Urinary Iodine Level Assessment and its Relation to Thyroid Function during Pregnancy

Thesis

Submitted for Partial Fulfilment of Master Degree
in **Internal Medicine**

By

Salma Said Hassan Tayeh
M.B.B.CH, Ain Shams University

Under Supervision of

Prof. Dr. Magda Shoukry Mohamed
Professor of Internal Medicine, Diabetes & Endocrinology,
Faculty of Medicine, Ain Shams University

Asst. Prof. Dr. Merhan Samy Nasr
Assistant Professor of Internal Medicine, Diabetes &
Endocrinology, Faculty of Medicine, Ain Shams University

Dr. Salah Hussien El-Halawany
Lecturer of Internal Medicine, Diabetes & Endocrinology,
Faculty of Medicine, Ain Shams University

Dr. Ahmed Mohamed Abbas
Lecturer of Gynecology and Obstetrics
Faculty of Medicine, Ain Shams University

Faculty of Medicine, Ain Shams University
2020

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to **Allah** *the Most Beneficent and Merciful.*

No words can describe my appreciation for Prof. Dr. Magda Shoukry Mohamed, *Professor of Internal medicine, Diabetes & Endocrinology, Faculty of Medicine, Ain Shams University, not only for his continuous encouragement and tremendous support, but also for believing in me and pushing me forward from my first steps in neurology and for being a role model in helping and teaching the younger.*

I am profoundly grateful to Asst. Prof. Dr. Merhan Samy Nasr*, Assistant Professor of Internal medicine, Diabetes & Endocrinology, Faculty of Medicine, for the enduring wisdom that this work retains from his invaluable years of expertise, for his determination to set this work straight from the beginning, and his relentless mentoring.*

I wish to express my genuine respect and gratefulness to Dr. Salah Hussien El-Halawany *for his enormous help, his constructive criticism, meticulous revision and guidance, that enabled me to accomplish this work*

My most sincere appreciation goes to Dr. Ahmed Mohamed Abbas*, Lecturer of Gynecology and Obstetrics, Faculty of Medicine, Ain Shams University, for his generous help and valuable recommendations, his sincere effort and tolerance were inspiring.*

I owe much debt and admiration for Dr. Mona Ali Abdel Wahed*, Lecturer of Radio-Diagnosis, Faculty of Medicine, Ain Shams University, for her everlasting support, continuous encouragement, for her dedication and genuine help, for being there every single step and his inspiring passion for this work.*

I am deeply thankful to Dr.Hoda Ezz El_Arab Abdel Wahab*, Fellow of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her great help, active participation.*

Salma Said Hassan Tayeh

List of Contents

List of Abbreviations

Abb.	Full term
AIT	*Autoimmune thyroiditis*
ANC	*Antenatal Clinic*
ART	*Assisted reproduction technologies*
ATA	*American Thyroid Association*
ATD	*Autoimmune thyroid disease*
CBM	*Carbimazole*
CNS	*Central nervous system*
FT_4	*Tetra iodothyronine*
hCG	*Human chorionic gonadotropin*
HG	*Hyperemesis gravidarum*
I	*Iodine*
ICCIDD	*International council for control of iodine deficiency disorders*
ID	*Iodine deficiency*
IDD	*Iodine deficiency disorders*
IH	*Isolated hypothyroxinemia*
IMR	*Infant Mortality Rate*
IOM	*Institutes of Medicine*
IQ	*Intelligence quotient*
IVF	*In vitro vertilization*
LT4	*Levothyroxine*
MID	*Mild iodine difficiency*
MMI	*Methimazole*
NTD	*Non-thyroidal diseases*
OH	*Overt hypothyroidism*
PTU	*Propylthiouracil*
RDA	*Recommended dietary allowance*
RIC	*Renal iodine clearance*

List of Abbreviations cont...

Abb.	Full term
RNI	*Recommended nutrient intake*
RR	*Relative risk ratio*
SH	*Subclinical hypothyroidism*
T3	*Triiodothyronine*
T_3	*Triiodothyronine*
TBG	*Thyroxine binding globulin*
TG	*Thyroglobulin*
Tg-Ab	*Thyroglobulin antibody*
TH	*Thyroid hormone*
THHG	*Transient Hyperthyroidism of Hyperemesis Gravidarum"*
TPOAb	*Thyroperoxidase antibody*
TRAb	*Thyroid Receptor Antibodies*
TSab	*Thyroid-stimulating antibody*
TSH	*Thyroid-stimulating hormone*
TV	*Thyroid volume*
UI	*Urinary iodine*
UIC	*Urinary iodine concentration*
UIE	*Urinary iodine excretion*
UNICEF	*United nations international children's emergency fund*
US	*United states*
USA	*United states of america*
USI	*Universal salt iodisation*
WHO	*World health organization*

List of Tables

List of Figures

ABSTRACT

Background: The global effort to prevent iodine deficiency disorders through iodine supplementation, such as universal salt iodization, has achieved impressive progress during the last few decades. However, iodine excess, due to extensive environmental iodine exposure in addition to poor monitoring, is currently a more frequent occurrence than iodine deficiency. Iodine excess is a precipitating environmental factor in the development of autoimmune thyroid disease.

Objective: To evaluate the urinary iodine level as a marker of iodine status in pregnant women in 3rd trimester and assess its relation to thyroid functions.

Methods: This Cross Sectional Study was conducted on 100 subjects with their ages ranging from 18-35 years old , pregnant females , at the third trimester , selected from Obstetric Out- patient Clinic of Ain shams University Hospitals . Samples were collected from participants in cairo , during the Spring and Summer from March to Novomeber.

Results: In our study, there was a significant negative correlation between Urinary Iodine level and TSH as Iodine difficient group has the Highest TSH, and the Highest Thyroid Volume, as there was a significant negative correlation between Urinary Iodine level and Thyroid Voulme.

Conclusion: TSH level and Thyroid Volume were significantly higher in Iodine difficient group than Excess iodine group, And FT4 level was lower in Iodine difficient group than excess iodine group.

Keywords: Urinary Iodine Level, Thyroid Function

INTRODUCTION

During pregnancy, profound changes in thyroid physiology occur, resulting in different thyroid-stimulating hormone (TSH) and free thyroxine (FT_4) levels compared to the non pregnant state, It has long been known that iodine is an essential component of Thyroid Hormone that is subject to physiologic changes during pregnancy, including an increased turnover and renal excretion, necessitating increased intake during pregnancy ***(Medici et al., 2015).***

The vast physiological changes in maternal hormones and their binding proteins complicate the assessment of normal levels of most hormones and the interpretation of the test's result during gestation, Under the influence of placental human chorionic gonadotropin (hCG), the levels of thyrotropin (thyroid stimulating hormone [TSH]) is decreased throughout pregnancy ***(Mankar et al., 2016).***

Also, the placenta of humans secrete huge amount of a hormone Called Hcg. TSH and Hcg are similar enough that hCG can bind and transduce signaling from the TSH receptor on the thyroid epithelial cells, When hCG levels are highest, a significant fraction of the thyroid stimulating activity is from hCG. The thyroid stimulating activity of hCG actually results in reduction in the levels of TSH ***(Mankar et al., 2016).***

This suggests that the upper limit for TSH should be 2.5 mIU/L in the first trimester, and 3.0 mIU/L in the second and third trimesters. Furthermore, the lower physiological limit could be 0.1 mIU/L in the first trimester, 0.2 mIU/L in the second, and 0.3 mIU/L in the third ***(Haddow et al., 2004).***

Failure to apply these trimester specific reference ranges almost certainly results in an underestimation of hypothyroidism and overestimation of hyperthyroidism ***(Stricker et al., 2007).***

Thyroid diseases in pregnancy include Overt hypothyroidism (OH) is defined as a low FT4 with high TSH levels. While worldwide iodine deficiency is the main cause of OH, in areas where iodine intake is sufficient, the most frequent cause is autoimmune thyroiditis ***(Casey et al., 2005).***

Other causes are prior thyroidectomy, radioiodine therapy, the use of drugs such as amiodarone, anti-thyroid drugs and lithium, congenital hypothyroidism, pituitary or hypothalamic disease, and immunoglobulin binding to the TSH receptor (blocking its activity). The frequency of OH is estimated to be between 0.2 and 1.0% ***(Casey et al., 2005).***

Subclinical hypothyroidism (SH) is defined as a normal FT4 with high TSH levels. SH is by far the most frequent thyroid dysfunction occurring in pregnancy. The prevalence of SH varies from one study to another, depending on the

definition of SH, ethnicity, iodine intake, and study design. In most cases, prevalence is between 1.5 and 4.0% ***(Casey et al., 2005).***

The condition of isolated hypothyroxinemia in pregnancy is defined as the presence of an FT4 value below the 2.5th percentile with a TSH level within the normal range ***(Morreale de Escobar et al., 2000).***

The leading cause of IH is iodine deficiency. Profound reduction of thyroid hormone during early fetal life results in irreversible brain damage ***(Morreale de Escobar et al., 2000).***

Iodine, an essential micronutrient, is found in every tissue in the body. The only known function of iodine is its role in the production of thyroid hormones, thyroxine, T_4, and triiodothyronine T_3, although it may also act as an anti-oxidant, anti-inflammatory, apoptotic, antiviral, and antibacterial agent ***(Panth et al., 2019).***

Thyroid hormones play essential roles in regulating energy homeostasis by modifying basal metabolic rate and thermogenesis ***(Panth et al., 2019).***

The detrimental effect of iodine deficiency and maternal hypothyroxinemia on fetal brain development is most probably related to reduced maternal thyroxine transfer to the fetus before the onset of fetal thyroid function ***(Morreale de Escobar et al., 2000).***

During the first trimester the fetus is completely dependent on maternal T4, and though T4 in the fetal compartment is about 100 times lower than in the maternal serum ***(Morreale de Escobar et al., 2000).***

Hyperthyroidism is defined as an excessive production of thyroid hormones by the thyroid gland. Causes of hyperthyroidism may be mainly divided into (1) immune and (2) non-immune thyroid disease ***(Glinoer and Spencer, 2010).***

Graves' disease is an autoimmune disease and may result in maternal and fetal complications if not properly controlled ***(Glinoer and Spencer, 2010).***

The most common cause of non-immune hyperthyroidism is "Transient Hyperthyroidism of Hyperemesis Gravidarum" (THHG), defined as "transient hyperthyroidism, limited to the first trimester of pregnancy, characterized by elevated serum FT4 and suppressed or undetectable serum TSH, in the absence of thyroid autoimmunity" ***(Glinoer and Spencer, 2010).***

The symptoms may worsen again during the postpartum period because of exacerbation of Graves' or because of the development of postpartum thyroiditis ***(Rotondi et al., 2008).***

The present recommendation by the American Thyroid Association is to use PTU for the treatment of maternal hyperthyroidism through 16 weeks of pregnancy. If ATD

therapy is required after 16 weeks gestation, it remains unclear ***(Alexander et al., 2017).***

Whether PTU should be continued or therapy changed to MMI. As both medications are associated with potential adverse effects and shifting potentially may lead to a period of less-tight control ***(Alexander et al., 2017).***

The outcome of pregnancy is closely related to early control of hyperthyroidism. Spontaneous abortion, gestational hypertension, premature delivery, low birth weight, placenta abruption, congestive heart failure and thyroid storms are the most serious complications, with incidence significantly increasing with poor control of the disease ***(Phoojaroenchanachai et al., 2001)***

Median urinary iodine concentration (UIC) is the most commonly used indicator of population iodine nutrition. However, its validity as an indicator of dietary intake relies on a stable relationship between dietary iodine intake and urinary excretion ***(Stilwell, 2008).***

Normal Values of Urinary iodine concentration for assessment of iodine status during pregnancy is (<150 (μg/L) = insufficient, 150–249 (μg/L) =Adequate, 250–499 (μg/L) = Above Requirements, (> or =)500 (μg/L) is Excessive ***(WHO/NMH/NHD, 2013).***

Iodine deficiency is defined by the WHO in terms of population median urinary iodine concentration (UIC). When the median UIC of school-age children is 50–99 mg/L, a population is considered mildly iodine deficient ***(Pearce et al., 2016).***

Based primarily on surveys of UIC in school-age children, an estimated 12 countries have excessive iodine intake, 116 have adequate iodine nutrition, and 25 remain iodine deficient; of the latter, 7 are moderately deficient, 18 are mildly deficient, and none are considered severely deficient. Worldwide, an estimated 1.9 billion individuals are at risk of iodine deficiency ***(Pearce et al., 2016).***

However, when pregnancy takes place in healthy women who live in areas with an inadequate iodine intake of approximately 50– 75 mcg/day, physiological adaptation is progressively replaced by pathological alterations, Pregnancy typically acts therefore to reveal the underlying lack of iodine ***(Glinoer, 2007).***

The more severe the iodine deficiency, the more pronounced are the consequences for the maternal and foetal thyroid glands ***(Glinoer, 2007).***

For healthy pregnant women with iodine sufficiency, the challenge of the maternal gland is to adjust the hormonal output