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Exploring Thyroid Dysfunction During Pregnancy: Implications for Anemia and Timing of Birth

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ABSTRACT

Background: Maternal thyroid dysfunction during pregnancy has significant implications for both maternal and fetal health, with hypothyroidism linked to adverse outcomes. Understanding its impact on fetal development is crucial for prenatal care. This study, focusing on haemoglobin levels, examines the relationship between maternal thyroid dysfunction, particularly hypothyroidism, and fetal development.

Methods: This cross-sectional study was conducted at Mc Gann's Teaching District Hospital, Shivamogga, and analyzed pregnant women with and without thyroid dysfunction-screening involved comprehensive assessments and thyroid function tests. Two groups were compared: thyroid dysfunction (Group 1) and normal thyroid (Group 2).

Results: Differences were observed in comparing haemoglobin levels between pregnant women with hypothyroidism (case group) and normal thyroid (control group). In the case group, term births had lower Hb levels (10-10.9 g/dL: 76%, 7-9.9 g/dL: 24%) than controls (>11 g/dL: 95%). Preterm births in the case group also showed lower Hb levels (7-9.9 g/dL: 86%) compared to controls (>10 g/dL: 87%).

Conclusion: Maternal hypothyroidism is associated with fetal development issues, particularly preterm delivery. Anemia resulting from hypothyroidism may contribute to preterm birth. These findings underscore the importance of thyroid screening and management during pregnancy to optimize maternal and fetal health outcomes. Further research is needed to understand underlying mechanisms and explore interventions.

Key-words: Gestational anaemia, Maternal, Thyroid dysfunction, Maternal hypothyroidism

INTRODUCTION

Thyroid dysfunction during pregnancy constitutes a carrying health concern, substantial prevalent repercussions for both maternal and fetal well-being.

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The thyroid gland is pivotal in overseeing the body's metabolic rate, influencing critical physiological processes such as cardiac and muscular function, cerebral development, and skeletal maintenance ^[1]. The intricate interplay of thyroid function during pregnancy underscores its indispensability, emphasizing the imperative need for vigilance and comprehensive management to safeguard the health of both expectant mothers and their offspring.

Anemia poses a pervasive global health challenge, impacting 33% of non-pregnant women and 38% of

pregnant women, with prevalence escalating throughout pregnancy^[2]. The World Health Organization categorizes anemia based on red blood cell morphology, with iron deficiency anemia (IDA) dominating 75% of pregnancyrelated cases ^[3]. Elevated iron demand during pregnancy heightens susceptibility to IDA. Compounding this, studies suggest a bidirectional relationship between anemia and thyroid function, implicating anemia in reduced thyroid peroxidase activity. To further elucidate the complex relationship between thyroid dysfunction and anemia, this study draws attention to Veltri et al.'s cross-sectional study conducted in the first trimester of pregnancy ^[4]. This intricate interplay, is observed during various stages of pregnancy, and the implications extend beyond pregnancy ^[5,6], encompassing non-pregnant women as well. Hence, it underscores the heightened risk of anemia associated with thyroid dysfunction ^[7,8].

MATERIALS AND METHODS

Design- This research followed a cross-sectional study design, aimed at finding the relationship between maternal thyroid dysfunction and gestational anemia among pregnant ladies visiting Obstetrics and Gynecology department of Mc Gann's Teaching District Hospital in Shivamogga.

Screening of population- All pregnant women with a positive pregnancy test (urine pregnancy test positive) were eligible for the study. The screening procedure involved comprehensive assessments, including routine clinical examinations. Blood pressure measurements and general health checks will be conducted. Blood tests will be performed to assess hematological parameters, including hemoglobin levels. Medical history reviews will identify pre-existing conditions or risk factors. For thyroid function assessment, thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) levels will be measured. Additionally, ultrasound imaging will evaluate fetal development during the first trimester. This ensures a thorough evaluation of both maternal and fetal health parameters.

Study Subjects- The study subjects comprise two groups: Group 1, consisting of 79 pregnant women diagnosed with thyroid dysfunction during the current pregnancy, and Group 2, including 79 pregnant women without thyroid dysfunction during the current pregnancy. **Hypothyroidism in Pregnancy**- Underactive thyroid gland in pregnancy, causing low thyroid hormone levels, potentially leading to complications for both mother and baby.

Preterm Delivery- Baby born before 37 weeks of pregnancy, increasing risk of health problems due to immature organs and systems.

Anemia in Pregnancy- Low red blood cell or hemoglobin levels less than 11g/dl ^[9] during pregnancy, causing fatigue, weakness, and increasing risk of childbirth complications. As per a study conducted by Marwaha *et al.* ^[10] on normal pregnant Indian women, the upper limit of the reference interval for TSH levels in the 95th percentile was 5.0 mIU/L. In our study involving normal pregnant women, the upper limit of the reference interval for TSH levels at 95% yielded a value of 4.98 mIU/L. Hence, a cutoff of 5 mIU/L was employed in our study.

Statistical Analysis- Descriptive characteristics of the study population were presented as median and mean \pm SD. Spearman correlation analysis assessed the relationship between TSH and Hb among the case and control groups (Table 2). Chi-square tests were utilized to analyze associations between the Gestational phase, anemia, and thyroid function in the whole population (Table 3), as well as among pregnant women with hypothyroidism (Table 5) and those with normal thyroid levels (Table 6). A chi-square test was also conducted to examine associations between anemia and the Gestational phase (Table 4). The significance level was set at p < 0.05 for all analyses.

Ethical approval- The Institutional Ethics Committee approved the study, Shimoga Institute of Medical Science, Shivamogga, Ref. No.: SIMS/IEC/876/2022-23.

RESULTS

Table 1 illustrates the characteristics of the study population, focusing on age, hemoglobin (Hb) levels, and thyroid hormone levels (T3, T4, and TSH) for both the case (maternal thyroid dysfunction) and control (normal thyroid function) groups. Notably, the case group displayed a lower median Hb level (9.09 g/dL) than the control group (12.3 g/dL), representing a substantial percentage decrease of approximately 26%. Conversely,

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the case group exhibited higher median T4 levels (14.09 μ g/ml) the control group (10.3 μ g/ml), reflecting a notable percentage increase of about 36%. Moreover, thyroid-stimulating hormone (TSH) levels were markedly elevated in the case group (median: 24.10 uIU/ml) compared to the control group (median: 4.52 uIU/ml), indicating a substantial percentage increase of approximately 433%.

Variable	Mean ± SD	Median			
Case					
Age	26.22 ± 3.93	26			
Hb	9.39 ± 1.22	9.09			
T3 ng/ml	1.23 ± 0.39	1.25			
T4 μg/ml	13.89 ± 3.86	14.09			
TSH uIU/ml	21.24 ± 6.52	24.10			
Control					
Age	25.23 ± 3.38	25.22			
Hb	12.18 ± 1.28	12.3			
T3 ng/ml	1.18 ± 0.41	1.18			
T4 μg/ml	11.36 ± 4.54	10.3			
TSH uIU/ml	4.28 ± 0.7	4.52			

Table 1: Characteristic of study population

The Spearman correlation analysis in Table 2 demonstrates a robust negative correlation (rs=-0.62, p=0) between TSH and Hb levels in the case group, suggesting that elevated TSH levels coincide with reduced Hb levels. Conversely, a weaker negative correlation (rs=-0.177, p=0.12) is observed in the control group, indicating a less pronounced association between TSH and Hb levels.

 Table 2: Spearman correlation analysis between TSH and

 Hb among Case and Control

Correlation Parameter	spearman correlation coefficient (rs)	p-value
Case TSH- Hb	-0.62	0
Normal TSH- Hb	-0.177	0.12

Table 3 depicts the Chi-square test results analyzing the association between Gestational phase and TSH levels in the study population. The findings indicate a significant relationship (p<0.00001) between TSH levels and delivery time. Preterm deliveries are notably more prevalent in the case group with elevated TSH levels

(73%) compared to the control group (26.6%). Conversely, term deliveries exhibit a more balanced distribution between the case and control groups.

Gestational	Case n	Control	Total	p-value
phase	(%)	n (%)		
Preterm	44 (73)	16 (26.6)	60	
			(100)	
Term	35	63 (64.2)	98	<0.00001
	(35.7)		(100)	<0.00001
Total	79 (50)	79 (50)	158	
			(100)	

Table 3: Chi square test of analysis of whole population for Gestational phase and TSH levels

The data presented in Table 4 illustrate the chi-square test results analyzing the association between anemia and the gestational phase. The analysis revealed a significant relationship between anemia and gestational phase (p < 0.00001). Among preterm births, 98.3% were anemic, whereas only 29.6% of term births were anemic. This suggests a higher prevalence of anemia among preterm births compared to term births. Overall, 55.7% of the total population studied was anemic, indicating a substantial occurrence of anemia during pregnancy across both gestational phases.

Table 4: Chi square test of analysis of whole populationfor anemia and delivery time

Gestational phase	Anemic n (%)	Non- anemic n (%)	Total	p-value
Preterm	59 (98.3)	1 (1.6)	60	<0.00001
ricterin			(100)	
Term	29 (29.6)	69 (70.4)	98	
			(100)	
Total	88 (55.7)	70 (44.3)	158	
			(100)	

Table 5 presents the results of the chi-square test examining the relationship between hypothyroidism in pregnant women and the occurrence of anemia across different gestational phases. The analysis demonstrated a statistically significant association between hypothyroidism and anemia (p = 0.0008). Among preterm births, 97.7% of pregnant women with hypothyroidism were anemic, compared to 71.42% of those with term births. Overall, 86.1% of pregnant women with hypothyroidism were anemic, indicating a higher prevalence of anemia in this group compared to non-anemic individuals.

Table 5: Chi square test of analysis of pregnant ladies
with hypothyroidism for anemia and delivery time

Gestational phase	Anemic n (%)	Non- anemic n (%)	Total	p-value
Preterm	43 (97.7)	1(2.3)	44	
			(100)	
Term	25	10 (28.6)	35	0 0008
	(71.42)		(100)	0.0008
Total	68 (86.1)	11 (13.9)	79	
			(100)	

Table 6 displays the results of the Fisher Exact test investigating the association between normal thyroid levels in pregnant women and the occurrence of anemia across different gestational phases. The analysis revealed a statistically significant relationship between normal thyroid levels and anemia (p<0.00001). Among preterm births, all pregnant women with normal thyroid levels were anemic, while in term births, only 6.34% were anemic. Overall, 25.3% of pregnant women with normal thyroid levels were anemic, indicating a lower prevalence compared to pregnant women with hypothyroidism.

Table 6: Fisher Exact test of analysis of pregnant ladieswith normal thyroid level for anemia and delivery time

Gestational phase	Anemic n (%)	Non- anemic n (%)	Total	p-value
Preterm	16 (100)	0	16 (100)	
Term	4 (6.34)	59 (93.65)	63 (100)	0.00001
Total	20 (25.3)	59 (74.68)	79 (100)	

DISCUSSION

The investigation into the characteristics of pregnant women with thyroid dysfunction compared to those with normal thyroid function reveals significant disparities in physiological parameters, particularly hemoglobin levels and thyroid hormone levels, underscoring the potential impact on maternal and fetal health outcomes.

The characteristics of our study population reveal notable differences in physiological parameters between pregnant women with thyroid dysfunction (case group) and those with normal thyroid function (control group). In our study, pregnant women with thyroid dysfunction exhibited distinct physiological differences compared to those with normal thyroid function, notably in hemoglobin levels and thyroid hormone concentrations. The significant decrease in hemoglobin levels and substantial increase in T4 and TSH levels among the case group suggest potential implications for maternal and fetal health outcomes. These findings underscore the importance of monitoring thyroid function during pregnancy and implementing tailored interventions to address the correlated risk.

While there is widespread agreement on the necessity of promptly treating overt maternal hypothyroidism, the potential risks associated with hypothyroidism remain uncertain. Additionally, the American Endocrine Society and the 2011 American Thyroid Association (ATA) guidelines advocate for interpreting thyroid function during pregnancy based on trimester-specific reference ranges derived from populations with optimal iodine intake. The European Thyroid Association echoes similar recommendations. This convergence in recommendations underscores the importance of consistent management practices to optimize maternal and fetal health outcomes, with one parameter being TSH levels typically considered within the range of 0.1-2.5 mIU/L. Further Gestational thyrotoxicosis exhibits a [11] higher prevalence among Asian populations compared to Western and other ethnic groups. Given the geographical variability in thyroid disorder prevalence during pregnancy, establishing trimester-specific reference ranges for thyroid profiles is imperative. Particularly for the Indian population, adhering to a universal upper cutoff limit of 2.5 mIU/L may not suffice, necessitating tailored guidelines to ensure accurate diagnosis and management of thyroid dysfunction in pregnant women. Our study revealed that with an upper cutoff of 5 mIU/L, preterm births were more prevalent in the case group with elevated TSH levels (73%) than controls (26.6%). At the same time, term deliveries showed a more balanced distribution. This observation aligns with findings in an updated systematic review and

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meta-analysis ^[12], suggesting a potential association between maternal thyroid dysfunction, elevated TSH levels, and preterm delivery.

Anemia and hypothyroidism are significant health concerns during pregnancy, posing risks to both maternal and fetal well-being ^[13]. Anemia, characterized by low red blood cell count or hemoglobin levels, can lead to maternal fatigue, impaired oxygen delivery, and adverse pregnancy outcomes. Hypothyroidism, marked by insufficient thyroid hormone production, disrupts metabolic processes crucial for fetal development and maternal health. The co-occurrence of anemia and hypothyroidism during pregnancy exacerbates these risks, warranting careful monitoring and management. The study observed a negative correlation between TSH and Hb levels, particularly pronounced in the case group, underscoring maternal thyroid dysfunction's potential influence on hemoglobin levels during pregnancy. These findings highlight the importance of early detection and management of thyroid dysfunction in pregnant women to reduce the linked risk, including anemia and potential adverse pregnancy outcomes.

The analysis across the entire study population reveals a significant correlation: heightened TSH levels are associated with a notably higher incidence of preterm delivery. The study also observed a significantly higher incidence of preterm deliveries in pregnant women with elevated TSH levels compared to those with normal TSH levels, indicating a potential correlation between maternal thyroid dysfunction and preterm delivery. This underscores the critical influence of maternal thyroid function on gestational outcomes. This was well documented in a study conducted by Negro *et al.* ^[14] and other studies ^{[15-17],} which suggest a potential association between higher TSH levels and adverse pregnancy outcomes like preterm delivery.

The analysis conducted across the entire study population highlights a significant association between anemia and the gestational phase, revealing a substantially higher prevalence of anemia among preterm births compared to term births. Moreover, the specific examination within the case population demonstrates a notable correlation between hypothyroidism and anemia, particularly evident in preterm births, indicating the necessity of targeted interventions for pregnant women with hypothyroidism to mitigate the risks associated with anemia and optimize maternal and fetal health outcomes. Further a study from Kumar et al. refer to hypothyroid women showing a higher incidence of preeclampsia, followed by anemia and other adverse outcomes such as abortions, meconium-stained liquor, preterm delivery, and premature rupture of membranes ^[18]. With the significant association observed between hypothyroidism and anemia, particularly evident in preterm births, underscores the critical role of thyroid function in maternal health during pregnancy. With nearly all hypothyroid pregnant women experiencing anemia in preterm deliveries ^[19-21], and a substantially higher prevalence overall, proactive monitoring and management of anemia become paramount, especially in this vulnerable population. These findings emphasize the necessity of integrated care approaches that address thyroid function and anemia to ensure optimal maternal and fetal outcomes.

CONCLUSIONS

Our study underscores the intricate interplay between thyroid dysfunction, anemia, and adverse pregnancy outcomes, particularly preterm birth. The observed association between hypothyroidism and anemia, notably in preterm deliveries, highlights the importance of proactive monitoring and management of both conditions during pregnancy. These findings emphasize the critical need for integrated care strategies that address thyroid function and anemia to optimize maternal and fetal health outcomes. By implementing tailored guidelines and comprehensive management approaches, healthcare providers can mitigate the risks associated with thyroid disorders and anemia, ultimately ensuring the well-being of both mother and child during pregnancy.

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