The use of thyroid stimulating hormone testing in pregnancy and post-partum at Rahima Moosa Mother and Child Hospital

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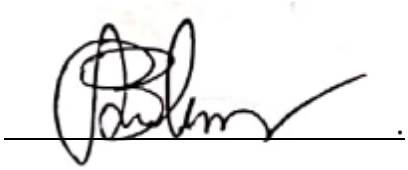
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Medicine in Obstetrics and Gynaecology.

Johannesburg, 2025

DECLARATION

I, Dr. Seele Buhobe, declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine (MMed) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.



Signature

Date: 15 May 2025

DEDICATION

This MMed is dedicated to my loving and supportive mother Ottiliah Buhobe and my brother Pusetso Buhobe.

PRESENTATIONS

SASOG 2024- 41st National Congress of the South African Society of Obstetricians and Gynaecologists.

ABSTRACT

Background: Thyroid disease is an uncommon but important cause of pregnancy and postpartum complications. Early diagnosis aids in preventing these complications. This study aimed to review the indications for TSH testing during pregnancy and evaluate the results and pregnancy outcomes of those tested at the Rahima Moosa Mother and Child Hospital.

Methods: This retrospective descriptive study was conducted at Rahima Moosa Mother and Child Hospital in Coronationville, Johannesburg. Medical records of pregnant women and women in the postpartum period who had their TSH tested between the 01st October and 31st December 2019 were retrieved and reviewed. The indication for investigating a TSH level, the TSH result, and pregnancy outcomes were evaluated.

Results: A total of 746 TSH samples were collected during the study period. Out of these, only 122 files were found and retrieved from the records department and reviewed. Only 82 (67.2%) of the patients had indications in line with American Thyroid Association (ATA) recommendations. Data showed that 106 (86.9%) of patients were euthyroid, 11 (9.0%) hypothyroid, and five (4.1%) were hyperthyroid. There was one low birth-weight baby born to a patient with hyperthyroidism, one low birth-weight baby, and one intrauterine fetal demise born to a patient with hypothyroidism. There were no maternal complications in patients found to be hyperthyroid, and only one pregnancy was complicated by sepsis in those patients found to be hypothyroid.

Conclusion: Thyroid disease screening during pregnancy and postpartum at Rahima Moosa Mother and Child Hospital did not adhere to ATA recommendations. This study has a higher prevalence of thyroid disease than the world-reported prevalence.

Keywords: thyroid stimulating hormone, TSH testing, pregnancy, postpartum, pregnancy outcomes, South Africa

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TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

List of Figures

LIST OF ABBREVIATIONS

ATA- American Thyroid Association

FGR- Fetal growth restriction

HCG- Human chorionic gonadotropin

HIV- Human Immunodeficiency virus

IUFD- intrauterine fetal death

NHLS- National health laboratory service

RMMCH- Rahima Moosa Mother and Child hospital

RPR- Rapid plasma reagin

T3- Triiodothyronine

T4- Thyroxine

TAI- Thyroid autoimmunity

TBG- Thyroid binding globulin

TRH- Thyroid releasing hormone

TSH- Thyroid stimulating hormone

JOURNAL ARTICLE (In the format for JEMDSA)

THE USE OF THYROID-STIMULATING HORMONE (TSH) TESTING IN PREGNANCY AND POST-PARTUM AT RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

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INTRODUCTION AND BACKGROUND

Thyroid disorders are well known to be the second most common endocrine disorders observed in pregnant women, following diabetes mellitus. These may either be hyperthyroidism or hypothyroidism and may present before conception, during pregnancy, or in the puerperium.[1] The overall prevalence of thyroid disease ranges between 5-7% of all pregnancies with differences depending on geographical location and ethnicity.[2,3] Hyperthyroidism is uncommon in pregnancy, affecting about 0.1-0.4% of pregnancies.[4] Overt hypothyroidism affects around 0.3-0.5% of all pregnancies, while subclinical hypothyroidism affects approximately 2-3% of all pregnancies.[5]

Prompt recognition and diagnosis are important to ensure treatment in pregnancy to prevent the consequences of the disease to both the mother and baby. Maternal complications of hyperthyroidism include an increased risk of pregnancy loss, gestational hypertension, preeclampsia, placental abruption, preterm labour, and serious complications like thyroid storm and congestive heart failure.[6,7] It has been shown that there is an odds ratio of 3.84 (1.82-7.29) for developing superimposed preeclampsia and an odds ratio of 3.0 (1.16-11.80) for admission to the ICU. There is also a relative risk of 1.8 for preterm delivery in these women.[8]

Fetal complications of maternal hyperthyroidism, on the other hand, include prematurity, low birth weight (<2500g), goitre, tachycardia, fetal hydrops, cardiac failure, early bone maturation, intrauterine growth restriction, and neurodevelopmental abnormalities.[6] There is a 1.3 relative risk for developing fetal growth restriction, with a relative risk of 1.8 for prematurity and 1.3 for low birth weight.[7] Women with uncontrolled disease are at higher risk for stillbirth with an odd ratio of 8.42 (2.01-35.2).[9]

Untreated hypothyroidism during pregnancy may lead to gestational hypertension (OR 1.20) and severe preeclampsia (OR 1.38).[9] These patients have 1.6 times the odds of developing gestational diabetes, 1.4 times the odds of preterm birth, and 1.3 times the odds of ICU

admission.[7] Hypothyroidism in pregnancy is also associated with several perinatal complications including major congenital anomalies, low APGAR score at 5 mins, an increased risk of neonatal ICU admission (OR 1.35), and a need for respiratory support.[10]

It is not recommended to routinely screen for thyroid disease during pregnancy, rather, patients who are at high risk for thyroid disease based on history and exam should be screened.[11] The American Thyroid Association (ATA) developed guidelines on the diagnosis and management of thyroid disease during pregnancy and postpartum. These guidelines recommend screening for thyroid disease in the following groups of individuals; patients with a personal history of thyroid dysfunction, with signs and symptoms of thyroid dysfunction, known to have thyroid antibodies, presence of a goitre or palpable thyroid nodule, those who had irradiation of the head or neck previously or prior thyroid surgery, patients older than 30 years, with type 1 diabetes or any autoimmune disease, history of miscarriage or preterm delivery, morbid obesity (body mass index (BMI) >40), on medication such as lithium and amiodarone, and residing in areas known with moderate to severe iodine deficiency.[11] Currently there are no guidelines on screening or management of thyroid disease in pregnancy or postpartum period in South Africa, however, the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA)/Association of Clinical Endocrinologists of South Africa (ACE-SA) guidelines for the management of hypothyroidism in adults recommend screening pregnant women with risk factors.[13]

In 2011, the American Thyroid Association (ATA) recommended the following reference ranges for thyroid stimulating hormone (TSH) levels to screen for thyroid disease during pregnancy:0.1–2.5 mIU/L, 0.2–3.0 mIU/L, and 0.3–3.0 mIU/L in the first, second and third trimester respectively.[11] This was amended in 2017, to make the upper limit 4.0mIU/L in early pregnancy if no trimester-specific reference exists for that population.[14]

Currently, South Africa has no population-specific, trimester-specific reference ranges. There has been very little research done in our setting, with only one small study done in Soweto looking at the causes, management, and outcomes of thyroid disease in pregnancy. In this retrospective study, they reviewed 88 women attending the Endocrine antenatal clinic at Chris Hani Baragwanath Academic Hospital over four years and found an overall prevalence of thyroid disease in pregnancy of 0.08% and a prevalence of 0.05% and 0.02% for Grave's disease and overt hypothyroidism respectively which is lower than reported internationally.[15] No studies have been done to evaluate our population-specific reference ranges or methods of

screening. The National Health Laboratory Services (NHLS) of South Africa uses a reference value of being 0.35-5.50 mIU/L which is not trimester-specific (Daya M 2021, oral communication, 20 April).

This study aimed to look at the use of TSH testing in pregnancy and the post-partum period at the Rahima Moosa Mother and Child Hospital (RMMCH), by determining the indications for TSH testing and to evaluate the results and pregnancy outcomes of those tested.

METHODS

This study was a retrospective descriptive study that described the indications for TSH testing, results, and pregnancy outcomes of women who had their TSH tested between 1st October and 31st December 2019. It was undertaken at the RMMCH, a 320-bed regional hospital in Coronationville. The obstetric unit of this hospital delivered 13974 women in 2019, 690 (5%) of these women were nursed in a high care and Intensive Care Unit setting. There were 2078 (14.6%) babies that were low birth weight (LBW), 46 fresh stillbirths, 164 macerated stillbirths (11.7/1000 births), and 156 (11.3/1000 births) early neonatal deaths.

Sampling and sample size: A list of all TSH tests and results performed during the study period was obtained from the NHLS and the corresponding maternity case files were then obtained from the records department. A total of 1080 TSH samples were pulled during the study period, 105 were paediatric patients and 229 were non-pregnant gynaecology patients; which were excluded from the study. The rest of the 746 samples were used to retrieve files from the records department. Only 122 of the 746 patient files requested from the records department were found and reviewed. It is not clear as to why most of the files were not found, but before the time of data collection the RMMCH records department had been flooded, and some files may have been destroyed, or some may have been moved to a different area for archiving.

Patient files were obtained from the records department and reviewed to obtain demographic details including age, race, gravidity, parity, and booking bloods. The gestational age at testing, indication for testing, TSH results, pregnancy outcomes including gestation at delivery, mode of delivery, and obstetric complications were obtained. Measured neonatal outcomes included the incidence of low birth weight/intrauterine growth restriction, the incidence of aplasia cutis, neonatal goiter, and evidence of thyrotoxicosis. Maternal complications measured included hypertensive disorders, thyroid storm, haemorrhage, and anaemia. All the TSH results obtained during the study period were interpreted using NHLS

(trimester non-specific) reference ranges whilst TSH results of the 122 patients whose files were reviewed were interpreted using ATA trimester-specific reference ranges, with patients with elevated TSH levels diagnosed as hypothyroid and those with low TSH levels diagnosed as hyperthyroid. The assessments and/or diagnoses made by the clinician during the visit the TSH was tested were taken as indications for testing. If there were more than one indication for testing, all the indications listed in the file were listed as the indication for testing.

Data analysis: Data was captured using Redcap 14.6.11 and analysed using Statistical software (STATA) version 17. The descriptive data was presented using means, ranges, medians, and standard deviations.

Ethical clearance and permission: The study received approval from the Human Research Ethics Committee of the University of the Witwatersrand. Clearance certificate number M220211. We obtained permission from the CEO of Rahima Moosa Mother and Child Hospital and the NHLS.

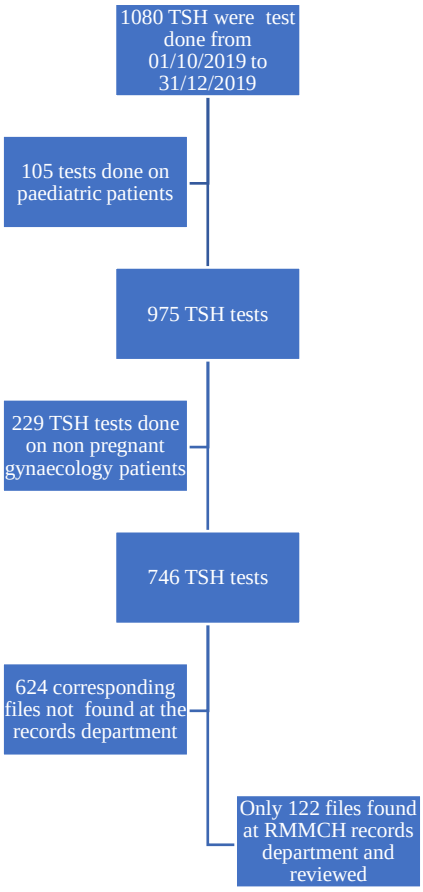

Figure 1: Data sampling

RESULTS

Of the 746 files requested from the RMMCH records department, only 122 files were found, retrieved, and analysed. The mean age of the individuals involved in the study was 30.9 years. There were 17 (13.9%) primigravidae, while 20 (16.4%) were grand-multiparous women. Only one (0.8%) patient was Rhesus antigen negative and had no atypical antibodies. With regards to rapid plasma reagin (RPR), 121 (99.2%) women had a negative test and one (0.8%) had no documented result. The study had 18 (14.8%) patients who were HIV positive. All 18 (14.8%) HIV-positive patients were on antiretroviral therapy. Out of the 122 patients, six (4.9%) women had pre-existing thyroid disease, six (4.9%) had diabetes, and 10 (8.2%) had chronic hypertension (Table I).

TSH testing was done during the antenatal period in 103 (84.4%) whilst the remaining 19 (15.6%) were tested in the postpartum period. The mean gestation at TSH testing for those tested antenatally was 23 weeks 1 day (9 weeks 3 days). Indications for testing included known thyroid disease seven (5.7%), a palpable goitre one (0.8), recurrent miscarriages 10 (8.2%), previous intrauterine demise 14 (11.5%), intrauterine demise in the current pregnancy 11 (9.1%), uncontrolled hypertension 16 (13.2%), known diabetic 15 (12.4%) and persistent tachycardia 17 (13.9%). Thirty-two (26.0%) of the patients had other indications (Table II). Based on ATA recommendation, 82 (67.2%) of the patients had appropriate indications for TSH testing while the remaining 40 (32.8%) had inappropriate indications.

A review of all the TSH results obtained during the study period using the NHLS (trimester non-specific) reference ranges showed that 590 (79.1%) were euthyroid, 99 (13.3%) were hypothyroid, while 57 (7.6%) were hyperthyroid (Table III).

Review of TSH results of the 122 patients included in the study using the ATA trimester-specific reference ranges showed that 106 (86.9%) were euthyroid, 11 (9.0%) were hypothyroid, and five (4.1%) were hyperthyroid (Figure 1).

Table I: Descriptive statistics

	Total (N = 122)
Age	
Median (Q1, Q3)	30.5 (27.0,36.0)
Race	
African	111 (91.0%)
Coloured	9 (7.4%)
White	2 (1.6%)
Gravidity	
1	17 (13.9%)
2	32 (26.2%)
3	31 (25.4%)
4	22 (18.1%)
≥5	20 (16.4%)
Parity	
0	28 (23.2%)
1	38 (31.1%)
2	33 (25.4%)
3	17 (13.9%)
4	5 (4.1%)
⩾5	1 (0.8%)
Rhesus Antigen	
Negative	1 (0.8%)
Positive	121 (99.2%)
HIV	
Negative	104 (85.2%)
Positive	18 (14.8%)
Syphilis screen (RPR)	
Negative	121 (99.2%)
Positive	0 (0.0%)
Not documented	1 (0.8%)
Medical conditions	
Thyroid disease	3 (2.5%)
Diabetes	6(4.9%)
Epilepsy	1 (0.8%)
Chronic Hypertension	10 (8.2%)
Body mass index (BMI)	
Median (Q1, Q3)	29.4 (25.3, 34.5)

Table II: Indications for TSH testing

	Total (N = 103)
Gestation at TSH testing	
Median (Q1, Q3)	24.0 (16.0, 31.0)
	Total (N=122)
Indication for TSH testing	
ANTENATAL	
Uncontrolled hypertension	16 (13.2%)
Diabetic	15 (12.4%)
Previous intrauterine demise	14 (11.5%)
Intrauterine demise in this pregnancy	11 (9.1%)
Recurrent miscarriages	10 (8.2%)
Pre-gestational thyroid disease	7 (5.7%)
Pre-hypertensive and high BMI	3 (2.5%)
Previous early neonatal death	3 (2.5%)
Previous first-trimester miscarriage	3 (2.5%)
Vomiting in early pregnancy	3 (2.5%)
Advanced maternal age	2 (1.6%)
Anaemia in pregnancy	2 (1.6%)
Previous preterm delivery	2 (1.6%)
Chronic palpitations	1 (0.8%)
Current Molar pregnancy	1 (0.8%)
Goitre	1 (0.8%)
Glycosuria	1 (0.8%)
Intrauterine growth restriction	1 (0.8%)
Persistent chest pain and bradycardia	1 (0.8%)
Poor obstetric history	1 (0.8%)
Pre-labour rupture of membranes	1 (0.8%)
Previous macrosomic baby	1 (0.8%)
Shortness of breath and hot flushes	1 (0.8%)
Uncontrolled epilepsy	1 (0.8%)
Young hypertensive	1 (0.8%)
POSTNATAL	
Persistent tachycardia	17 (13.9%)
Postpartum psychosis	2 (1.6%)

Table III: Analysis of all Thyroid stimulating hormone results obtained during the study period.

	N=746	**N=122**
Hyperthyroidism	57 (7.6%)	5 (4.1%)
Hypothyroid	99 (13.3%)	11 (9.0%)
Euthyroid	590 (79.1%)	106 (86.9%)

The median body mass index (BMI) of patients in this study was 29.4Kg/M^2 (25.3, 34.5) which according to the World Health Organization, is considered as class I obesity.[16] The median TSH level was 1.9mIU/L (1.2, 2.8). Mean gestational age at delivery was 35 weeks 6 days with 50 patients (41.0%) delivering vaginally, 68 (55.7%) delivered via caesarean section and four (3.3%) had no documentation of their delivery. With regards to delivery, 102 (83.6%) deliveries were live births, 16 (13.1%) stillbirths, and the remaining four (3.3%) had no documentation of their delivery. Of the 102 live births, 14 (13.7%) and 3 (2.9%) babies had an APGAR score of less than seven at one and five minutes of life respectively. No cord blood nor neonatal TSH sample testing was done for babies born to mothers with abnormal TSH results. Median birth weight was 2750.0g (2250.0, 3280.0). There were 18 (14.7%) fetal/neonatal complications and 14 (11.4%) maternal complications. (Table IV).

Table IV: Pregnancy outcomes, fetal, neonatal, and maternal complications

	Total N=122
Gestational age at deliver	
Median (Q1, Q3)	38.0 (35.0, 39.0)
Live birth	
No	16 (13.1%)
Yes	102 (83.6%)
Not documented	4 (3.3%)
Live Births	**N=102**
Baby discharged to mother	82 (80.4%)
Baby admitted as a lodger	1 (1.0%)
Baby admitted to neonatal ICU	19 (18.6%)
If not a live birth	**N=16**
Fresh still birth	1 (6.3%)
Macerated stillbirth	14 (87.5%)
Miscarriage	1 (6.3%)
Birth weight	
Mean (SD)	2620.4 (917.8)
Median (Q1, Q3)	2750.0 (2250.0, 3280.0)
Fetal/Neonatal complications	**N=122**
No	100 (82.0%)
Yes	18 (14.7%)
Not documented	4 (3.3%)
Complications	**N=122**
Low birth weight	2 (1.6%)
Intrauterine fetal demise	16 (13.1%)
Maternal complications	N=122
Hypertension	6 (4.9%)
Postpartum psychosis	1 (0.8%)
Sepsis	7 (5.7%)

Table V shows that there were no maternal complications noted in the group that had hyperthyroidism, while there was only one maternal complication noted in those with hypothyroidism which was puerperal sepsis. The rest of the 13 maternal complications noted in this study were seen in euthyroid patients. Six patients had hypertension, puerperal sepsis

occurred in 6 patients and post-partum psychosis in 2. In this study, there were 18 (14.6%) fetal/neonatal complications, 15 (83.3%) of which were seen in euthyroid patients while 3 (16.7%) were seen in patients with abnormal thyroid function. Only one (20%) fetal/neonatal complication was noted in those patients who had hyperthyroidism, 2 (18.2%) fetal/neonatal complications in those patients who had hypothyroidism, and 15 (14.2%) in those patients who were euthyroid.

Table V: Pregnancy outcomes, fetal, neonatal and maternal complications in the different groups.

	Hyperthyroid	Euthyroid	Hypothyroid
	(N = 5)	(N = 106)	(N = 11)
Gestational Age at delivery			
Median (Q1, Q3)	38.5 (36.5, 41.0)	38.0 (35.0, 39.0)	38.0 (34.0, 38.0)
Mode of delivery			
Normal vaginal delivery	2 (40.0%)	45 (42.5%)	3 (27.3%)
Caesarean section	2 (40.0%)	58 (54.7%)	8 (72.7%)
Undocumented	1 (20.0%)	3 (2.8%)	0 (0.0%)
If caesarean section			
Emergency	2 (100.0%)	42 (72.4%)	7 (87.5%)
Elective	0 (0.0%)	16 (27.6%)	1 (12.5%)
Live birth			
No	0 (0.0%)	15 (14.6%)	1 (9.1%)
Yes	4 (80.0%)	88 (85.4%)	10 (90.9%)
Undocumented	1(20.0%)	3 (2.8%)	0 (0.0%)
Fetal/Neonatal Complications			
	1 (20.0%)	15 (14.2%)	2 (18.2%)
Fetal/Neonatal Complications			
Low birth weight	1 (20.0%)	0 (0.0%)	1 (9.1%)
Other	0 (0.0%)	15 (14.2%)	1 (9.1%)
Maternal Complications			
Sepsis	0 (0.0%)	6 (5.7%)	1 (9.1%)
Other	0 (0.0%)	2 (1.8%)	0 (0.0%)

DISCUSSION

Thyroid disease in pregnancy is an uncommon but important cause of morbidity and possible mortality for both the mother and the fetus. Early detection and treatment are important to prevent potential complications. During this study, we analyzed the records of women who were screened for thyroid disease during pregnancy and/or after delivery, using TSH. The reasons for testing included the presence of signs and symptoms of thyroid disease, a previous or current history of thyroid disease or autoimmune disorders, previous pregnancy complications, and complications in the current pregnancy. The majority of these indications (67.2%) were appropriate and in line with the recommendation of the ATA which discourages universal screening of thyroid disease and encourages screening of high-risk individuals.[15]

There were some inappropriate indications which are not in line with international guidelines such as a history of glycosuria, premature rupture of membranes, uncontrolled epilepsy, and anaemia in pregnancy.

Analysis of the TSH results of the 122 patients whose files were reviewed in this study showed that 13.1% of the patients had a thyroid disorder, with 5.4% having hyperthyroidism which is higher than the prevalence of 0.75% reported by Singh.[17] In Indore, India, Gupta et al conducted a larger study examining 865 pregnant women with risk factors for thyroid disease during pregnancy. Their TSH levels were tested during the antenatal period, revealing a prevalence of 3.4%, which was also lower than the prevalence observed in this study.[18]

This study found a 9.0% prevalence of hypothyroidism and this was higher than the prevalence of 0.49% reported by Turunen, but was less than the prevalence of 22.5% reported by Awede in Benin.[2,19] Unlike the present study, Awade conducted a study on pregnant women in the antenatal clinic who had no prior history of thyroid disorders and were not taking any medication that could potentially affect thyroid hormone metabolism. The study measured their TSH levels.[19]

Iodine deficiency is an important public health issue and an important cause of hypothyroidism. The requirements of iodine in pregnancy increase to almost double that of a non-pregnant woman.[19] South Africa has instituted a mandatory iodine fortification of foods, particularly salt to about 46-60mgof iodine per kilogram (kg) of salt. This has resulted in 52.5% of households using adequately iodised salt versus the international goal of 90%.

Despite this low household penetrance, South Africa is considered a sufficiently iodinated country and this may account for the prevalence being lower than in Awede's study.[19.20]

Only 14.7% of patients with abnormal TSH results developed fetal/neonatal complications. Compared to only 9.1% of hypothyroid patients, 20% of hyperthyroid patients gave birth to low-weight babies. This is significantly higher than the 2.25% prevalence reported by Saki.[21] Thyroid hormones are essential for the growth and development of a fetus during pregnancy. They are necessary for the overall increase in fetal mass and to trigger the development of somatic cells. Both hypo and hyperthyroidism have been linked to the occurrence of fetal growth restriction (FGR) and low birth weight in babies born to mothers who have these conditions. [22]

This study showed that about 4.1% of the pregnancies were complicated by hypertensive disorders in pregnancy. These complications were seen in euthyroid patients. None of the patients who had abnormal TSH results developed any hypertensive disorder of pregnancy. This was lower than the 6.3% occurrence reported by Saki and may be due to our small sample size.[21] The association between thyroid disease in pregnancy (particularly hypothyroidism) and pre-eclampsia is poorly understood. The presence of thyroid disease may lead to patients developing of pre-eclampsia, potentially due to decreased plasma protein levels and increased endothelin levels. [23] Some experimental studies have shown that in hypothyroidism there is a decreased production of nitric oxide and this leads to endothelial cell dysfunction hence leading to the development of pre-eclampsia.[24] In a study conducted in the Eastern Cape Province (South Africa), Businge et al found an association between severe iodine deficiency with elevated thyroglobulin and a higher risk of severe preeclampsia/eclampsia in the studied population. The researchers also noted that as the level of iodine deficiency increased, serum nitric oxide levels decreased, resulting in a higher severity of preeclampsia.[25]

LIMITATIONS

The study had a small sample size because most maternity records were not found and therefore did not have clinical information for 624 patients. This may not be a true representation of the pattern of testing and, therefore, the prevalence of thyroid disease in this population, making drawing conclusions from this data difficult.

Another limitation of the study is the use of assessment and diagnosis to determine the indication for testing. This may have led to recording an assumption of what the indication for testing was instead of what the true indication for testing was.

CONCLUSION

In conclusion, screening for thyroid disease in pregnancy and the postpartum period in Rahima Moosa Mother and Child Hospital did not follow the recommendations from the ATA. This study has a higher prevalence of thyroid disease than the internationally reported prevalence.

RECOMMENDATIONS

Large, high-powered studies must be conducted to determine the prevalence of thyroid disease in pregnancy in the South African population and to determine trimester-specific reference ranges.

Local protocols on screening for thyroid disease in pregnancy and postpartum should be developed and should include a guide on when to screen.

Considerations should be made for universal screening at the primary care level to ensure we do not miss patients with thyroid disease in pregnancy but this would be costly.

Disclosure statement: The researcher and co-authors have no conflict of interest to declare.

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APPENDIX A: PROTOCOL

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

THE USE OF THYROID STIMULATING HORMONE TESTING IN PREGNANCY AND POST-PARTUM AT RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

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MMed (O&G) Proposal

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TABLE OF CONTENTS

1.0 ABBREVIATION LIST

ATA- The American Thyroid Association

HCG- Human chorionic gonadotropin

HIV- Human Immunodeficiency virus

IUFD- intrauterine fetal death

NHLS- National health laboratory service

RMMCH- Rahima Moosa Mother and Child hospital

T3- Triiodothyronine

T4- Thyroxine

TAI- Thyroid autoimmunity

TBG- Thyroid binding globulin

TRH- Thyroid releasing hormone

TSH- Thyroid stimulating hormone

2.0 INTRODUCTION AND BACKGROUND

Thyroid disease is counted among those disorders that cause morbidity and mortality in pregnancy. It is estimated that overt hypothyroidism complicates 3 in 1000 pregnancies while overt hyperthyroidism affects 2 in 1000 pregnancies in countries on the Western hemisphere (2). The prevalence and impact of thyroid disease in pregnancy have not been widely investigated in our setting and therefore there is limited data to direct protocols and policy. This study aims to examine the use of TSH in pregnancy and the postpartum period in Rahima Moosa Mother and Child Hospital and by extension find out the burden of disease associated with thyroid disorders.

3.0 LITERATURE REVIEW

Thyroid hormones are iodinated metabolites of tyrosine that are synthesised in the thyroid gland's follicular cells. These include T3 which has three iodine molecules and T4 which has four iodine molecules. They are produced through a complex process involving iodine trapping, oxidation, and coupling (4). Thyrotropin-releasing hormone (TRH) is produced in the hypothalamus and triggers the anterior pituitary to release thyroid stimulating hormone (TSH) which will stimulate the thyroid gland to produce T3 and T4. Hormone levels are maintained through a negative feedback system (4).

Thyroid hormones control metabolism, growth, and many other body functions. They are important in the function of every organ system in the body including the heart, central nervous system, the autonomic system, bones, the gastrointestinal system, the reproductive system and metabolism by binding to intranuclear receptors which activate genes to increase metabolic rate and thermogenesis. This increased metabolic rate leads to increased oxygen and energy consumption (4).

Thyroid hormones are integral in the process of normal growth and development of the fetus. The thyroid gland of the fetus begins producing hormones after the first trimester. Before this gestation, thyroid hormones required by the fetus are obtained from the mother (2). The level of the hormones in the fetus are therefore affected by the gestational age, maternal nutrition, placental permeability of maternal thyroid hormones and the endocrine condition of the fetus (5). Thyroid hormones are responsible for the general growth of fetus and also are responsible for the development of its brain and other in early pregnancy (5). They also control the levels and effectiveness of other hormones and growth factors such as

catecholamines and insulin-like growth factors which are required for fetal development (5). Another key role that these hormones play in pregnancy is to promote terminal differentiation of fetal tissue close to term; by doing so, they ensure activation of physiological processes such as pulmonary gas exchange, thermoregulation, hepatic gluconeogenesis and cardiac adaptation which are essential for the survival at birth (5).

Normal pregnancy entails substantial changes in thyroid function. The maternal thyroid is affected by 3 main factors:

High levels of oestrogen in early gestation stimulate the production of a binding globulin isoform which is less rapidly degraded by the body and therefore ultimately results in a decrease in serum concentration of free T4 (6). There is an increase in TSH that accompanies this decrease in serum-free but is rarely detected on routine thyroid testing (6).

The first trimester of pregnancy is characterised by high levels of human chorionic gonadotropin (hCG) which has a similar alpha subunit. This similarity leads to a cross-reaction with the TSH receptors and therefore results if a temporary rise in T4 and a partial suppression of TSH (6).

Reduced availability of iodine- this results from the action of the placenta which de-iodinates the maternal T4 and increases the turnover of T4 (2).

In normal pregnancies, despite the above physiological changes, the thyroid gland is able to maintain a euthyroid state with very little changes in serum TSH and T4. However, in women with limited reserves as seen in thyroid autoimmunity and iodine deficiency, hypothyroidism may develop (2).

THYROID DISORDERS

Thyroid dysfunctions include hypothyroidism and hyperthyroidism. Hypothyroidism may either be overt or sub-clinical, Overt hypothyroidism is thyroid hypofunction characterised by abnormally increased TSH and low FT4 levels, whereas subclinical hypothyroidism is thyroid hypofunction that is asymptomatic. Patients usually have a high TSH but the FT4 levels remain normal (2). Overt hypothyroidism affects about 3 in 1000 pregnancies and is characterised by signs and symptoms that can be mistaken for normal signs and symptoms of pregnancy. The first signs are usually fatigue, constipation, muscle cramps, and cold intolerance. Later on, patients develop insomnia, weight gain, intellectual slowness, and voice changes (6).

Autoimmune thyroiditis (Hashimoto's thyroiditis) has been noted as the number one cause of hypothyroidism. Here, there is an infection of the thyroid (usually painless) with subsequent enlargement of the gland. Other causes of hypothyroidism to note include thyroid surgery, thyroid irradiation, and, most importantly, iodine deficiency. Secondary causes of hypothyroidism are usually due to the pituitary, while tertiary causes are due to the hypothalamus and are rare (2).

Varul et al. report a 4.8% prevalence of hypothyroidism in their Indian population. They attributed this high prevalence (compared to the prevalence in Western countries) to iodine deficiency. They also reported a mean age of presentation of 25.19±4.17 as opposed to the mean age of presentation in Western countries of 27±6 years. This was a reflection that women in India get married earlier in life and conceive earlier in life. The mean gestation at presentation was reported to be 10.03 weeks (7).

Overt hyperthyroidism is characterised by a low TSH level and a high free T4, while subclinical hyperthyroidism is asymptomatic and characterised by low TSH and normal FT4

levels (1). This condition is rare, in Western countries 0.5% to 1.3% of cases are due to Grave's disease, while only 0.1 % result from autonomous thyroid production. Patients usually complain of palpitations, anxiety, diarrhoea, easy fatiguability, and muscle pain (1). The most common cause of hyperthyroidism in pregnancy is Grave's disease. This auto-immune disorder is characterised by the production of thyroid-stimulating hormones by the body, which binds and stimulates TSH receptors on the thyroid gland. Another unique cause of hyperthyroidism in pregnancy is gestational transient thyrotoxicosis which is usually associated with excessive vomiting due to elevated levels of hCG, which stimulates TSH receptors and leads to transient hyperthyroidism (2).

Postpartum thyroiditis is the development of hypothyroidism or thyrotoxicosis in a woman who had no clinical signs or evidence of thyroid disease before pregnancy within a year of delivery (8). The thyrotoxicosis arises due to the loss of the immune suppression present during pregnancy, which leads to the onset or exacerbation of auto-immune thyroid disease. Patients usually present with signs that include palpitations, lethargy, and irritability and experience palpitations. The diagnosis is confirmed by chemistry that shows a low or undetectable TSH and a high free T4 (9).

DIAGNOSIS OF THYROID DISORDERS

The diagnosis of any thyroid disorder is made by measuring serum TSH which is more sensitive than T4. Only after the TSH is noticed to be deranged can the T4 be quantified (10). The ATA recommends that each population establish TSH reference ranges for their patients according to their gestation and if no reference ranges have been established, the panel recommends for the first trimester, decreasing the lower and upper limit of a non-pregnant individual by 0.4 mU/L and 0.5mU/L respectively. This corresponds to an upper limit of

4.0mU/L. After the late first trimester, TSH levels return to those of a non-pregnant individual (11).

The Rahima Moosa NHLS does not have established trimester-specific TSH reference ranges for our population. The reference ranges used are only adjusted to age, with the normal TSH range in adults (both female and male) being 0.35-5.50 mIU/L (12).

COMPLICATIONS OF THYROID DISODERS

Overt hypothyroidism has been noted to increase the risk of complications in pregnancy. They are particularly at risk of developing miscarriages, stillbirth, and abruption placentae. They are also prone to developing preeclampsia and delivering low-birth-weight babies (1).

Uncontrolled hypothyroidism (either overt or subclinical) at conception is associated with a 31.4% rate of miscarriages as compared to that of 4% in euthyroid patients. Patients with a TSH of less than 2µIU with TAI have a significantly higher rate of stillbirths and this suggests that autoimmunity contributed to the loss of some pregnancies (13). Because of this increase in rate of miscarriages in subjects with TAI suggestions have been made that the presence of TAI may be a marker of general immune imbalance and therefore would account for the rejection of the fetal graft (14).

Manninsto et al reported that there is a 1.8-time increased risk of hyperthyroid women developing preeclampsia compared to the controls. They also noted that along with this increased risk of pre-eclampsia, there is an increased risk of early preterm birth, 4.8 times increased in risk of late preterm labour, and 3.7 times increased risk management in an intensive care unit (15).

In 1999, Tim et all demonstrated that untreated hypothyroidism in pregnancy caused a decrease in intelligence. This was evidenced by a 7 drop in IQ points when compared to

children born to euthyroid mothers. It was also noted that the children had difficulties attaining developmental milestones by age 7-9 years (16).

Another study from Denmark showed that in addition to having higher risks of miscarriage, stillbirth, preterm birth, and lower birth weight, women diagnosed with hyperthyroidism had a higher risk of having a child with attention deficit hyperactivity disorder than control participants (17).

THYROID DISODERS IN OUR SETTING

In a study by Nicolaou et al in Chris Hani Baragwanath Academic Hospital, they found that of the 88 patients with thyroid disease, 58 had hyperthyroidism while only 30 were hypothyroid. The most common cause of hyperthyroidism was noted to be Grave's disease affecting 83%. They reported 6 fetal losses, 4 of which were IUFDS while 2 were spontaneous miscarriages. In this study 20% of the live births were delivered prematurely with low birth weights (less than 2500g) while 80% were normal birth weights with a mean birth weight of 2895g (18).

4.0 AIMS AND OBJECTIVES

4.1 AIM

This study aims to review the use of TSH testing at Rahima Moosa Mother and Child Hospital from October 2019 to December 2019 in pregnant and post-partum women in the first six weeks postpartum.

4.2 OBJECTIVES

1. To determine the number of TSH tests done in pregnant women or women in the first six weeks post-partum at RMMCH from October 2019 to December 2019.
2. To describe the indications for the THS testing in the patients included.
3. To describe the results of the TSH in the patients.
4. To describe the pregnancy outcomes of the women who had their TSH tested.

5.0 METHODS

5.1 STUDY DESIGN

This retrospective descriptive study will involve reviewing patient files from the selected study period.

5.2 STUDY SETTING

The study will be conducted in Rahima Moosa Mother and child hospital, a 320-bed regional hospital in Coronatioville. In 2019 the hospital delivered 13974 women, six hundred and ninety (5%) of these women were nursed in a high care and Intensive Care Unit setting and five died due to various causes. In the same year the hospital 13989 babies were delivered, 2078 (14.6%0 of these were low birth weight, 46 (0.3%) were fresh still births, 164 (1.2%) were macerated still births while 156 (1%) became early neonatal deaths.

5.3 STUDY SUBJECTS

All the pregnant women and women in the first six weeks post-partum treated in Rahima Moosa Mother and Child Hospital who had their thyroid stimulating hormone tested between October and December 2019.

5.4 SAMPLE SIZE

A list of all the pregnant women who had their thyroid function tested during the study period will be sourced from the National Health Laboratory Services (NHLS) and their files will be reviewed. A sample size of 200 women is expected.

5.5 DATA MANAGEMENT AND ANALYSIS

De-identified data will be collected and captured using the REDCap data management system and exported into STATA version 17 for analysis. Categorical variables will summarised by frequency and percentage tabulations. Continuous variables will be assessed for normality using the Shapiro-Wilk test and where applicable, data will be summarised using means and

standard deviations or medians interquartile ranges and ranges. The demographic profile of the study population will be analysed and these will include age, parity and gestational age. The absolute number of TSH tests done will be determined, gestational age at testing and indication for testing will be determined. Details of the TSH results will be evaluated using ATA trimester-specific ranges classified as normal, hypothyroid or hyperthyroid. The prevalence of hypothyroidism will be calculated as the number of patients with a high TSH (i.e. >5.5 mIU/L) over the total number of patients tested in that period while that of hyperthyroidism will be calculated as the number of patients that had a low TSH (i.e. <0.35 mIU/L) over the total number of women tested. Data analysis will be done with the aid of STATA.

6.0 ETHICS

- The protocol will be submitted to the postgraduate research committee of the department of Obstetrics and Gynaecology of the University of the Witwatersrand.
- Approval to conduct the study will be obtained from the Chief executive officer of Rahima Moosa Mother and Child Hospital.
- Approval will be requested from the manager of the National Health Laboratory Services to obtain patient information.
- The study will be registered in the National Health Research Database.
- All the information obtained will be treated with highest level of confidentiality, the patient identifiers will be removed, the data sheet will have study numbers – the researcher will keep a list of study numbers and the corresponding patient details separately.

7.0 TIMELINE

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb
Literature Review	X	X												
Preparing Protocol			X	X										
Protocol Assessment					X	X								
Ethics Application							X	X						
Collecting Data									X	X				
Data Analysis											X	X		
Paper Write up													X	
Final Submission														X

8.0 FUNDING

All costs will be incurred by the researcher and are estimated at R6500.

ITEM	COST
Printing data sheet	R500
Printing dissertation	R500
Publication	R5500
Total	R6500

9.0 PROBLEMS

There may be difficulties retrieving all the required files due to loss or misplacement.

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APPENDIX B: DATA COLLECTION SHEET

THE USE OF TSH IN PREGNANCY AND POST PARTUM PERIOD

Record ID	_____
Age	_____
Race	◯ Asian ◯ Black ◯ Coloured ◯ Mixed race ◯ White ◯ Other ◯ Undocumented
Gravidity	◯ 1 ◯ 2 ◯ 3 ◯ 4 ◯ 5 ◯ >5
Parity	◯ 0 ◯ 1 ◯ 2 ◯ 3 ◯ 4 ◯ 5 ◯ >5
Medical Condition	☐ None ☐ Thyroid disease ☐ Diabetes ☐ Epilepsy ☐ Asthma ☐ Cardiac ☐ Tuberculosis ☐ Chronic Hypertension/Gestations HTN/PET/HELLP syndrome ☐ Connective tissue disorder ☐ Other
If Diabetes	◯ Type 1 ◯ Type 2 ◯ Gestational
If other Medical condition: specify	_____
Rhesus status	◯ Negative ◯ Positive ◯ Not Documented
If Negative	◯ No Antibodies ◯ Antibodies present

If antibodies present, Titer	_____
Syphilis screen	◯ Negative ◯ Positive ◯ Not documented
If Positive RPR Titer	_____
If positive was she treated	◯ Yes ◯ No
HIV status	◯ Negative ◯ Positive ◯ Not documented
If positive	◯ Not on treatment ◯ On treatment
If Positive Viral load	_____
If Positive CD4 count	_____
Height	_____
Weight at booking	_____
Body Mass Index	_____
Last Normal Menstrual Period	_____
Gestational age at first USS	_____
Expected date of delivery	_____
Final Expected date of delivery according to ACOG	_____

Indication for TSH testing	◯ Known Thyroid disease ◯ Goitre ◯ Exopthalmos ◯ Cardiac disease ◯ Recurrent miscarriages ◯ Previous Intrauterine demise ◯ Intrauterine demise in this pregnancy ◯ Uncontrolled Hypertension ◯ Diabetic ◯ Persistent tachycardia ◯ Other
If THyroid disease	◯ Hypothyroidism ◯ Hyperthyroidism
If persistent tachy	◯ Pre-delivery ◯ Post delivery
If other	_____
Date/Gestation at TSH testing	_____
TSH result	_____
T4 taken	◯ Yes ◯ No
If yes, date /gestation at testing	_____
If yes, T4 Result	_____
Thyroid Antibodies	◯ Yes ◯ No
If yes, Results	_____
TSH repeat	◯ Yes ◯ No
If yes, Date/Gestation at repeat testing	_____
If yes, TSH repeat result	_____
T4 repeat	◯ Yes ◯ No
Date/Gestation of T4 repeat	_____

T4 repeat results	_____
TSH repeat 2	◯ Yes ◯ No
Date/Gestation of repeat 2	_____
TSH Repeat 2 Results	_____
Gestational Age at delivery	_____
Mode of delivery	◯ Normal vaginal delivery ◯ Caesarean section
If NVD	◯ Spontaneous ◯ Assisted delivery
If caesarean section	◯ Emergency ◯ Elective
Indication of caesarean section	◯ Fetal distress ◯ Prolonged labour ◯ previous caesarean section ◯ GPHT/PET/HELLP Syndrome ◯ Other
If Other, SPECIFY	_____
Live birth	◯ Yes ◯ No
If yes	◯ Baby discharged to mother ◯ Baby admitted as lodger ◯ Baby admitted to16B ◯ Baby admitted to ICU
If 16b	_____
If ICU	_____
If no	◯ Fresh still birth ◯ Macerated still birth ◯ Miscarriage
Birth Weight	_____
APGAR 1min	_____

APGAR 5min	_____
Cord Blood TSH	◯ Yes ◯ No
If yes	_____
Neonatal TSH	◯ Yes ◯ No
If yes	_____
Neonatal Complications	◯ Yes ◯ No
If Yes to Neonatal Complications	◯ Goitre ◯ Thyrotoxicosis ◯ Aplasia cutis ◯ Fetal growth restriction ◯ None ◯ Other
If Other, specify	_____
Maternal Complications	☐ Haemorrhage ☐ Anaemia ☐ Hypertension ☐ Sepsis ☐ Thyroid storm ☐ None ☐ Other
If other, SPECIFY	_____
If Haemorrhage	◯ APH ◯ PPH
If hypertension	◯ Chronic HTN ◯ Gestational HTN ◯ Pre-eclampsia (PET) ◯ Chronic HTN it superimposed PET ◯ Eclampsia
Diagnosis based on TSH results	◯ Euthyroid ◯ Hypothyroid ◯ Hyperthyroid

APPENDIX C: APPROVAL FROM HOSPITAL

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Rahima Moosa Mother and Child Hospital
Enquiries: Adjunct Professor Ashraf Coovadia
Tel: 011 470 9284/9100
Email: Karen.Marshall@wits.ac.za

TITLE OF RESEARCH PROJECT:
"THE USE OF THYROID STIMULATING HORMONE TESTING IN PREGNANCY AND POST-PARTUM AT RAHIMA MOOSA MOTHER AND CHILD HOSPITAL"

NAME OF SUPERVISOR:
Dr Amy Wise

NAME OF RESEARCHER:
Dr Seele Buhobe
Department of Obstetrics and Gynaecology
University of the Witwatersrand

NHRD REF NO: GP_202110_052

Dear Dr Buhobe,

Permission is granted for you to conduct the research as indicated in the title above.

The terms under which this permission is granted is contained in the Researcher Declaration form that you have signed. Failure to comply with these conditions will result in the withdrawal of such permission.

It is crucial for you to inform the Research Coordinator, Karen Marshall of the actual start and end dates of your study. This could be done by e-mail.

Should the study commence more than 12 months after receipt of this approval letter you will have to go through the process of applying again.

You are strongly advised to keep a signed copy of the declaration form to ensure that the terms of this agreement are always complied with.

Yours sincerely,

DR FREW BENSON
Acting Chief Executive Officer
Rahima Moosa Mother and Child Hospital

Date: 28-01-2022

APPENDIX D: APPROVAL FROM NHLS

Academic Affairs and Research
Modderfontein Road, Sandringham, 2031
Tel: +27 (0)11 386 6155
Fax: +27 (0)11 386 6296
Email: babatyi.kgokong@nhls.ac.za
Web: www.nhls.ac.za

05 July 2022

Applicant: Seele Buhobe
Institution: University of the Witwatersrand
E-mail Address: seelebuhobe@yahoo.com
Cell: 081 030 7989

Project Title: THE USE OF THYROID STIMULATING HORMONE TESTING IN PREGNANCY AND POST-PARTUM AT RAHIMA MOOSA MOTHER AND CHILD HOSPITAL
Reference Number: PR2122585

Research Application Type(s):
1. Request for Data

RE: APPROVAL LETTER: REQUEST TO ACCESS NHLS RESOURCES FOR RESEARCH PURPOSES

This letter serves to advise that the application requesting permission to conduct the above-mentioned research using the listed NHLS resources has been reviewed and **"Approved"**. Please note that the approval is granted on the condition that you comply with the NHLS Research Material and Data Access Policy and requirements stated below.

1. All material and data requested shall be used as per the research protocol submitted to the NHLS and as approved by the relevant Health Research Ethics Committee (HREC) in South Africa.
2. Access to the NHLS material and/or data shall be limited to the minimum required for successful completion of the approved study and shall be made available ***without patient names***.
3. Confidentiality shall be maintained at the participant and institutional level and there shall be no disclosure of personal information or confidential information.
4. The material and/or data obtained from the NHLS shall be anonymised and not, for any reason, be used to track or recruit patients as no pre-approval/consent is obtained from patients.
5. Processes shall be discussed with the relevant NHLS departments (i.e. Corporate Data Warehouse (CDW), NHLS Laboratory Management, Operations Office, etc.) and agreed upon.
6. Any amendments to the study requirements, including the use of the material and/or data for purposes not initially disclosed to the NHLS) shall be cleared by an approved HREC and submitted to the NHLS for approval via the AARMS system – https://aarms.nhls.ac.za.
7. The NHLS shall be acknowledged as a source of material and/or data in any output, such as abstracts and journal articles, emanating from the project.
8. A final report of the research study and any published output resulting from this study shall be submitted to the NHLS via AARMS

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. The NHLS entities tasked with providing the material and/data may have additional requirements for access. Data related queries may be directed to NHLS CDW, email: zarina.sabat@nhls.ac.za; contact number: 011 386 6074 and sample related queries (if applicable) shall be directed to the relevant business manager.

pp. Dr. Babatyi Malope-Kgokong

Dr Babatyi Malope-Kgokong 05/07/2022
National Manager: Academic Affairs and Research

APPENDIX E: FACULTY APPROVAL

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

29 March 2022
Person No: 2422289
PAG

Dr S Buhobe
P O Box 822
0000
Botswana

Dear Dr Seele Buhobe

Master of Medicine in Obstetrics and Gynaecology: Approval of Title

We have pleasure in advising that your proposal entitled *The use of Thyroid stimulating hormone testing in pregnancy and post-partum at Rahima Moosa Mother and Child Hospital* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX F: PERMISSION FROM ACADEMIC HEAD

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

OBSTETRICS AND GYNAECOLOGY
School of Clinical Medicine

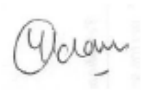
Department of Obstetrics and Gynaecology
Chris Hani Baragwanath Academic Hospital, PO Bertsham 2013, South Africa. Telephone: t 27 11 933 8156 .Fax 2711 938 1534

To: Ethics Committee,

Re: Permission for research to ethics committee- Dr S BUHOBE

Dr Buhobe is a registrar in the department of Obstetrics and Gynaecology. His research is entitled "The use of thyroids stimulating hormone testing in pregnancy and postpartum at RMMCH". This is a retrospective study using clinical and biochemical findings of blood samples pulled from eligible patients. The thyroid stimulating hormone is sent for testing as part of standard care at this hospital.
Dr Wise is the acting head of department at RMMCH and is also his supervisor and therefore cannot give permission for the study.

Yours sincerely



Professor Y. Adam
Clinical Head and Adjunct Professor
Obstetrics and Gynaecology Department
Chris Hani Baragwanath Academic Hospital
The University of the Witwatersrand

Date: 10 March 2022

APPENDIX G: ETHICS CLEARANCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research and Innovation)

TO: Dr S Buhobe
School of Clinical Medicine
Department of Obstetrics and Gynaecology
Medical School
University

E-mail: seelebuhobe@yahoo.com

CC: Supervisor: Dr A Wise
<amyjulietwise@yahoo.co.uk>
and <HREC-Medical Research Office@wits.ac.za>

FROM: Mr Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2022/08/02

REF: R14/49

PROTOCOL NO: **M220211** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.)

PROJECT TITLE: *The use of thyroid stimulating hormone testing in pregnancy and post-partum at Rahima Moosa Mother & Child Hospital*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr S Buhobe

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220211

NAME: (Principal Investigator) — Dr S Buhobe

DEPARTMENT: — School of Clinical Medicine
Department of Obstetrics and Gynaecology
Medical School
University

PROJECT TITLE: — *The use of thyroid stimulating hormone testing in pregnancy and post-partum at Rahima Moosa Mother & Child Hospital*

DATE CONSIDERED: — 2022/02/25

DECISION: — Approved unconditionally

CONDITIONS:

NOTE: — If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>

SUPERVISOR: — Dr A Wise

APPROVED BY: — Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: — 2022/08/02

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **February** and therefore reports and re-certification will be due in the month of **February** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

17 AUGUST 2022
Date

APPENDIX H: JEMDSA AUTHOR GUIDELINES

Author Guidelines

Manuscripts submitted to JEMDSA must be in the form of *Original Research, Scientific letters, Clinical Review Articles, Critical appraisals of Clinical Trials (CATs), Protocols for Debate, Brief Reports, Case Reports, Correspondence, Clinical Quiz, Opinion or Forum Papers and Editorials.* The Journal will consider the publication of National Guidelines, Conference Proceedings, Supplements, Press Releases and Book Reviews.

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5. Ethics committee approval.
6. Conflicts of interest.

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Correspondence to the Editor-in-Chief:
Prof Joel Dave, e-mail: joeldave@endocrine.co.za

Technical manuscript preparation
All JEMDSA papers must comply with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (Ann Intern Med 2000; 133:229-231 [editorial]; http://www.icmje.org, full text). All articles must be typed in 12 pt Times New Roman with 1.5 spacing. Small tables and figures (1/4–1/2 page) may be included in the manuscript. If

tables are large (i.e. 1 page landscape) or if images are large in file size (> 500 KB), they must be uploaded as separate supplementary files. Research articles should have a structured abstract not exceeding 200 words (50 for short reports) comprising: Objectives, Design, Setting, Subjects, Outcome measures, Results and Conclusions. Refer to articles in recent issues for guidance on the presentation of headings and subheadings.

Abbreviations
These should be spelt out when first used in the text and thereafter used consistently. Scientific measurements: These should be expressed in SI units except: blood pressure should be given in mmHg and haemoglobin values in g/dl. If in doubt, refer to 'uniform requirements' above. Illustrations: Figures consist of all material that cannot be set in type, such as photographs and line drawings. If any tables or illustrations submitted have been published elsewhere, the author should obtain written consent to republication from the copyright holder and the author(s). All illustrations, figures etc must be of high resolution/quality, preferably jpeg or equivalent but not PowerPoint, and must be uploaded as separate supplementary files.

References
References should be inserted in the text as superior numbers and should be listed at the end of the article in numerical and not in alphabetical order. Authors are responsible for verification of references from the original sources. References should be set out in the Vancouver style using approved abbreviations of journal titles; consult the List of Journals in Index Medicus for these details.

Unpublished observations and personal communications may be cited in the text, but not in the reference list. Sample references can be found at: http://www.nlm.nih.gov/bsd/uniform_requirements.html

Articles in Journals

- *Standard journal article*
  Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7.
- *More than six authors:*
  Rose ME, Huerbin MB, Melick J, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

Books

- *Personal author(s)*
  Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

Electronic Material

- *Journal article on the Internet*
  Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 3 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm. Accessed 3 June 2007

- *Monograph on the Internet*
  Foley KM, Gelband H, editors. Improving palliative care for cancer [monograph on the Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap.edu/books/0309074029/html/. Accessed 6 January 2007
- *Homepage/Web site*
  Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/. Accessed 3 May 2008

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3. All author details (full names, qualifications and affiliation) must be provided.
4. The full contact details of corresponding author (tel, fax, e-mail, postal address) must be on the manuscript.
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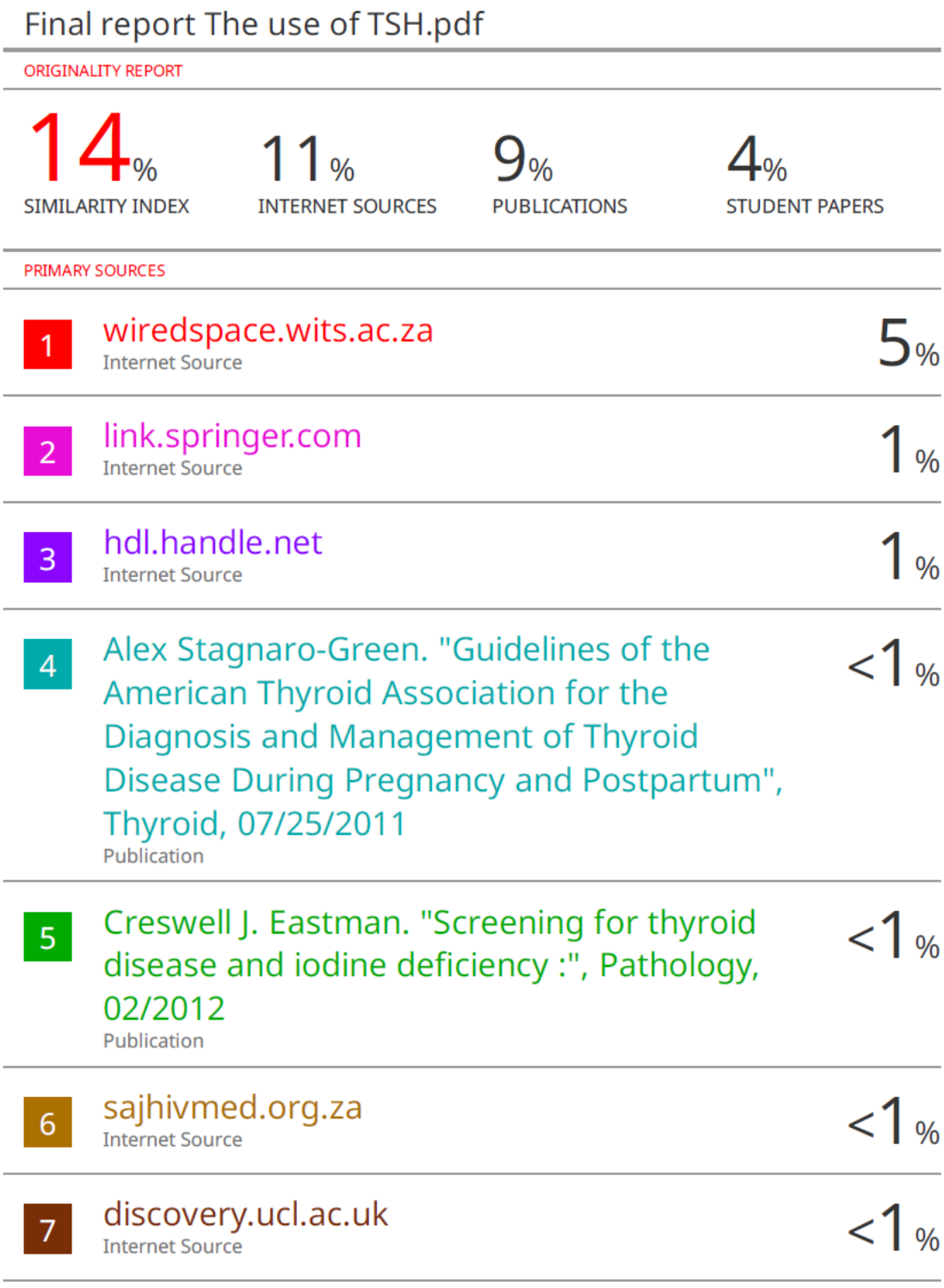
7. Please consult the guide on Vancouver referencing methods at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
8. It must be clear where every figure and table should be placed in the text. If possible, tables and figures must be placed in the text where appropriate. If too large or impractical, they may be featured at the end of the manuscript or uploaded as separate supplementary files.
9. All photographs must be at 300 dpi and clearly marked according to the figure numbers in the text. (Figure 1, Table II, etc.)
10. Scientific measurements: These should be expressed in SI units except: blood pressure should be given in mmHg and haemoglobin values in g/dl. If in doubt, refer to 'uniform requirements' above.
11. All numbers below ten, without percentages or units, must be written in words.
12. Figure numbers: Arabic; Table numbers: Roman,

13. Abbreviations: These should be spelt out when first used in the text and thereafter used consistently.
14. The submission must be reviewed by a language expert proficient in UK English.

APPENDIX I: TURNITIN REPORT



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