomes for mother and the fetus.

Material and Method: This prospective cohort study was conducted at Chemical Pathology and Endocrinology department, Reference laboratory at Rawalpindi in collaboration with Gynaecology department of tertiary care hospital at Rawalpindi from 28 August 2023 to 28 February 2024. Pregnant women without diagnosed endocrine disorders in third trimester were included in this study and observed till delivery for feto-maternal outcomes. Blood samples were collected after a detailed history. Fetomaternal outcomes were compared between women with thyroid disorders and euthyroid participants by using the chi-square test and odds ratios to calculate the estimated risk.

Results: Among 174 pregnant women enrolled, 152 (87.35%) were euthyroid and 22 (12.65%) had thyroid dysfunction. The frequency of anaemia (36.4% vs 5.3%), pre-eclampsia (18.2% vs 3.3%) and low APGAR score (27.3% vs 3.9%) were higher in females with thyroid dysfunction with a p value <0.05 . However, no significant differences were observed in cesarean section, gestational diabetes mellitus, preterm labor, NICU admission, or low birth weight ($p>0.05$). Thyroid dysfunction was associated with increased odds of anaemia (OR 6.91), pre-eclampsia (OR 5.53), and low APGAR score (OR 6.91), whereas associations with other maternal and neonatal outcomes were not statistically significant.

Conclusion: Pregnant women with thyroid dysfunction have a higher risk of adverse feto-maternal outcomes. Early detection and management of thyroid dysfunction could help prevent these complications.

Keywords: Euthyroid, Feto-maternal outcomes, Pregnancy, Thyroid dysfunction.

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INTRODUCTION

In pregnancy thyroid disorders are the second most prevalent endocrine abnormalities after diabetes mellitus, but their diagnosis is challenging [1]. Pregnancy involves significant physiological and hormonal adaptations that increase maternal thyroid hormone levels and may predispose women to thyroid dysfunction. When thyroid disorders complicate pregnancy, the risk of adverse maternal, fetal, and neonatal concerns rises [2].

Adequacy of maternal thyroid hormones play a key role in maintaining pregnancy and supporting placenta [1]. During the initial weeks of gestation, transplacental transfer of maternal T4 is particularly

important for fetal neurodevelopment. While the fetal thyroid begins synthesizing hormones during the second trimester, the fetus remains dependent on maternal T4 and iodine throughout pregnancy [3,4]. Deficiency of iodine is the leading preventable cause of thyroid dysfunction and neurodevelopmental defects worldwide [5]. In iodine-replete or mildly deficient populations, autoimmune thyroid disease is more common. Untreated overt hypothyroidism may be associated with miscarriage, pre-eclampsia, preterm birth, prematurity and postpartum hemorrhage, while overt hyperthyroidism, most often due to Graves' disease, increases risks of pre-eclampsia, preterm labor, decreased fetal growth, and maternal heart failure [5].

In pregnancy overt hypothyroidism is associated with adverse feto-maternal outcomes, including impaired neurodevelopment in offspring, therefore judicious levothyroxine treatment is strongly recommended⁶. Gestational thyrotoxicosis is more common in Asian populations, including Pakistan, and prevalence varies geographically. Population and different reference ranges in each trimester for thyroid function

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are recommended to facilitate early detection and to prevent complications [7].

This study aims to determine the frequency of thyroid disorders during pregnancy in this region and illuminate the association between thyroid dysfunction and feto-maternal outcomes compared to euthyroid pregnant females.

MATERIAL AND METHODS

This was a prospective cohort study, carried out at the Department of Chemical Pathology and Endocrinology of a reference laboratory in collaboration with tertiary care hospital Rawalpindi from 28th August 2023 to 28th February 2024. The study was conducted after approval of Institutional Ethical board with approval certificate vide reference number Cons-CHP-6-READ-IRB/23/2776 dated 21st August 2023. The WHO calculator was used to determine the sample size with frequency of adverse pregnancy outcomes (Pre-eclampsia) in 20% in thyroid dysfunction women and 16.8% in euthyroid women with confidence interval of 95% and margin of error 5% [3]. A total of 174 pregnant females in their third trimester of pregnancy were selected by non-probability consecutive sampling after taking written informed consent. All pregnant females aged 20-45 years, who came for checkup at Gynaecology department of a Tertiary care hospital and were referred to Endocrine Clinic of Reference laboratory of Rawalpindi, as per inclusion criteria after 24 weeks of pregnancy were registered in this study after taking the informed consent, while subjects having known thyroid or other endocrine disorders were excluded. A detailed history, including obstetric history was recorded from these subjects. Approximately 3-5 ml blood was drawn from all participants and stored in serum separator tubes, centrifuged at 3500 RPM for 5 minutes, analyzed on same day and stored at 2-8°C for 5 days after testing as per laboratory protocol. Thyroid hormone levels (TSH, Total T3 and Free T4) were analyzed on automated chemiluminescent immunoassay. Based on the laboratory reference ranges (T3: 1.08–3.14 nmol/L, T4: 10.3–34.7 pmol/L, and TSH: 0.4–4.5 mIU/L), participants were classified as euthyroid, overt hypothyroid, overt hyperthyroid, subclinical hypothyroid, or subclinical hyperthyroid. Euthyroidism was defined as normal serum T3, FT4, and TSH concentrations. Overt hypothyroidism was defined as elevated TSH (>4.5 mIU/L) with decreased T4 (<10.3 pmol/L), while subclinical hypothyroidism was defined as elevated TSH with normal T3 and FT4 concentrations. Overt hyperthyroidism was defined as suppressed TSH

(<0.4 mIU/L) with elevated T3 (>3.14 nmol/L) and/or FT4 (>34.7 pmol/L), whereas subclinical hyperthyroidism was defined as suppressed TSH with normal T3 and FT4 concentrations. These pregnant women were followed till delivery of baby. Adverse maternal outcomes like Caesarian section (C-section), Preeclampsia, Anaemia, Gestational Diabetes Mellitus (GDM) and Preterm Labor were noted, along with fetal consequences, such as low APGAR score, LBW and NICU admission. All biochemical and clinical information were recorded on a predesigned proforma.

The data was analyzed using SPSS (Statistical Software Package) version 21. Qualitative variables like thyroid status, maternal and fetal outcomes were expressed as percentages and frequencies, whereas quantitative variables like age was expressed as mean $\pm$ SD. Independent sample “t” test was used to compare quantitative variables, and chi square test was used to evaluate categorical variables like frequencies feto-maternal outcomes between different thyroid disorders and euthyroid patients; a *p* value of less than 0.05 was considered statistically significant. To assess the probability of adverse fetal and maternal outcomes in euthyroid and thyroid disease patients (with deranged Thyroid Profile), the odds ratio was computed.

RESULTS

Out of total 174 pregnant females screened, 152 (87.4%) had normal thyroid functions (Euthyroid), and 22 (12.6%) had thyroid dysfunction. Among these 22 subjects with thyroid dysfunction, 11 (50.0%) had subclinical hypothyroidism, 8 (36.4%) had overt hypothyroidism and 3 (13.6%) had subclinical hyperthyroidism (Figure-I). Mean age of selected females was approx. 30.96 ($\pm$ 6.13) years; with mean age of Euthyroid females were 30.78 ($\pm$ 6.06) years and females of thyroid dysfunction 32.18 ($\pm$ 6.64) years and no statistical significance was seen when compared by independent sample test (*p* 0.32) as shown in Table- I.

When compared by Chi square test, the frequency of anaemia (36.4% vs 5.3%), pre-eclampsia (18.2% vs 3.3%) and low APGAR score (27.3% vs 3.9%) were higher in patients with thyroid dysfunction as compared to euthyroid females (*p* value <0.05). These were a negligible difference in frequencies of emergency LSCS, GDM, preterm labor, NICU admission and low birth weight (LBW) (*p*-value >0.05). NICU admission rate was high in neonates born to thyroid dysfunction females (40.9%) as

compared euthyroid female (23.0%) but, it was statistically insignificant as depicted in Table-I.

Odds ratio for feto-maternal outcomes during pregnancy showed that the risk of all feto-maternal complications was higher in thyroid dysfunction

females than euthyroid females. The risks were more significant for preeclampsia, anaemia, and low APGAR score 5.53, 6.91 and 6.91 respectively as shown in Table-II.

Table-I: Comparison of fetomaternal adverse outcomes in pregnant subjects with thyroid dysfunction and euthyroid group

Maternal outcomes	Thyroid dysfunction	Euthyroid	p-value
Preeclampsia	18.2%	3.3%	0.003
Anaemia	36.4%	5.3%	0.000
C-section	27.3%	19.1%	0.370
GDM	4.5%	3.3%	0.763
Preterm labor	22.7%	15.8%	0.414
Fetal outcomes			
LBW	27.3%	20.4%	0.461
Low APGAR score	27.3%	3.9%	0.000
NICU admissions	40.9%	23.0%	0.071

Table-II: Odds ratio of fetomaternal adverse outcomes in pregnant subjects with thyroid dysfunction and euthyroid group

Outcomes	Thyroid dysfunction Odds with 95% CI	Euthyroid Odds 95% CI
Preeclampsia	5.527 (19.032-1.605)	0.846 (1.032-0.693)
Anaemia	6.909 (16.525-2.889)	0.672 (0.932-0.489)
C-Section	1.429 (3.047-0.671)	0.899 (1.174-0.688)
GDM	1.382 (11.284-0.169)	0.987 (1.086-0.897)
Preterm Labor	1.439 (3.379-0.613)	0.918 (1.163-0.724)
LBW	1.337 (2.834-0.631)	0.914 (1.195-0.699)
Low APGAR Score	6.909 (19.538-2.443)	0.757 (0.980-0.585)
NICU Admission	1.777 (3.174-0.994)	0.768 (1.099-0.536)

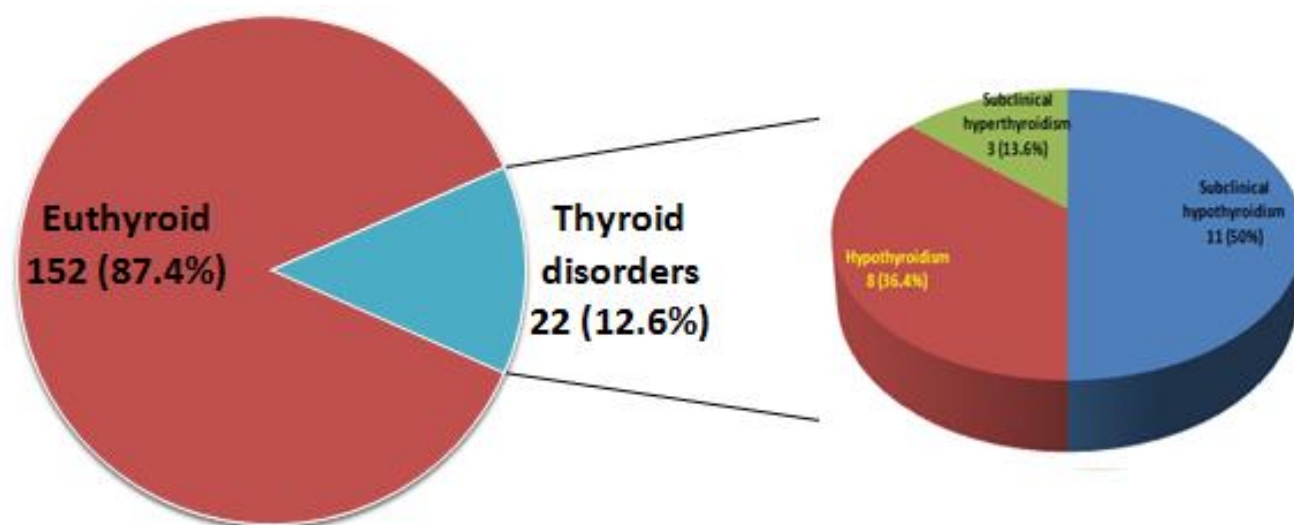


Figure-I: Frequency of thyroid disorders among pregnant females (n=174)

DISCUSSION

After diabetes, thyroid disorders are the most prevalent endocrine disorders among women in their reproductive years [1]. However, depending on a number of factors, the prevalence of thyroid diseases during pregnancy and the consequences they cause

for both the mother and the fetus vary widely across different locations. Due to regional variations in the iodine content of common salt, the geographic location may play a critical role in the frequency of thyroid disorders [6]. Locally 29.4% of the sample population in a multicenter, cross-sectional

population survey carried out in Lahore was found outside of the typical thyroid reference range⁷. Thyroid dysfunction was identified in 45.4% of a sample comprising pregnant women with a history of poor obstetric outcomes in another multicenter comprehensive study [8].

The current study showing 12.65% frequency of thyroid dysfunction among pregnant females offers valuable regional data from Rawalpindi region of Pakistan and the frequency in this study is consistent with previous data documented in another study including 5.4% of post thyroiditis cases [9] and in the nearby South Asian nations [10], where 10–13% of pregnant women experience thyroid dysfunction, due to iodine deficiency, family history, dietary habits, geographic distributions, or autoimmune disorders.

In the present study, out of 12.6% patients diagnosed with thyroid dysfunction, subclinical hypothyroidism (SCH) was the most common abnormality, followed by overt hypothyroidism and subclinical hyperthyroidism, highlighting the importance of thyroid monitoring during pregnancy, in our setups. The greater burden of subclinical hypothyroidism had been documented in other studies as well [10]. The finding, that SCH is the most prevalent thyroid anomaly during gestation in South Asia is supported by a prevalence of 7–13% documented in other studies as well [5, 6].

The slightly higher mean age observed among females with thyroid dysfunction compared to euthyroid women in our study was not statistically significant, a finding that is consistent with previous regional studies indicating that thyroid dysfunction during pregnancy may occur across a broad reproductive age range rather than being age-related [7].

This study demonstrates a significantly higher frequency of anaemia and preeclampsia among pregnant females with thyroid dysfunction compared to euthyroid counterparts. The odds of anaemia (OR 6.91) and preeclampsia (OR 5.53) were markedly elevated, indicating a strong association between thyroid dysfunction and adverse maternal outcomes. Thyroid hormones play an important role in erythropoiesis, and hypothyroidism can lead to iron shortage and normocytic anaemia [11]. The link between hypothyroidism and anaemia has been extensively explored in regional [12] and Asian literature [13]. Furthermore, the prominent relationship between thyroid dysfunction and preeclampsia in this study is consistent with findings from Indian [14] and Bangladeshi [12] cohorts, where preeclampsia (16% in hypothyroid, 21% in

hyperthyroid) were more frequent in pregnancies with thyroid-dysfunctions, may further predispose affected women to hypertensive disorders of pregnancy.

Among fetal outcomes, a low APGAR score at birth was associated with maternal thyroid dysfunction, with a nearly sevenfold increased risk (OR 6.91). Thyroid hormones are required for fetal neurodevelopment and cardiovascular adaptation at birth; thus, maternal thyroid insufficiency may impair neonatal physiological resilience, resulting in lower APGAR ratings. The NICU admissions and low birth weight (LBW) were more common among neonates born to mothers with thyroid disease, although the differences were not statistically significant. Similar trends have been documented in other Pakistani¹³ and sub-continental [14,15] researches, where increased NICU admissions were observed [16]. Current study's higher NICU admission rate (40.9%) despite its statistical insignificance is clinically eloquent and signals possible subclinical neonatal impairment.

The significance of thyroid health during pregnancy is further supported by the overall higher likelihood of unfavorable feto-maternal outcomes among females with thyroid dysfunction in comparison to euthyroid pregnant women, findings in line with mounting data with regional literature [17, 18].

Even subclinical thyroid dysfunction which is frequently regarded as benign, have shown significant links with unfavorable outcomes in this study. These results underscore the critical need for comprehensive thyroid screening during early pregnancy, especially in high-risk communities, given Pakistan's high fertility rate, widespread iodine shortage, and minimal antenatal endocrine screening. Associated maternal and newborn morbidity can possibly be addressed by early detection and prompt treatment of thyroid dysfunction [19,20].

This study's strength rests in its comparative design and geographical relevance. However, at the same time it has limitations like low sample size and the lack of trimester-specific thyroid reference values in our population, which may affect risk estimates. Multicenter investigations with larger sample size especially using trimester-specific thyroid reference values are recommended to validate these results and educate individuals about the defined consequences of thyroid dysfunction, with ultimate goal towards greater range of safe and healthy pregnancies.

CONCLUSION

Pregnant women with thyroid dysfunction have a higher risk of adverse feto-maternal outcomes. Early detection and management of thyroid dysfunction could help prevent these complications.

RECOMMENDATION

Considering adverse pregnancy outcomes due to thyroid dysfunction, at least one-time screening for thyroid function test by TSH be mandatory.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Muhammad Anwar: Project development/conception, Data analysis, interpretation of results, literature search, critical reviews, final approval, responsible for every aspect of the research

Fawaad Sana: Data collection and processing, critical analysis and literature search manuscript writing, final approval, responsible for every aspect of the research

Sajida Shaheen: Project conception, interpretation of results, literature search, critical reviews, final approval, responsible for every aspect of the research

Ayesha Shuja: Data collection and processing, literature search, manuscript writing, critical reviews, final approval, responsible for every aspect of the research

Hajra Hafeez: Data collection and processing, literature search, manuscript writing, final approval, responsible for every aspect of the research

Muhammad Younas: Data collection and processing, literature search, manuscript writing, critical reviews, final approval, responsible for every aspect of the research

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