Dedication

To my parents

To my wife

To my family

And to my colleagues

Isam

Acknowledgements

Allah says: "Who just thank, thanks for himself." (Verse 40 Alnaml). Prophet says: "Who does not thank people he does not thank Allah". It is beautiful thanks and gratitude that is credited to my family, so I can extend my deepest thanks and gratitude to my supervisor Dr Ghada Abdurrahman Elfadil and Dr Abdelgadir Ali Elmugadam whom are kindly guided me to accomplish this research. Thanks to Dr Isam Farah, Dr Omer Abdu Liemon, Dr Abd allah Ibrahim Eltiraifi whom are senior consultants of medicine for their support the research by clinical examination for the study groups and releasing out of the cases. Thanks for Omdurman teaching hospital central laboratory. Asia medical center laboratory, and albogaa special medical center laboratory for their support by collection of the specimens , specimens storage , and their analysis . Thanks to patients and volunteers for their support by their specimens and special in formations Finally thanks to all who helped me to accomplish this research

Abstract

High titers of antibodies to anti thyrotropin receptor(TRA-Ab), and Thyroperoxidase antibodies(TPO-Ab) are the hallmarks of human autoimmune thyroid diseases. The aim of this study was to assess the antibodies in Sudanese hyperthyroidism (mean age 33.22±10.04, range 19-59 years) with hyperthyroidism and graves' disease. One hundred Sudanese patients with hyperthyroidism(50with hyperthyroidism and clinically diagnosed with graves' disease, 50 with hyperthyroidism and clinically diagnosed without graves' disease), and fifty apparently healthy as control group, age and sex were matched. Study done in Endocrinology Outpatient Clinic at Omdurman Teaching Hospital, Khartoum state, Sudan, during the period June 2011 to June 2013.

Thyroid function test (FT3, FT4, and TSH) was determined by using fully automated chemical analyzer (ROCH ELECSYS) with COBAS kits, and anti Thyroperoxidase antibodies, and anti thyrotropin receptor antibodies were determined by ELISA technique with Euro immune Kits. Analysis of the data was performed using the SPSS , P < 0.05 considered significant.

Study showed that there were significantly high serum FT3, anti TRA, TPO antibodies among the Sudanese patients with Graves disease compared with patients with hyperthyroidism. 90% of patients with graves' disease had positive TRA antibodies, and 16% had positive TPO antibodies.

In conclusion, the parameters, FT3, anti-TRA- Ab, and anti-TPO-Ab can be used as a biochemical panel for differential diagnosis of Graves' disease from hyperthyroidism.

المستخلص

تتميز امراض الغدة الدرقيةالمناعيةالداتية بمعدلات عالية من الاجسام المضادة لمستقبلات الثيروتروبين 0

Thyroperoxidase وإنزيم الثيروبيروكسيديز وThyroperoxidase والنين الدين يعانون من الدراسة هو قياس الاجسام المناعية المضادة للعدة الدرقية لدي المرضي السودانيين الدين يعانون من فرط نشاط الغدة الدرقية فرط نشاط الغدة الدرقية عير المناعي وكذلك المرضي الدين يعانون من فرط نشاط الغدة الدرقية المزمن(داء قريفز)(متوسط الاعمار 22 و33±10 ومدي مقداره 15 الى59 ستة

الدين شاركوا في هدة الدراسة عدد 50 من المرضي الدين يعانون من داء قريفز وتم تشخص حالاتهم بواسطة استشاري الطب الباطني وغير خاضعين لعلاج وعدد 50 مريض يعلنون من فرط نشاط الغدة الدرقي غير المزمن وتم تشخيص حالاتهم بواسطة استشاري الطب الباطني وعدد متطوع صحيح علي ما يبدو 0تمت مطابقة النوع العمر لدى عينات الدراسة

الدراسة أجريت في عيادة الغدد الصماء العيادات الخارجية في مستشفى أم درمان التعليمي الخرطوم اختبار وظيفة الغدة الدرقية (FT4، FT3، وTSH) تم تحديد باستخدام محلل كيميائى الى بالكامل (ELECSYS ROCH) مع مجموعات كوباس وتم تحديد الأجسام المضادة الثيروتروبين والثيروبيروكسيديز بواسطة تقنية ELISA مع أطقم المناعة اليورو. تم إجراء تحليل البيانات 0.05> P کأی مع اختبار باستخدام کبیرة. تعتبر مربع وأظهرت الدراسة أن هناك ارتفاع كبير في مستوي FT3 والأجسام المضادة TPO بين المرضى السودانيين المصابين بمرض جريفز مقارنة مع المرضى الذين يعانون من فرط نشاط الدرق. وكان 90% من المرضى الذين يعانون من مرض جريفز الأجسام المضادة TRA إيجابيه وكان 16٪ TPO الأجسام المضادة إيجابية.

وفي الختام,يمكن أن تستخدم ر FT3 ،TRA-AB ،TPO-AB في تشخيص داء قريفز

Contents

Subject	page NO
Dedication	I
Acknowledgements	п
Abstract	III
ـــــالمستخلص	IV
Contents	VI
List of tables	IX
List of figures	X
Abbreviations	XI
Chapter one	1
1.1Introduction	1
1.2 Rationale	3
1.3 Objectives	3
Chapter two Literature review	7
2.1. Thyroid gland	7
2.1.1Thyroid-stimulating hormone	8
2.1.1.2 Thyroxin(T4)	10
2.1.1.3Triiodothyronine(T3)	10
2.1.1.4 Calcitonin	11
2.1.2 Disorders of thyroid gland	12

2.1.2.1 Classifification of endocrinophasis16		
2.1.2.1.1 :Hypothyroidism16		
2.1.2.1.2 Hyperthyroidism(thyrtoxicosis)17		
2.1.2.1.2.1 Graves disease18		
2.1 .2.1.2.1.1 Historical background		
2.1 .2.1.2.1.2 Clinical Manifestations of graves' disease18		
2.1 .2.1.2.1.3 Autoimmunity and graves' disease19		
2.1 .2.1.2.1.4 Graves disease and pregnancy20		
2.1 .2.1.5 GieneticFactorsforgravesdisease22		
2.1 .2.1.2.1.6 Complications of graves' disease23		
Chapter (3)		
3.Materials and Methods		
3.1 Study design27		
3.2 Study area and period27		
3.3Study population27		
3.4 Inclusion criteria27		
3.5 Exclusion criteria27		
3.6 Ethical consideration28		
3.7 Data collection and samples process27		
3.7.1 Measure ment of thyroid hormons and antibodies27		
3.7.1.1 Measurement of serum TSH		
3.7 .1.1 .1 principle of TSH 27		
3.7.1.1.2 procedure of TSH		
3.7.1.2. free thyroxin(FT4)28		
3.7.1.2.1Test principle for free thyroxin: (appendix-II)28		
3.7.1.2.2:procedures for FT4: (appendix-II)28		
3.7.1.3. free tetraiodothyronine(FT328		

3.7.1.3.1principle of free tetraiodothyronine(FT328
3.7.1.3.2 procedure of free tetraiodothyronine(FT328
$measurement of thy rotrop in recepter antibodies (TSHRABS) \\ \\ and \\ \\$
Thyroperoxidase antibodies (TPODABS)levels29
3.7.1.4. SHRABS :
3.7.1.4.1 Principles for TSHRABS29
3.7.1.4.2 procedure for(TRAbs)30
3.7.1.5 TPOABS 31
3.7.1.5.2 principle for (TPOAbs31
3.7.1.5.2 procedure for (TPOAbs) 31
Quality control32
.Data analysis32
Chapter Four
4. Results33
Chapter five
5.1 Discussion46
5.5.2Conclusion50
5.3 Recommendations52
References53
Appendices62

List of tables;

Table(4.1): Comparison between means of TSH, FT3,FT4, TPO, TRA in
Sudanese patients with hyperthyroidism, hyperthyroidism and clinically
diagnosed without graves' disease, Sudanese patients with graves'
disease, compared with control group39
Table(4.2): Comparison between means of TSH, FT3,FT4, TPO, TRA in
Sudanese patients with hyperthyroidism and clinically without Graves disease
compared with Graves disease group39
Table (4.3): cross tabulation between hyperthyroidism, Graves disease and
family history41
Table(4.4): cross tabulation between TPO antibodies and cases41
Table (4.5): cross tabulation between TRA antibodies and cases42

List of figures:

Fig (4.1): shows correlation between TRA antibodies and FT3 among
Sudanese patients with Graves disease. Significant positive correlation43
Fig(4.2): shows correlation between TRA antibodies and TPO among Sudanese
patients with Graves disease, Significant positive correlation43

Abbreviations

FT3	Free triiodothyronine
FT4	Free tetraiodothyronine
GD	Graves disease
TPOAbs	Thyroid peroxidase anti bodies
TRAbs	Thyroid recepter anti bodies
TSH	Thyroid stimulating hormone
DIT	Di iodo tyrosine
MIT	Mono iodo tyrosine
TMB	Tetra methyl Benzedine
ELISA	Enzyme linked immunosorpent assay
rpm	Round per minute
nm	nanometer
mIU/L	Mili international unit per liter
Pg/ml	Pico gram per milliliter
ng/dl	Nano gram per deciliter
Pmol/ml	Pico mol per milliliter
μL	Micro liter
U/L	Unit per liter
SD	Standard deviation