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ASSOCIATION OF MATERNAL SUBCLINICAL HYPOTHYROIDISM AND LOW BIRTH WEIGHT AMONG PREGNANT WOMEN ADMITTED FOR DELIVERY AT A TERTIARY CARE HOSPITAL IN KARACHI

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ABSTRACT

Background: Maternal thyroid function is important for fetal growth and development, while low birth weight (LBW) is associated with adverse neonatal and later-life outcomes. The relationship between maternal subclinical hypothyroidism (SCH) and LBW remains inconsistent across studies.

Objective: To determine the frequency of SCH among pregnant women admitted for delivery and compare the frequency of LBW among women with and without SCH.

Methods: A descriptive cross-sectional study was conducted in the Department of Gynecology, Memon Medical Institute Hospital, Karachi, from 15 November 2022 to 30 August 2023. A total of 164 pregnant women aged 15–49 years, admitted for delivery and with gestational age >28 weeks, were enrolled through non-probability consecutive sampling. SCH was defined as TSH >5 IU/mL with normal T3 and T4. LBW was defined as birth weight <2.5 kg. Associations were assessed using chi-square/Fisher exact tests, with $p<0.05$ considered statistically significant.

Results: SCH was identified in 24/164 (14.6%) women, while LBW occurred in 43/164 (26.2%) neonates. LBW was observed in 15/24 (62.5%) women with SCH compared with 28/140 (20.0%) women without SCH (reported p=0.00; conventionally expressed as $p<0.001$). From the reported 2×2 table, the risk ratio for LBW was 3.13 (95% CI 1.99–4.92) and the odds ratio was 6.67 (95% CI 2.65–16.80).

Conclusion: SCH was relatively frequent in this hospital-based sample and was associated with a substantially higher frequency of LBW. Further prospective and adequately powered studies are needed to clarify the relationship and its clinical implications.

KEYWORDS: subclinical hypothyroidism; pregnancy; low birth weight; maternal thyroid dysfunction; fetal growth; Karachi.

What this study adds. In this tertiary-care hospital sample, maternal subclinical hypothyroidism was present in 14.6% of participants and was accompanied by a substantially higher observed frequency of low birth weight. The study provides locally relevant data from Karachi and highlights the need for larger prospective studies using trimester-specific thyroid reference ranges.

INTRODUCTION

Birth weight is an important indicator of fetal growth, development, nutrition and intrauterine exposures. Low birth weight is associated with neonatal morbidity and mortality and may also be linked to increased risk of chronic disease later in life.[1–4]

Thyroid disease is relatively common among women of reproductive age. Normal maternal thyroid function is important for fetal growth and neurocognitive development, and observational studies have suggested associations between maternal thyroid dysfunction and adverse pregnancy outcomes, including fetal growth restriction and small-for-gestational-age birth.[5,6]

During pregnancy, fetal thyroid hormone availability depends substantially on maternal thyroid hormone transfer, particularly during the first 18–20 weeks of gestation. Mild thyroid-function abnormalities such as SCH and hypothyroxinemia are more common than overt thyroid disease.[7] However, evidence regarding their association with LBW is inconsistent. Some studies have reported higher rates of LBW among women with SCH, whereas others have not demonstrated a significant difference.[7–11]

Local Pakistani data also show substantial variation in the reported prevalence of SCH during pregnancy. Studies cited in the dissertation reported prevalences of 12.1% in Karachi, 19.35% in another Pakistani cohort, and 1.6% in a multicenter study.[12–14] Such variation may reflect differences in population characteristics, diagnostic thresholds, timing of testing and study settings.

Given the limited and inconsistent local evidence, the present study was undertaken to determine the frequency of SCH among pregnant women admitted for delivery at a tertiary care hospital in Karachi and to compare the frequency of LBW between women with and without SCH.

MATERIALS AND METHODS

Study design and setting. This descriptive cross-sectional study was conducted in the Department of Gynecology, Memon Medical Institute Hospital (MMIH), Karachi, from 15 November 2022 to 30 August 2023. The dissertation states that 164 pregnant women were included and assessed for SCH and subsequently followed until delivery for assessment of birth weight.

Sample size and sampling. Sample size was calculated using the OpenEpi calculator based on a previously reported SCH frequency of 12.1%, a 5% margin of error and 95% confidence level, resulting in a sample of 164 participants. Non-probability consecutive sampling was used.

Eligibility. Women aged 15–49 years, admitted for delivery in the labor room, with gestational age >28 weeks were eligible, irrespective of parity, gravida or booking status. Women with multiple fetuses, previous bad obstetric history, autoimmune disease or recurrent miscarriage were excluded.

Data collection and laboratory assessment. After institutional ethical and CPSP approval and written informed consent, baseline information was recorded using a predesigned proforma. Variables included age, residence, family monthly income, height, weight, BMI, gestational age, diabetes, hypertension, smoking, family history of thyroid disease, booking status and mode of delivery. A 3-mL blood sample was obtained aseptically and sent to the hospital laboratory for thyroid assessment. Participants were followed until delivery and neonatal birth weight was recorded.

Definitions. SCH was defined in the dissertation as TSH >5 IU/mL with normal T3 (0.8–2.2 ng/mL) and T4 (50–120 ng/mL). LBW was defined as neonatal birth weight <2500 g at birth.

Statistical analysis. Data were analyzed using SPSS version 25. Quantitative variables were summarized as mean±standard deviation or median (IQR), as appropriate, and normality was assessed with the Shapiro–Wilk test. Categorical variables were presented as frequencies and percentages. The association between SCH and LBW was assessed using chi-square or Fisher exact test. Stratification was performed for age, residence, family income, BMI, gestational age, diabetes, hypertension, smoking, booking status, mode of delivery, parity, gravida and family history of thyroid disease. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 164 pregnant women were included. The mean maternal age was 28.19±7.07 years, mean BMI was 23.71±2.08 kg/m², and mean gestational age was 36.21±2.68 weeks. Mean maternal TSH was 3.44±1.57 IU/mL and mean neonatal birth weight was 2.83±0.42 kg. Rural residence was reported in 92 (56.1%) participants, diabetes in 33 (20.1%), hypertension in 24 (14.6%), smoking in 10 (6.1%), and a family history of thyroid disease in 33 (20.1%). Most women were booked (142, 86.6%), and 96 (58.5%) delivered vaginally. The complete baseline profile is summarized in Table 1.

Variable	Value
Sample size	164
Maternal age, years	28.19 ± 7.07
Monthly family income, thousand PKR	76.98 ± 29.05
Height, cm	155.90 ± 1.99
Weight, kg	57.58 ± 4.59
BMI, kg/m²	23.71 ± 2.08
Gestational age, weeks	36.21 ± 2.68
T3, ng/mL	1.51 ± 0.37
T4, ng/mL	86.53 ± 18.81
TSH, IU/mL	3.44 ± 1.57
Birth weight, kg	2.83 ± 0.42
Rural residence	92 (56.1%)
Diabetes	33 (20.1%)
Hypertension	24 (14.6%)
Smoking	10 (6.1%)
Family history of thyroid disease	33 (20.1%)
Booked	142 (86.6%)
Vaginal delivery	96 (58.5%)
Caesarean delivery	68 (41.5%)

Interpretation of Table 1. The study population represented women admitted for delivery at a tertiary-care hospital, with a mean gestational age close to term. More than half of participants were from rural areas, while approximately one-fifth had diabetes or a family history of thyroid disease. The distribution of BMI was relatively balanced between the predefined normal and high groups, and just over half of the pregnancies were

classified as pre-term according to the study definition. These characteristics are important when interpreting the primary association because maternal metabolic, obstetric and sociodemographic factors can influence fetal growth. The table therefore provides the clinical context for the subsequent comparison of birth weight by thyroid status.

Table 1. Baseline characteristics of the study population. Values are presented as mean±SD or frequency (%), according to the dissertation.

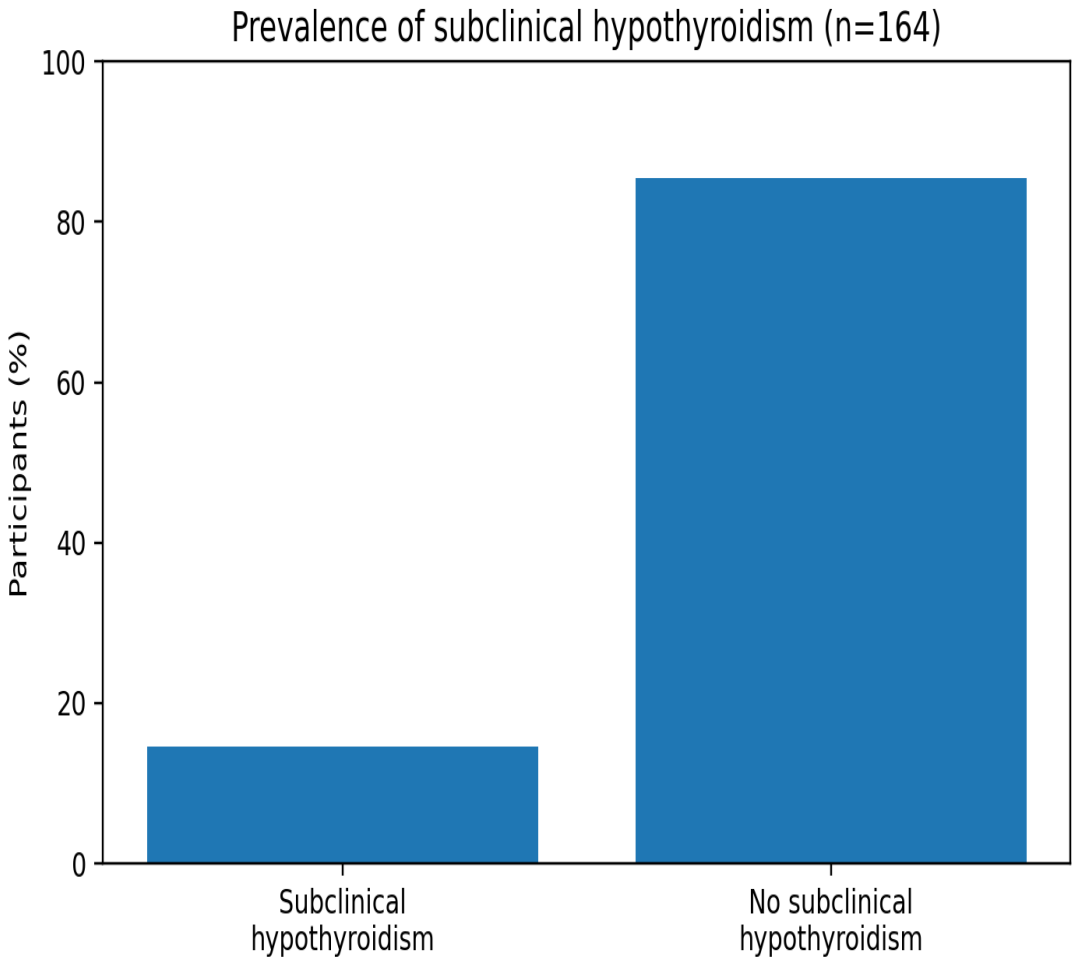

Figure 1. Frequency of subclinical hypothyroidism in the study population (n=164).

Interpretation of Figure 1. SCH was identified in 24 of 164 participants (14.6%), while 140 (85.4%) did not meet the dissertation's biochemical definition of SCH. The figure visually emphasizes that SCH affected a minority of the cohort, but the prevalence was sufficiently high to permit comparison of LBW outcomes between thyroid-status groups.

Outcome	**SCH, n (%)**	**No SCH, n (%)**	**Total, n (%)**
Low birth weight (<2.5 kg)	15 (62.5)	28 (20.0)	43 (26.2)
Birth weight ≥2.5 kg	9 (37.5)	112 (80.0)	121 (73.8)
Total	24 (100)	140 (100)	164 (100)

Interpretation of Table 2. The table demonstrates a marked difference in the frequency of LBW according to maternal thyroid status. Nearly two-thirds of women with SCH delivered a neonate weighing less than 2.5 kg, whereas one-fifth of women without SCH had an LBW neonate. The observed difference is statistically significant and clinically notable. Because the study was observational and single-center, however, the result should be interpreted as an association rather than proof that SCH caused reduced birth weight. The derived risk ratio and odds ratio quantify the strength of the association but do not substitute for adjusted prospective analyses.

Table 2. Association between maternal subclinical hypothyroidism and low birth weight. The dissertation reports p=0.00; this is expressed as p<0.001 in the manuscript.

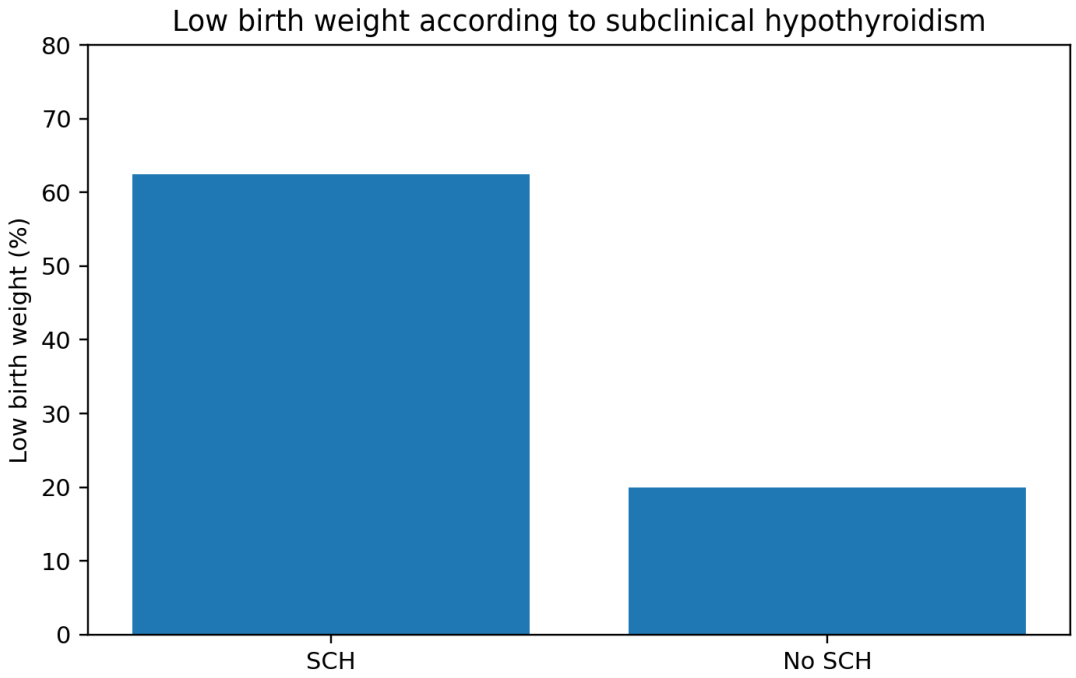

Figure 2. Frequency of low birth weight according to maternal subclinical hypothyroidism status.

Interpretation of Figure 2. The figure shows a substantially greater proportion of LBW among women with SCH (62.5%) than among women without SCH (20.0%). The visual separation between the groups is consistent with the statistically significant association reported in Table 2. This figure should be interpreted together with the underlying counts because the SCH group contained only 24 participants.

The principal association is presented in Table 2. LBW occurred in 15 of 24 women with SCH (62.5%), compared with 28 of 140 women without SCH (20.0%). Thus, the absolute difference in observed LBW frequency between the two groups was 42.5 percentage points. The dissertation reported p=0.00; for journal presentation this should be reported as p<0.001 rather than p=0.00. Using the reported 2×2 counts, the calculated risk ratio was 3.13 (95% CI 1.99–4.92) and the calculated odds ratio was 6.67 (95% CI 2.65–16.80). These effect estimates were derived from the dissertation counts and were not originally reported in the dissertation.

Exploratory stratified analyses were also performed for age, gestational age, BMI, family income, mode of delivery, booking status, family history of thyroid disease, diabetes, hypertension, smoking, parity, gravida and residence. The dissertation reported statistically significant associations in several strata, whereas some strata were non-significant. Because the analysis relied on stratification rather than a multivariable regression model and several subgroups were small, these findings should be regarded as exploratory and should not be interpreted as independent adjusted effects.

DISCUSSION

The present study found SCH in 14.6% of pregnant women admitted for delivery. This frequency falls within the broad range reported in the Pakistani studies cited in the dissertation: 12.1% in a Karachi tertiary-care study, 19.35% in a study by Perveen et al., and 1.6% in a multicenter Pakistani study.[12–14] Differences between studies may be related to population characteristics, gestational age at testing, laboratory reference ranges and diagnostic definitions.

An important finding was the markedly higher frequency of LBW among women with SCH. LBW occurred in 62.5% of women with SCH compared with 20.0% among women without SCH, with a highly significant association in the dissertation (p=0.00; expressed here as p<0.001). The magnitude of the observed association was substantial, with a derived risk ratio of 3.13 and odds ratio of 6.67 based on the reported contingency table.

These findings are directionally consistent with evidence suggesting that maternal thyroid dysfunction may influence fetal growth. The systematic review and meta-analysis cited in the dissertation reported an association between subclinical maternal thyroid dysfunction/autoimmunity and intrauterine growth restriction.[5] Monen et al. reported that maternal thyrotropin was independently related to small-for-gestational-age neonates at term.[7] Chen et al. reported a higher frequency of LBW in women with SCH than in euthyroid women (5.97% vs 2.11%).[8]

Conversely, the relationship is not uniformly demonstrated. Kumru et al. found no clear adverse effect of thyroid dysfunction and autoimmunity on pregnancy outcomes in a low-risk population, while Maraka et al.'s systematic review emphasized heterogeneity in the evidence regarding SCH in pregnancy.[10,11] Wang et al., specifically cited in the dissertation, reported no meaningful difference in LBW between women with SCH and

euthyroidism (2.38% vs 2.77%).[15] Thus, the strong association observed in the present study should be interpreted in the context of its single-center design and relatively small sample.

Biologically, maternal thyroid hormones contribute to fetal development, particularly before the fetal thyroid becomes fully functional.[6] The association between SCH and impaired fetal growth may therefore reflect altered maternal-fetal thyroid hormone availability or pathways involving placental function and fetal growth. However, the present study was observational and did not establish causality.

The study has several strengths. It used a predefined sample-size calculation, consecutive recruitment, laboratory assessment of thyroid function, direct measurement of neonatal birth weight and assessment of multiple clinical and sociodemographic variables. These features support the internal consistency of the primary comparison. Nevertheless, several limitations must be considered. The study was single-center and hospital-based, used non-probability sampling, and included a relatively small number of women with SCH. The cross-sectional design limits causal inference. The dissertation did not report thyroid peroxidase antibody status, treatment status, or trimester-specific thyroid reference ranges, and no multivariable regression was performed. Residual confounding by maternal, placental or fetal factors therefore cannot be excluded.

Despite these limitations, the findings provide locally relevant evidence that maternal SCH may be associated with increased LBW frequency. Prospective multicenter studies with larger samples, trimester-specific thyroid reference ranges, antibody assessment and multivariable adjustment are needed to determine whether SCH independently predicts LBW and whether treatment modifies this risk.

CONCLUSION

Subclinical hypothyroidism was identified in 14.6% of pregnant women in this tertiary-care hospital sample and was associated with a substantially higher frequency of low birth weight. The findings suggest that maternal thyroid dysfunction may be an important marker of adverse fetal growth in this setting. However, because of the observational single-center design and absence of multivariable adjustment, the findings should not be interpreted as establishing causality or as sufficient evidence for universal screening. Larger prospective multicenter studies using trimester-specific biochemical criteria and appropriate adjustment for maternal and obstetric confounders are warranted.

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