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Original Article

Urine Iodine Concentration Trends During Pregnancy in The North-Central Region of Nigeria

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Abstract

Background: Pregnancy is a hyperdynamic state that significantly strains the mother's iodine stores due to the demands of the foetus. Iodine deficiency poses significant risks during pregnancy, affecting maternal and foetal health. Thyroid hormones, which are vital for brain development, rely on iodine, and deficiencies can lead to conditions like hypothyroidism and goitre. Monitoring urinary iodine concentration (UIC) is crucial for assessing iodine status, especially in pregnancy, where iodine plays a pivotal role in neurodevelopment. The aim of this study is to determine the urine iodine concentration changes and its adequacy in pregnancy.

Methodology: This descriptive cross-sectional study was conducted over a period of nine (9) months (June 2019–February 2020). The study comprised a cohort of 250 pregnant women who were attending their antenatal clinic visits. These participants were selected randomly using a table of random numbers. Spot Urine samples were analysed using the Sandell-Kolthoff technique to measure UIC. The data were analysed using Statistical Package for Social Sciences (SPSS) version 21 (IBM, Chicago, IL, USA).

Results: The mean ± SD urine iodine concentration in the 1st, 2nd , 3rd was (192.02 ± 40.71 µg/L; 185.49 ± 32.94 µg/L I;186.54 ± 35.35 µg/L; p=0.135) respectively Urine iodine Concentration across the 3 trimesters <150 µg/L(<0.01); 150-250 µg/L(<0.01); >250 µg/L(<0.01). The participants' chronological ages ranged from 17 to 44 years. The mean ± SD, 1st, 2nd , 3rd (26.40 ± 4.70; 27.00 ± 5.10; 28.20 ± 5.20; p=0.211) years respectively. The Pearson (-0.439; p <0.05) of urine iodine concentration and thyroglobulin.

Conclusion: This study highlights the continued need for public health initiatives that promote iodine awareness and the use of iodized salt among women of reproductive age. Furthermore, the inclusion of thyroglobulin measurement alongside urinary iodine concentration may provide a more comprehensive assessment of thyroid function during pregnancy.

Keywords: Urine iodine concentration, pregnancy, thyroid function test, Thyroid status, Thyroid-stimulating hormone, free thyroxine

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Introduction

Iodine is an essential micronutrient crucial for various physiological functions, particularly in pregnancy. It plays a vital role in the synthesis of thyroid hormones, which are essential for brain development and overall growth, especially during foetal development [1]. Iodine deficiency can have severe implications, leading to conditions like hypothyroidism, goitre, and even intellectual disabilities [2]. During pregnancy, iodine deficiency can significantly impact both maternal and infant outcomes, affecting brain and nervous system development [3]. Adequate iodine intake is crucial during pregnancy to support maternal adaptation and provide the foetus with the necessary thyroid hormones and iodine [4]. The significance of iodine in pregnancy is underscored by its role in foetal neurogenesis and the development of the brain and nervous system [5]. Studies emphasise the importance of ensuring sufficient dietary iodine intake and monitoring urinary iodine levels throughout pregnancy to support optimal neurodevelopment [6]. Maternal iodine status has been linked to neurodevelopmental outcomes in children, highlighting the importance of maintaining adequate iodine levels during pregnancy [7]. Moreover, iodine deficiency during pregnancy is common in various regions, including Europe and the USA, necessitating interventions to address this issue [7]. Urinary iodine concentration (UIC) serves as a reliable indicator of iodine intake, with more than 90% of iodine excreted in urine over a 24-hour period [8]. Monitoring UIC is crucial in assessing iodine status and guiding interventions to prevent deficiencies, especially in pregnant women [9]. Additionally, iodine's role in energy-yielding metabolism, gene expression, embryogenesis, growth, and cognitive function underscores its significance in various physiological processes [10]. Iodine is a critical micronutrient essential for thyroid hormone synthesis and overall health, particularly during pregnancy. Serum thyroglobulin (Tg) concentration is considered to reflect thyroid volume in both iodine-deficient and iodine-excessive settings [11]. In iodine deficiency, high Tg concentration results from TSH stimulation of the thyroid, leading to thyroid enlargement [12]. Adequate iodine intake is vital to prevent deficiencies that can have far-reaching implications for maternal and child health. Monitoring urinary iodine concentration and ensuring sufficient iodine intake are key strategies to support optimal outcomes during pregnancy. The aim of this study is to determine the urine iodine concentration changes and its adequacy in pregnancy.

Methods

Ethical consideration

Prior to their enrolment in the study, each potential participant was required to provide informed and written consent. Strict confidentiality was upheld throughout the duration of this study and disclosure of the procedures to be undertaken by the participants. This study adhered to ethical standards in accordance with the Declaration of Helsinki and was ethically approved as a component of a broader study by the Health Research Ethics Committee of Benue State University Teaching Hospital (registration code: **BSUTH/CMAC/HREC/101/V.I/52**).

Study Design and Setting

This study was conducted at multiple hospitals and involved a descriptive cross-sectional analysis of pregnant women. The study required the examination of data gathered from the participants throughout the course of the research. The study was conducted over a period of approximately nine (9) months, from June

2019 to February 2020. The process of enlisting individuals from the antenatal clinic and collecting samples for serum thyroid function tests, urine iodine, laboratory analysis, and assessment of thyroid dysfunction in pregnancy were all carried out during the specified 9 months. The study sample was selected from Makurdi, a city located in north-central Nigeria. The participants were selected from various healthcare facilities, including Benue State University Teaching Hospital (B.S.U.T.H.), Federal Medical Centre (F. M. C) Makurdi, Family Support Programme Clinic Makurdi, First Fertility Hospital Makurdi, and Foundation Hospital Makurdi. The laboratory of the Chemical Pathology Department of B. S. U. T. H, Makurdi conducted data and sample analysis.

Study Population

The study consisted of 250 pregnant women in Makurdi who were attending their regular antenatal clinic visits. The subjects were chosen using a basic random sampling procedure, employing a table of random numbers. The flow chart (**Figure 1**) illustrates the systematic process of participant selection, including those who were excluded for not meeting the eligibility criteria and those ultimately included in the study. The participants were provided with information about the study, obtained their signed consent, and completed questionnaires.

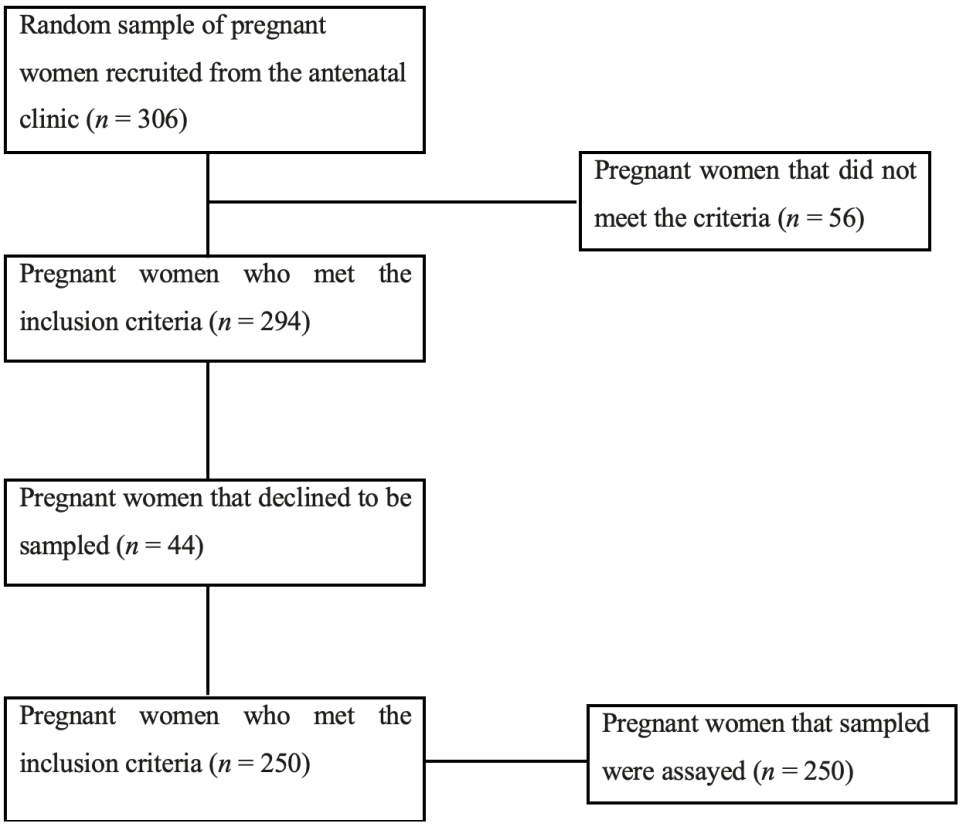

Fig. 1 Flowchart of the recruitment of pregnant women into the study.

Inclusion Criteria

- Participants were women in the first, second, and third trimesters of their pregnancy attending routine antenatal clinic visits.
- No history of thyroid dysfunction

Exclusion Criteria

- Participants who had thyroid disease or were seriously or chronically
- Participants taking specific medications such as lithium, amiodarone, anti-seizure drugs, interferon alpha (IFN-α), hormone replacement therapy (HRT), i.e oestrogen, and rifampicin;

Sample Collection and Analysis

A spot urine sample was collected in a wide-mouthed sterile urine bottle were promptly tested within an hour for urine iodine concentration using the Sandell-Kolthof technique. Non-fasting samples were obtained by collecting venous blood. A volume of 5 ml of blood was drawn using a syringe and needle in a sterile manner and placed into a simple Vacutainer tube. The samples were centrifuged using a tabletop centrifuge (StatSpin Express) at a speed of 3000 revolutions per minute for a duration of 10 minutes. The resulting serum samples were then transferred into cryovials and stored at a temperature of -20°C. The serum samples were analysed using the ultrasensitive enzyme-linked immunosorbent assay (ELISA) technique provided by Monobind Inc.® (AccuBind® ELISA kits, California, USA) for the purpose of assessing thyroid function. The analysis was conducted using an automated system equipped with a microstrip reader (STAT-FAX 303, USA).

Thyroglobulin assay

Samples collected for the Tg assay were stored at -20°C before analysis. Serum Tg was measured by a quantitative enzyme-linked immunoassay (ELISA) technique using a kit from the Tg AccuBind® ELISA test system supplied by Monobind Inc. It had an analytical sensitivity of 0.4 ng/ml. The performance characteristics of thyroglobulin were determined. The reference Interval was 3.5 – 56ng/ml, with the coefficient of variance of 4.2% within assay and 5.7% between assays, the interference included antibodies against Tg.

Urine Iodine Assay

Spot urine samples were collected early in the morning, voided into a sterile urine container (5–10 ml), and stored at -4 °C until analysis(these analyses were done immediately, not beyond a duration of 3 hours; therefore, the temperature used for storage). Urine iodine was measured by a quantitative Sandell-Kolthoff technique.

Sandell-Kolthoff technique

Urine is digested with ammonium persulfate. Iodide is the catalyst in the reduction of ceric ammonium sulfate (yellow) to cerous form (colourless) and is detected by the rate of colour disappearance (Sandell-Kolthoff reaction) with decreased absorbance measured at 420nm. The reference value for urinary iodine concentration (UIC) cut-off value for adequacy was 150-249 µg/L [13], and on the other hand, UIC values <150 µg/L suggested urine iodine concentration inadequacy. The Performance characteristics of this Sandell Kolthoff technique determined a reference interval of urine iodine concentration at 150 – 249µg/l with a coefficient of variance at 4.2% within assay and 6.2% between assays. The interference included L-Ascorbic acid.

Data Analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21(IBM, Chicago, IL, USA). The Shapiro-Wilk test was used to assess the normality of data distribution. The data was analysed using the student's t-test and one-way analysis of variance (ANOVA) statistical tools. Results were presented as mean ± standard deviation (SD), and categorical variables were presented as numbers or percentages. Significance was defined as $p < 0.05$, while $p < 0.01$ indicated a high level of statistical significance.

Results

Characteristics of the study population

A total of 250 pregnant participants were enrolled in the study and categorized by trimester into first, second, and third groups. Specifically, there were 51 participants in the first trimester, 114 in the second, and 85 in the third trimester. The mean ± SD gestational ages for the first, second, and third trimesters were 9.0 ± 2.70, 20.0 ± 3.70, and 33.3 ± 4.10 weeks, respectively. The gestational ages across the trimester were statistically significant ($p<0.01$).

The participants' chronological ages ranged from 17 to 44 years. The mean ± SD ages were 26.40 ± 4.70 years for the first trimester, 27.00 ± 5.10 years for the second trimester, and 28.20 ± 5.20 years for the third trimester, as seen in Table 2. There was no statistical difference ($p=0.211$) in the chronological age of participants in this cohort.

The adequacy of urine iodine for each trimester was illustrated in **Table 1** for different levels at <150 µg/L, 150-250 µg/L and >250 µg/L. To ensure adequate iodine intake in pregnant women, the World Health Organization (WHO) recommends monitoring their iodine status by collecting spot-urine samples and comparing the median urinary iodine concentration (UIC) to the cut-off value for adequacy, which is typically set between 150-249 µg/L [11].

Table 1 Comparison of Maternal Iodine Status and Thyroid Function Parameters Across Pregnancy Trimesters

Variables	First trimester *(n=51)*	Second trimester *(n=114)*	Third trimester *(n=85)*	*p*
Age (years)				
Mean ± SD	26.40 ± 4.70	27.00 ± 5.10	28.20 ± 5.20	0.211
Gestational age (weeks)				
Mean ± SD	9.00 ± 2.70	20.00 ± 3.70	33.30 ± 4.10	<0.01
Urine iodine Concentration (µg/l)				
Mean ± SD	192.02 ± 40.71	185.49 ± 32.94	186.54 ± 35.35	0.135
Urine iodine Concentration (µg/l) n(%)				
<150	3(1.2)	45(18)	3(1.2)	<0.01
150-250	8(3.2)	102(40.8)	4(1.6)	<0.01
>250	10(4.0)	73(29.2)	2(0.8)	<0.01
Thyroglobulin n(%)				
Normal	45(18%)	103(41.2%)	79(31.6%)	<0.01
Elevated	3(1.2%)	8(3.2%)	5(2.0%)	<0.01
Decreased	3(1.2%)	3(1.2%)	1(0.4%)	<0.01
Thyroglobulin (ng/ml)				
Mean ± SD	21.35 ± 20.15	22.29 ± 17.50	25.54 ± 24.33	0.44
Thyroid status n(%)				

Subclinical hypothyroidism	2(0.8)	4(1.6)	6(2.4)	
Overt hypothyroidism	-	4(1.6)	8(3.2)	<0.05
Subclinical hyperthyroidism	-	4(1.6)	-	0.00
Overt hyperthyroidism	1(0.4)	-	-	0.00
Euthyroidsim	48(19.2)	102(40.2)	71(28.4)	<0.01

The mean urinary iodine concentration (UIC) values across the three trimesters of pregnancy in a cohort of 250 participants. The mean ± SD UIC values were 192.02 ± 40.71 µg/L in the first trimester, 185.49 ± 32.94 µg/L in the second trimester, and 186.54 ± 35.35 µg/L in the third trimester, as seen in **Table 1**. Although there is a slight decrease in mean UIC from the first to the second trimester, and a minimal increase in the third trimester, the overall differences in UIC across the three trimesters were not statistically significant (P = 0.135). This suggests that urinary iodine concentration remained relatively stable throughout pregnancy in this population, with values consistently within the WHO-recommended adequate range for pregnant women (150–249 µg/L). The thyroglobulin level, Mean ± SD in the first, second and third trimester (21.35 ± 20.15; 22.29 ± 17.50; 25.54 ± 24.33; P=0.44), respectively depicted a gradual increase as pregnancy progressed due to the improvement of thyroid gland function as the action of hCG wanes.

Table 2: Proportion of Thyroid Dysfunction Stratified by Thyroglobulin Status During Pregnancy

Thyroid status	Elevated TG(%)	Decreased TG(%)	Total(%)
Hypothyroid	8(3.2)	2(0.8)	10(4)
Hyperthyroid	-	-	-
Euthyroid + abnormal TG	7(2.8)	6(2.4)	13(5.2)
True euthyroid	-	-	227(90.8)

TG=Thyroglobulin

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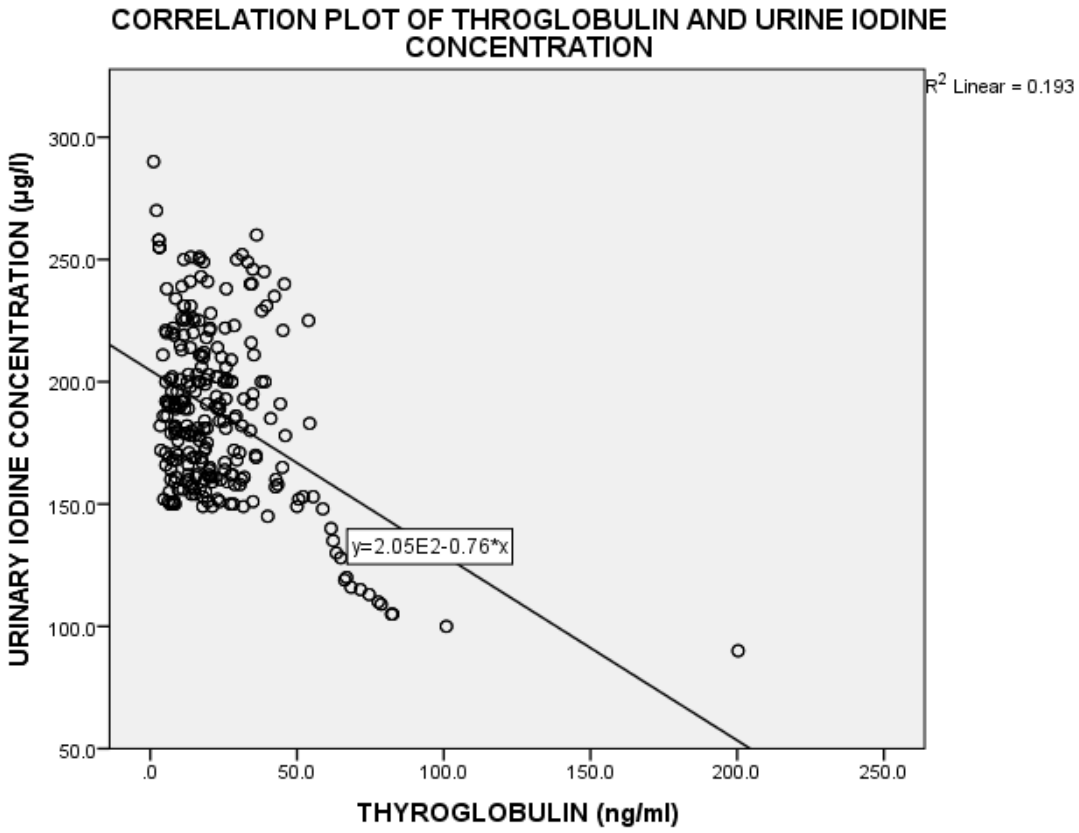
The proportion of participants with different thyroid statuses was assessed alongside their corresponding thyroglobulin concentrations, categorized as either elevated or decreased (Table 2). Notably, a greater number of participants who were clinically euthyroid were identified as having abnormal thyroid function when thyroglobulin levels were considered, findings that would have been overlooked using standard thyroid function tests alone. Furthermore, combining thyroglobulin measurement with urinary iodine concentration appears to be a justified and valuable approach during pregnancy.



The Pearson correlation between urine iodine concentration and thyroglobulin was negative, with most participants falling between 0-100ng/ml in thyroglobulin levels and urine iodine concentration falling between 150-250 µg/L. Pearson correlation (-0.439; $p < 0.01$) with a coefficient of correlation ($r^2 = 0.143$)(Figure 2). The UIC vs Thyroglobulin plot in Figure 2 was utilised in our previous study that analysed thyroglobulin as an evolving Biomarker of iodine reserve in thyroid dysfunction assessment in pregnancy

Discussion

The thyroid gland is important in pregnancy because the thyroid hormones are important in the development of the foetus, and its deficiency has adverse effects on the mother and the foetus, such as low IQ and postpartum thyroiditis [15]. Pregnancy, being a hyperdynamic state, can alter the function of thyroid hormones.

This study assessed the concentration of urine iodine and observed that UIC < 150 µg/L in the first, second, and third trimesters was 1.2% vs. 3.2% vs. 4.0%, respectively. This showed that there was an increasing number of participants with less suboptimal UIC as pregnancy progressed. On the other hand, there were far more participants who were adequately supplemented with iodine that fell within the normal levels for UIC at 150-250 µg/L. The first, second, and third trimesters were observed to be 18.0% vs. 40.8% vs. 29.2% respectively. Notably, more participants in the second trimester were sufficiently supplemented with iodine, which was reflected in their UIC levels falling within the normal range. A third group was participants who had a UIC of >250 µg/L: 1.2% vs 1.6% vs 0.8% in the first, second, and third trimesters, respectively. 88% of the participants were within the normal UIC levels of 150-250 µg/L compared to 8.4% (UIC <150 µg/L) and 3.6% (>250 µg/L). Therefore, approximately 92% were adequately supplemented with dietary iodine that corresponded to the UIC's adequate and very adequate ranges. This is in keeping with the implementation of the universal salt iodization scheme in Nigeria, which has made it a sufficiently iodine country, as expected [12] [16]. Notably, there was no statistical significance (p=0.135) in the mean values of UIC compared across all trimesters.

There is a universal risk associated with iodine deficiency during pregnancy. However, there is a crucial need to assess the iodine status of pregnant women in Nigeria, as there is a decline in iodine supplementation in some rural communities with little or no health facilities or access to healthcare in pregnancy. Studies in regions like Ghana and Nepal have highlighted the prevalence of iodine deficiency among pregnant women, emphasizing the importance of monitoring UIC to identify deficiencies [17] and [18]. Additionally, research in Poland revealed that a significant proportion of pregnant women had insufficient iodine intake, as indicated by low median ioduria levels [19]. Furthermore, a study in Iran assessed pregnant women's urinary iodine excretion in areas with adequate iodine intake, emphasizing the importance of evaluating iodine status even in regions considered to have sufficient iodine levels [20]. The findings of this study underscore the need for comprehensive monitoring of iodine status in pregnant women in Nigeria to prevent adverse outcomes associated with iodine deficiency during pregnancy. Additionally, the important role of thyroglobulin in ascertaining the levels of urine iodine in participants attending routine ANC.

Monitoring UIC levels and implementing interventions to address iodine deficiency are essential to ensuring optimal maternal and foetal health outcomes in Nigeria. Public health strategies focusing on iodine supplementation and iodine-rich diets may be necessary to address potential deficiencies and improve the iodine status of pregnant women in the region. There should be events and campaigns that sensitize women of reproductive age to supplement their diets with diets rich in iodine or use iodized salt.

Conclusion

This study observed the trends of urine iodine in pregnancy, and this population was generally well-supplemented with iodine, as reflected in their optimal urine iodine concentration. However, there was still a percentage of pregnant women below the UIC reference range. The importance of public health programs to educate women on the importance of iodine and using iodized salt during the reproductive age is crucial and cannot be overlooked. Thyroglobulin is also a marker that is important in conjunction with UIC to determine pregnant individuals with abnormal thyroid function, even in euthyroid states.

Limitation of the Study

A 24-hour urine sample for determining the iodine-to-creatinine ratio would provide a relatively accurate assessment of urinary iodine concentration. However, the main challenge was the laborious collection process and the need for proper urine preservation. Although socioeconomic background data were initially planned for inclusion, they were omitted owing to incomplete records resulting from logistical handling and storage limitations. Some of the participants took iodine-containing supplements, and prenatal vitamins were not; state this as a key limitation. However, the inclusion of thyroglobulin and urine iodine concentration ascertained the level of iodine intake by the participants.

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