E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.48047/ijprt/16.01.329

Research Article

Maternal Thyroid Biochemistry in Pregnancy and Its Relationship with Physiological Changes and Infant Developmental Outcomes

Ommia Kalsoom[1], Muhammad Zahid[2], Muhammad Salman Khan[3], Amber Zaidi[4], Iffat Mushtaq[5], Fazal Rahim[6]

[1]Professor, Department of Physiology, Women Medical College, Abbottabad, Pakistan
[2]Associate Professor, Department of Physiology, Nowshera Medical College, Nowshera, Pakistan
[3]Assistant Professor, Department of Physiology, Gomal Medical College MTI, Dera Ismail Khan, Pakistan
[4,5]Assistant Professor, Department of Biochemistry, NUST School of Health Sciences (NSHS), National University of Sciences and Technology (NUST), Islamabad, Pakistan
[6]Assistant Professor, Department of Physiology, Bacha Khan Medical College, Mardan, Pakistan

Corresponding Author: Muhammad Zahid, Associate Professor, Department of Physiology, Nowshera Medical College, Nowshera, Pakistan**,** Email: drzahidktk@gmail.com
Received: 07.01.26, Revised: 25.04.26, Accepted: 06.05.26

ABSTRACT

Background: Maternal thyroid hormones have been demonstrated to be critical for normal pregnancy physiology, fetal growth and early neurodevelopment. Thyroid biochemical status can change during pregnancy due to changes in thyroid hormone needs, iodine needs and maternal metabolism. Undiagnosed or undiagnosed and untreated thyroid disease can lead to poor maternal, neonatal and infant developmental outcomes.

Objective: To determine the relationship between maternal thyroid biochemical status during pregnancy, pregnancy-related physiological changes, and infant developmental outcomes.

Methodology: The study was a prospective observational analytical study done at Women Medical College, Abbottabad, from February 2024 to September 2024. The number of pregnant women who were singleton pregnancies and enrolled in the study was 86, using non-probability consecutive sampling. Maternal demographic information, obstetric history, physiological parameters, and thyroid biochemical markers (TSH, fT3, and fT4) were documented. Participants were divided into 2 groups; euthyroid and thyroid dysfunction using the hospital laboratory reference ranges. Pregnancy and neonatal outcomes such as birth weight, preterm delivery, Apgar score, admission to the NICU and developmental milestones of the babies were measured. The SPSS version 26 was used to analyze data. The statistical methods used were Chi-square test, independent sample t-test, correlation analysis, and logistic regression. A p value of < 0.05 was considered statistically significant.

Results: Out of 86 pregnant women, 54 (62.8%) were euthyroid, while 32 (37.2%) had thyroid dysfunction. Women with thyroid dysfunction had significantly lower mean hemoglobin levels than euthyroid women (10.42 ± 1.19 g/dL vs. 11.20 ± 1.24 g/dL, p=0.006), and anemia was more frequent in this group (p=0.019). Infants of mothers with thyroid dysfunction had lower mean birth weight (2.61 ± 0.42 kg vs. 2.89 ± 0.39 kg**,** p=0.003), higher frequency of low birth weight (p=0.016), preterm birth (p=0.048), NICU admission (p=0.041), and developmental delay (p=0.008). Maternal TSH showed a positive correlation with infant developmental delay score (r=0.392, p<0.001), while FT4 showed a negative correlation (r=-0.337, p=0.002). On logistic regression, maternal thyroid dysfunction remained a significant predictor of infant developmental delay (OR=3.84, 95% CI: 1.29–11.43, p=0.016).

Conclusion: Maternal thyroid dysfunction during pregnancy was significantly associated with anemia, low birth weight, preterm birth, NICU admission, and delayed infant developmental milestones. Higher maternal TSH and lower FT4 levels were linked with poorer developmental outcomes. Routine antenatal thyroid assessment may help in early detection and timely management of thyroid dysfunction, particularly in high-risk pregnant women.

Keywords: Maternal thyroid dysfunction, pregnancy, TSH, FT4, birth weight, developmental delay, infant milestones.

INTRODUCTION

Thyroid function is an important factor in the maintenance of normal maternal physiology during pregnancy. During pregnancy, there are significant endocrine, metabolic and hemodynamic changes, and these changes contribute to the need for more thyroid hormones. Maternal thyroid hormones play a

role in placental function, fetal growth and fetal brain development. In early pregnancy, maternal thyroxine is heavily relied upon by the fetus, prior to the development of its own thyroid gland. So, slight thyroid dysfunction in the mother can affect fetal development and early postnatal growth (1-3).

Thyroid dysfunction in pregnancy can manifest as either overt hypothyroidism, subclinical hypothyroidism, overt hyperthyroidism, subclinical hyperthyroidism or isolated thyroid hormone changes. Of these, subclinical hypothyroidism is common as many women may have elevated TSH and no clinical symptoms. Physiological changes during pregnancy, such as the rise in thyroxine-binding globulin, the need to increase iodine intake and the stimulating effect on the thyroid gland of human chorionic gonadotropin (hCG), can make interpretation of thyroid biochemistry more complex. Present literature has highlighted that thyroid dysfunction in pregnancy can have a negative impact both on the mother's and fetus' health, especially if undiagnosed or untreated (4-6).

Several negative pregnancy outcomes have been associated with maternal thyroid imbalance. These include such complications as anemia, hypertensive disorders of pregnancy, gestational diabetes, miscarriage, preterm delivery, fetal growth restriction, low birth weight, and increased neonatal intensive care admission. Researchers in India conducted a prospective cohort study, which found increased rates of adverse maternal and fetal outcomes in hypothyroid women versus euthyroid women, including low birth weight and preterm birth. The results emphasize the need to assess thyroid biochemical status as a part of maternal risk assessment in pregnancy (7, 8).

Maternal thyroid status also affects infant neurodevelopment as well as pregnancy and neonatal outcomes. Thyroid hormones play a role in neuronal migration, myelination, synapse formation and maturation of the fetal central nervous system. A hypothyroid mother may have an impact on the early motor, language, and social development of her fetus. The relationship between maternal thyroid dysfunction and neonatal or child neurodevelopmental outcomes has recently been investigated, but results are inconsistent depending on the time of thyroid evaluation, severity of the thyroid dysfunction, treatment status, iodine status, and duration of follow up of the infants (9-11).

Developmental milestones serve as an early clinical sign of neurological and physical development. A failure to hold to the neck, sit up, crawl, stand, walk, babble or interact socially may be an indicator of underlying developmental issues. Several maternal and neonatal risk factors such as maternal anemia, thyroid dysfunction, premature delivery, low birth weight, and neonatal illness have been shown to affect these milestones. So, assessing infant development in relation to maternal thyroid biochemistry could be useful in identifying infants at risk early (12).

Antenatal screening in Pakistan is usually conducted on anemia, blood pressure, diabetes, fetal growth and delivery complications, but not always routine screening of thyroid is done in all pregnant women. There is little local information on the relationship between maternal thyroid biochemistry, physiological changes during pregnancy and infant developmental outcomes. This gap is clinically significant as thyroid dysfunction is a manageable and clinically detectable condition. If adverse neonatal and developmental consequences are to be minimized, early recognition during the pregnancy may play a role (13).

The present study was therefore conducted to determine the relationship between maternal thyroid biochemical profile during pregnancy, pregnancy-related physiological changes, and infant developmental outcomes. The study specifically assessed maternal TSH, FT3, and FT4 levels, categorized maternal thyroid status, and evaluated their association with maternal physiological parameters, birth outcomes, and infant developmental milestones.

METHODOLOGY

This study was carried out in Women Medical College, Abbottabad from February 2024 to September 2024, which spanned 8 months. The purpose of the study was to determine whether the relationship between maternal thyroid biochemical status, physiologic changes of pregnancy, and infant developmental outcomes differs. A prospective observational analytical study design was used because the present study was set up to observe the thyroid parameters of the mother during pregnancy, and their correlation with the physiological changes in the mother and developmental milestones in the infant without introducing any intervention.

The study population was pregnant women attending Women Medical College (WMC), Abbottabad in the obstetrics and gynecology clinic. Using a non-probability consecutive

sampling, a total of 86 pregnant women who meet the eligibility criteria were enrolled. This sampling technique was chosen because all the pregnant women who came to the hospital during the study period were sampled until the required sample size was obtained.

Pregnant women of reproductive age with a confirmed singleton pregnancy were included in the study. Women who agreed to take part, and who provided informed consent, and who could be contacted for follow-up until the time of infant developmental assessment were included.Women who agreed to participate, who gave informed consent, and who were able to be contacted until the time of infant developmental assessment were included. Women who had multiple pregnancy, known fetal congenital anomaly, chronic renal disease, severe liver disease, uncontrolled diabetes mellitus, autoimmune disease, and history of medication that affects the thyroid function were excluded. Women who did not have complete laboratory data or had been lost to follow-up prior to infant developmental assessment also were not included in the final analysis.

Before data collection, ethical approval was obtained from the institutional ethical review committee of Women Medical College, Abbottabad. The objective and methodology of the study was explained to all the participants and written informed consent was obtained prior to enrollment. All information collected was kept confidential by using study codes rather than patient names. Participants were told their participation was voluntary and they did not have to do anything if they refused to participate that would impact their usual care.

A structured proforma specifically developed for the study was used to collect data. Demographic data of the mother was collected, such as age, place of residence, education, socioeconomic status, occupation, parity, gravida status, gestational age at registration, and body mass index. Obstetric history, booking status, previous pregnancy outcomes and pregnancy related complications were also recorded. Blood pressure, pulse rate, weight, height and body mass index were measured during clinical examination. Hemoglobin level was noted to evaluate anemia, weight gain, anemia, pregnancy-induced hypertension and gestational diabetes mellitus were recorded when applicable.

Biochemical parameters of maternal thyroid evaluated: serum TSH, FT3 and FT4. A blood sample was withdrawn, aseptically and analyzed in the hospital laboratory, following standard laboratory procedure. The participants were divided into two groups according to thyroid biochemical results: Euthyroid and thyroid dysfunction. Thyroid dysfunction encompassed subclinical hypothyroidism, overt hypothyroidism and subclinical hyperthyroidism, based on the hospital's laboratory reference ranges. The following thyroid markers were analyzed as main markers: TSH, FT3 and FT4.

Post-delivery data on pregnancy and neonatal outcomes were collected. Infant variables were gestational age at birth, birth weight, low birth weight (< 5.5 kg), APGAR score at 1 minute and 5 minutes after birth, admission to NICU, neonatal jaundice, feeding difficulty, and preterm birth. Low birth weight was defined as birth weight of less than 2.5 kg and premature birth as delivery before 37 completed weeks. The following variables were added on so as to determine if early neonatal outcomes were correlated with maternal thyroid biochemical imbalance.

Follow-up assessment of developmental outcomes used developmental milestone evaluation based on age-appropriate developmental milestones. Domains of development included: gross motor, fine motor, language and social development. Recorded milestones were social smile, neck holding, sitting unsupported, crawling, standing with assistance, walking, babbling, responding to sound and eye contact. Infants were classified as normal development or developmental delay if they failed to meet age-appropriate expectations for development. Data was gathered by interviewing the mothers and by clinical follow-up and on child health records.

Infant developmental delay was the primary outcome variable and maternal thyroid biochemical markers, such as TSH, FT3, FT4 and thyroid status category, were the main independent variables. Other explanatory variables were maternal hemoglobin level, gestational age, body mass index, parity, pregnancy-related complications, birth weight, and preterm birth. The association of maternal thyroid biochemistry and infant developmental outcomes was studied, as well as pregnancy-related physiologic changes.

Data were inputted and analyzed using SPSS (version: 26). Continuous variables like maternal age, gestational age, BMI, hemoglobin, TSH, FT3, FT4, weight at birth and age of milestone achievement were expressed as mean and standard deviation. Categorical variables like parity, residence, anemia, thyroid status, low birth weight, preterm birth, admission to NICU and developmental delay were presented as frequencies and

percentages. The chi-square test was used to evaluate associations of categorical variables. Mean values were compared between euthyroid women and thyroid dysfunction women using independent sample t-test. Pearson correlation was used for normally distributed continuous variables and Spearman correlation was used for not normally distributed continuous variables. Logistic regression analysis was conducted to determine the factors predicting infant developmental delay. A p-value of < 0.05 was deemed to be significant.

All procedures were conducted according to ethical principles for human research. No experimental drug or intervention was given to the participants. Laboratory tests and clinical assessments were performed as part of maternal and infant evaluation, and the collected data were used only for research purposes. The methodology was structured to ensure reliable assessment of the relationship between maternal thyroid biochemical status, physiological changes during pregnancy, and infant developmental outcomes.

RESULTS

In total 86 pregnant women participated in the study. The mean maternal age was 27.84 ± 4.91 years, most of the subjects were in the age group 26-30 years. The mean gestational age at enrollment was 22.63 ± 6.48 weeks. Of the participants, 49 (57.0%) had multiple pregnancies and 37 (43.0%) had a single pregnancy. In terms of residence 51 (59.3%) women lived in urban areas, and 35 (40.7%) in rural areas. The mean maternal body mass index was 25.62 ± 3.87 kg/m². Thirty-two (37.2%) women were anemic and 10 (11.6%) had pregnancy induced hypertension.

Table 1: Maternal demographic and obstetric characteristics of study participants, n=86

Variable	Frequency / Mean	Percentage / SD
Maternal age, years	27.84	±4.91
Gestational age at enrollment, weeks	22.63	±6.48
BMI, kg/m²	25.62	±3.87
Hemoglobin, g/dL	10.91	±1.28
Primigravida	37	43.0%
Multigravida	49	57.0%
Urban residence	51	59.3%
Rural residence	35	40.7%
Anemia	32	37.2%
Pregnancy-induced hypertension	10	11.6%
Gestational diabetes mellitus	7	8.1%

The mean serum TSH level was 3.18 ± 1.74 mIU/L, while the mean FT3 and FT4 levels were 3.09 ± 0.58 pg/mL and 1.04 ± 0.23 ng/dL, respectively. In terms of thyroid biochemical status 54 (62.8%) women were euthyroid, 20 (23.3%) had subclinical hypothyroidism, 8 (9.3%) had overt hypothyroidism and 4 (4.6%) had subclinical hyperthyroidism. In all, 37.2% (32/86) pregnant women were found to have abnormal thyroid function.

Table 2: Distribution of maternal thyroid biochemical parameters

Thyroid variable	Mean ± SD / Frequency	Percentage
TSH, mIU/L	3.18 ± 1.74	—
FT3, pg/mL	3.09 ± 0.58	—
FT4, ng/dL	1.04 ± 0.23	—
Euthyroid	54	62.8%
Subclinical hypothyroidism	20	23.3%
Overt hypothyroidism	8	9.3%
Subclinical hyperthyroidism	4	4.6%
Any thyroid dysfunction	32	37.2%

Physiological parameters of pregnancy were different between thyroid status. The mean level of hemoglobin was found to be lower in women with thyroid dysfunction than in those with euthyroidism (10.42 ± 1.19 g/dL vs. 11.20 ± 1.24 g/dL, p=0.006). The thyroid dysfunction group also had more cases of anemia (53.1%) compared to the euthyroid group (27.8%), with the difference being statistically significant (p=0.019). A total of 18.8% of women with thyroid dysfunction experienced pregnancy induced hypertension, compared to 7.4% of euthyroid women and the difference was not statistically significant (p=0.112). There was a

slight increase in gestational diabetes in women with thyroid dysfunction, but this was not significant (p=0.314).

Table 3: Pregnancy-related physiological changes according to maternal thyroid status

Variable	Euthyroid n=54	Thyroid dysfunction n=32	p-value
Hemoglobin, g/dL	11.20 ± 1.24	10.42 ± 1.19	0.006
BMI, kg/m²	25.21 ± 3.69	26.31 ± 4.10	0.204
Anemia	15 (27.8%)	17 (53.1%)	0.019
Pregnancy-induced hypertension	4 (7.4%)	6 (18.8%)	0.112
Gestational diabetes mellitus	3 (5.6%)	4 (12.5%)	0.314
Preterm delivery	5 (9.3%)	8 (25.0%)	0.048

Maternal thyroid status was also compared to infant outcomes at birth. There was a significant difference between the infants of mothers with thyroid dysfunction and those of euthyroid mothers in their mean birth weight (2.61 ± 0.42 kg vs 2.89 ± 0.39 kg, p=0.003). There was a total of 13 (15.1%) pre-term deliveries, with a higher rate in the thyroid dysfunction group (p=0.048). In 12 (14.0%) newborns, admission to NICU was required, with significantly more infants of mothers with thyroid dysfunction being admitted to NICU than those of mothers without thyroid dysfunction (p=0.041). Twenty (20.9%) infants had low birth weight, which was more common in the thyroid dysfunction group (p=0.016).

Table 4: Infant birth outcomes according to maternal thyroid status

Infant outcome	Euthyroid n=54	Thyroid dysfunction n=32	p-value
Birth weight, kg	2.89 ± 0.39	2.61 ± 0.42	0.003
APGAR score at 5 minutes	8.61 ± 0.84	8.09 ± 1.03	0.014
Low birth weight	7 (13.0%)	11 (34.4%)	0.016
Preterm birth	5 (9.3%)	8 (25.0%)	0.048
NICU admission	4 (7.4%)	8 (25.0%)	0.041
Neonatal jaundice	6 (11.1%)	7 (21.9%)	0.174

Follow-up with the infant developmental milestones was conducted. In 17 (19.8%) babies overall developmental delay was noted. Infants of mothers who had thyroid dysfunction were more likely to be born with a delay (34.4%) than infants of mothers who were euthyroid (11.1%). This difference was statistically significant (p=0.008). Infant mothers with thyroid dysfunction had a higher mean age for holding the neck and sitting without support and standing with support, suggesting delayed milestones. The difference was statistically significant for neck holding (p=0.021), sitting without support (p=0.018) and standing with support (p=0.026).

Table 5: Infant developmental milestones according to maternal thyroid status

Developmental variable	Euthyroid n=54	Thyroid dysfunction n=32	p-value
Neck holding, months	3.34 ± 0.58	3.71 ± 0.76	0.021
Sitting without support, months	6.42 ± 0.82	6.91 ± 0.96	0.018
Crawling, months	8.14 ± 1.03	8.57 ± 1.11	0.071
Standing with support, months	9.36 ± 1.14	9.94 ± 1.20	0.026
Social smile, months	2.12 ± 0.41	2.28 ± 0.49	0.101
Babbling, months	6.71 ± 0.94	7.09 ± 1.02	0.083
Overall developmental delay	6 (11.1%)	11 (34.4%)	0.008

There was a significant positive correlation between maternal TSH and the infant developmental milestone score (r=0.392, p<0.001), indicating that higher maternal TSH levels were related to delayed achievement of developmental milestones. There was a significant negative correlation between FT4 levels and developmental delay score (r=-0.337, p=0.002) suggesting that lower levels of maternal FT4 would correspond to poorer developmental performance. Maternal hemoglobin and infant birth weight were

negatively related to developmental delay score, that is, lower birth weight and hemoglobin were associated with delayed infant milestone scores.

Table 6: Correlation of maternal biochemical and physiological variables with infant developmental delay score

Variable	Correlation coefficient, r	p-value
Maternal TSH	0.392	<0.001
Maternal FT3	-0.118	0.279
Maternal FT4	-0.337	0.002
Maternal hemoglobin	-0.286	0.008
Gestational age at delivery	-0.251	0.020
Birth weight	-0.371	<0.001
APGAR score at 5 minutes	-0.224	0.038

On logistic regression analysis, maternal thyroid dysfunction was found to be a significant predictor of infant developmental delay. The infants of mothers with thyroid dysfunction were 3.84 times more likely to be developmentally delayed (OR=3.84, 95% CI=1.29-11.43, p=0.016) than those of mothers with euthyroidism. Low birth weight was also a significant independent risk factor for developmental delay (OR=3.21, 95% CI: 1.05–9.81, p=0.041). Anemia in the mother was associated with higher likelihood of developmental delay in the child, but this was not statistically significant (p=0.062).

Table 7: Logistic regression analysis for predictors of infant developmental delay

Predictor	Odds Ratio	95% CI	p-value
Maternal thyroid dysfunction	3.84	1.29–11.43	0.016
Maternal anemia	2.61	0.95–7.19	0.062
Low birth weight	3.21	1.05–9.81	0.041
Preterm birth	2.47	0.81–7.53	0.112
NICU admission	2.18	0.69–6.87	0.184

Overall, the results indicated that thyroid dysfunction in mothers during pregnancy was prevalent and was significantly related to decreased levels of maternal hemoglobin, higher prevalence of anemia, preterm delivery, low birth weight, NICU admission, and delayed infant developmental milestones. Infant developmental outcome was significantly related to higher maternal TSH and lower FT4 levels. The findings indicate that maternal thyroid biochemical abnormalities during pregnancy could affect pregnancy physiology and early infant development.

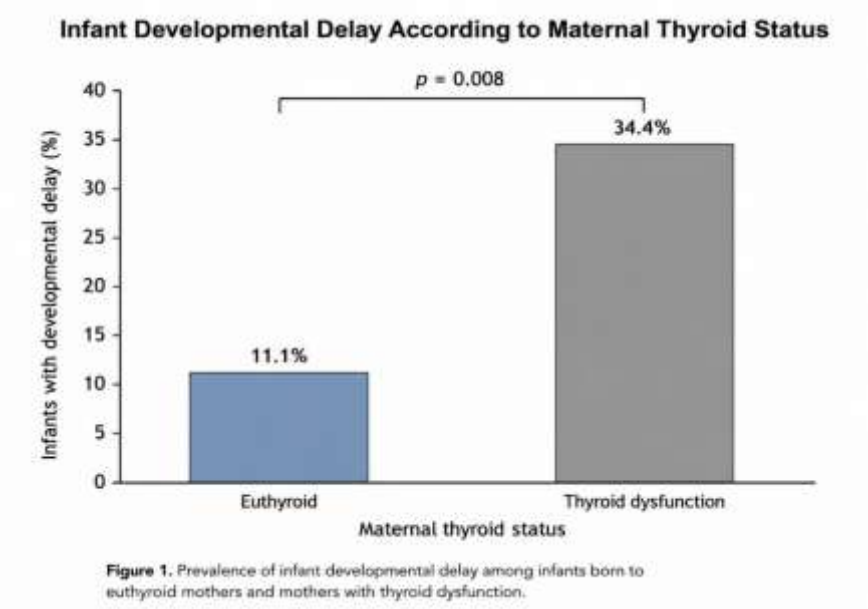

Figure 1: Prevalence of infant developmental delay among infants born to euthyroid mothers and mothers with thyroid dysfunction

DISCUSSION

The present study assessed maternal thyroid biochemistry during pregnancy and its relationship with pregnancy-related physiological changes and infant developmental outcomes. In this study, thyroid dysfunction was observed in 37.2% of pregnant women, while 62.8% were euthyroid. Subclinical hypothyroidism was the most frequent abnormality, followed by overt hypothyroidism and subclinical hyperthyroidism. This finding suggests that altered thyroid function is not uncommon during pregnancy and may remain clinically important even when symptoms are mild or absent. Pregnancy itself produces major endocrine and metabolic changes, and thyroid hormones play an essential role in maternal adaptation, placental function, fetal growth, and fetal brain development. Recent literature also supports that thyroid dysfunction during pregnancy is associated with adverse maternal, fetal, and neonatal outcomes, emphasizing the importance of antenatal thyroid evaluation (14, 15).

The present study showed that the level of hemoglobin was significantly lower in women with thyroid dysfunction than in euthyroid women. Women who had thyroid problems also had a higher prevalence of anemia, and this relationship was statistically significant. The finding could be attributed to the involvement of thyroid hormones in the mechanism of erythropoiesis, oxygen consumption, and overall metabolic control. Hypothyroid states can also decrease the response to erythropoietin and cause decreased red cell production, and pregnancy increases iron demand as well as plasma volume expansion. Thus, maternal thyroid dysfunction and anemia can compound the physiological reserve of the mother during pregnancy. In this study, women with thyroid dysfunction had higher rates of maternal BMI, PHT and gestational diabetes but these relationships were not statistically significant. This could be because of the small number of subjects or because of the fact that these pregnancy complications have a multifactorial etiology (16).

The study also revealed that the mean birth weight of infants of mothers with thyroid dysfunction was significantly lower than the mean birth weight of infants of euthyroid mothers. Thyroid dysfunction group had a higher prevalence of LBW, preterm delivery and admission to NICU. The importance of these findings is clinical since thyroid hormones are linked to the growth and development of the placenta, fetal metabolism, and intrauterine growth. To substantiate the biological significance of thyroid imbalance in fetal growth, a large individual-participant meta-analysis was reported, in which maternal subclinical hypothyroidism was linked to an increased risk for small-for-gestational-age birth and low birth weight (15). In the same vein, new research and reviews have indicated that mothers with thyroid disorders could be at a higher risk for negative fetal and neonatal outcomes such as low Apgar scores, fetal growth restriction, and preterm birth (14, 17).

A total of 19.8% of infants in the present study exhibited developmental delay. Developmental delay was more likely to occur in infants of mothers with thyroid dysfunction than in infants of mothers without thyroid dysfunction. Gross motor milestones were reported as delayed more especially in neck holding, sitting without support and standing with support. This discovery helps validate the notion that maternal thyroid hormones play a role in early fetal brain maturation, neuronal migration, myelination and synaptic development in particular, around the time when the fetus relies heavily on the maternal thyroxine. A recent study of thyroid dysfunction in pregnancies showed poorer neonatal neurodevelopment outcomes for those exposed to maternal thyroid dysfunction (18). However, not all studies found in the literature are congruent; some large studies reported little or no relationship between prenatal levels of thyroid hormones and subsequent school achievement or neurodevelopmental diagnoses, hinting that the timing of exposure, degree of thyroid dysfunction, treatment status, iodine status, and duration of follow-up may have an impact on outcome (19).

In the present study, Pearson correlation revealed that TSH was significantly correlated with the delayed developmental milestones and FT4 was significantly correlated with developmental delay score. This suggests that hypothyroidism (high TSH, low FT4) can be associated with less optimal early infant developmental performance. Poor maternal physiological status (maternal hemoglobin) and adverse neonatal outcomes (GESTATIONAL AGE, BW, APGAR) were also negatively correlated with developmental delay, suggesting that poor maternal physiological status and adverse neonatal outcomes may be associated with delayed development. These

results indicate that thyroid function per se is not associated with infant developmental outcome, but may be linked to the overall influence of maternal thyroid dysfunction, anemia, preterm delivery, and low birth weight (20).

Logistic regression analysis also found maternal thyroid dysfunction to be an independent predictor of infant developmental delay. Infants of mothers with abnormal thyroid function were 3.84 times more likely to have developmental delay than were infants of mothers with normal thyroid function. Low birth weight was also an independent risk factor for developmental delay. This discovery reinforces the importance of thyroid monitoring in pregnancy, especially as thyroid dysfunction is a potentially detectable and manageable condition. The effect of early identification and treatment on the outcomes of mother and child may minimize adverse outcomes and warrant further research with larger longitudinal studies to establish the long-term developmental outcomes (21).

There are some limitations to the findings of this study. It was performed in a single center and a small number of subjects (86) that may reduce the generalizability of the study. Neurodevelopmental outcome measures (cognition, language, school performance and behavioral outcomes) were not assessed at long-term follow-up; developmental milestones were assessed at early follow-up. Maternal thyroid antibody status and iodine levels were not considered in the primary analysis, as this may affect maternal thyroid function and fetal development. In spite of these restrictions, the study offers locally relevant evidence of the association between maternal thyroid biochemistry, changes in physiology during pregnancy and infant developmental outcomes.

CONCLUSION

This study concluded that maternal thyroid dysfunction during pregnancy was significantly associated with adverse maternal, neonatal, and infant developmental outcomes. Women with thyroid dysfunction had lower hemoglobin levels and a higher frequency of anemia. Infants born to mothers with thyroid dysfunction had lower birth weight, higher rates of preterm birth and NICU admission, and a greater frequency of developmental delay. Higher maternal TSH and lower FT4 levels were significantly correlated with delayed infant milestones.

The findings suggest that maternal thyroid biochemical imbalance during pregnancy may influence both pregnancy physiology and early infant development. Routine antenatal assessment of thyroid function, especially in high-risk pregnant women, may help in early identification and timely management of thyroid dysfunction. Further multicenter studies with larger sample sizes and longer infant follow-up are recommended to confirm these findings and evaluate long-term neurodevelopmental outcomes.

REFERENCES

1. Lucaccioni L, Ficara M, Cenciarelli V, Berardi A, Predieri B, Iughetti L. Long term outcomes of infants born by mothers with thyroid dysfunction during pregnancy. 2020;92(1):e2021010.
2. Lee SY, Cabral HJ, Aschengrau A, Pearce EN. Associations between maternal thyroid function in pregnancy and obstetric and perinatal outcomes. The Journal of Clinical Endocrinology & Metabolism. 2020;105(5):e2015-e23.
3. Murillo-Llorente MT, Llorca-Colomer F, Pérez-Bermejo MJ. Relationship between thyroid status during the first trimester of pregnancy and neonatal well-being. Nutrients. 2021;13(3):872.
4. Anifantaki F, Pervanidou P, Lambrinoudaki I, Panoulis K, Vlahos N, Eleftheriades M. Maternal prenatal stress, thyroid function and neurodevelopment of the offspring: A mini review of the literature. Frontiers in Neuroscience. 2021;15:692446.
5. Eng L, Lam L. Thyroid function during the fetal and neonatal periods. Neoreviews. 2020;21(1):e30-e36.
6. Bohn MK, Adeli K. Physiological and metabolic adaptations in pregnancy: importance of trimester-specific reference intervals to investigate maternal health and complications. Critical Reviews in Clinical Laboratory Sciences. 2022;59(2):76-92.
7. Huget-Penner S, Feig DS. Maternal thyroid disease and its effects on the fetus and perinatal outcomes. Pediatric Diabetes. 2020;40(9):1077-84.
8. Kolobarić A, Delić L, Raguž MJ. Can the pathological conditions of the thyroid gland during pregnancy affect the course and outcome of pregnancy and the parameters of the newborn? Archives of Basic and Clinical Research. 2023;2(2):108-18.
9. Lopes-Pereira M, Roque S, Costa P, Quialheiro A, Santos NC, Goios A, et al. Impact of iodine supplementation during preconception, pregnancy and lactation on

maternal thyroid homeostasis and offspring psychomotor development: protocol of the IodineMinho prospective study. 2020;20(1):693.
10. Fetene DM, Betts KS, Scott JG, Alati R. Maternal prenatal thyroid function and trajectories of offspring emotional and behavioural problems: findings from the ALSPAC cohort. European Child & Adolescent Psychiatry. 2020;29(6):871-9.
11. Marty S, Beekhuijzen M, Charlton A, Hallmark N, Hannas BR, Jacobi S, et al. Towards a science-based testing strategy to identify maternal thyroid hormone imbalance and neurodevelopmental effects in the progeny–part II: how can key events of relevant adverse outcome pathways be addressed in toxicological assessments? 2021;51(4):328-58.
12. Zhou Y-L, Ren J-B, Ding R, Yu T-T, Fan J-X. Effects of maternal internal environment on early life growth and development. In Utero Pediatrics: Research & Practice. Springer; 2023. p. 49-78.
13. Liang C, Han Y, Ma L, Wu X, Huang K, Yan S, et al. Low levels of arsenic exposure during pregnancy and maternal and neonatal thyroid hormone parameters: The determinants for these associations. 2020;145:106114.
14. Vamja R, M Y, Patel M, Vala V, Ramachandran A, Surati B, et al. Impact of maternal thyroid dysfunction on fetal and maternal outcomes in pregnancy: a prospective cohort study. Clinical Diabetes and Endocrinology. 2024;10(1):50.
15. Derakhshan A, Peeters RP, Taylor PN, Bliddal S, Carty DM, Meems M, et al. Association of maternal thyroid function with birthweight: a systematic review and individual-participant data meta-analysis. The Lancet Diabetes & Endocrinology. 2020;8(6):501-10.
16. Li S, Wu Y, Zhang S-J, Li G, Xiang YT, Zhang W-Z, et al. Higher maternal thyroid resistance indices were associated with increased neonatal thyroid-stimulating hormone—analyses based on the Huizhou mother-infant cohort. 2022;13:937430.
17. Wang F, Zhang Y, Yuan Z, Li Y, Liu S, Zeng X, et al. The association between iron status and thyroid hormone levels during pregnancy. 2022;74:127047.
18. Ge GM, Leung MTY, Man KKC, Leung WC, Ip P, Li GHY, et al. Maternal thyroid dysfunction during pregnancy and the risk of adverse outcomes in the offspring: A systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism. 2020;105(12):3821-41.
19. Anifantaki F, Pervanidou P, Lambrinoudaki I, Panoulis K, Vlahos N, Eleftheriades M. Maternal prenatal stress, thyroid function and neurodevelopment of the offspring: A mini review of the literature. 2021;15.
20. Davies K, Camm E, Atkinson E, Lopez T, Forhead AJ, Murray A, et al. Development and thyroid hormone dependence of skeletal muscle mitochondrial function towards birth. 2020;598(12):2453-68.
21. Miranda RA, de Moura EG, Lisboa PC. Adverse perinatal conditions and the developmental origins of thyroid dysfunction, lessons from animal models. Endocrine. 2023;79(2):223-34.