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**REVIEW ARTICLE**

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# Evaluation of effect of Noncancerous Thyroid Disease on Haematological Parameters and Coagulation Profile in Sudanese Females at Reproductive Age

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## ABSTRACT

***Thyroid hormones have a crucial role in metabolism and proliferation of blood cells. Thyroid dysfunction induces different effects on blood cells such as anaemia, erythrocytosis, leukopaenia, thrombocytopaenia, and in rare cases causes' pancytopaenia. It alters RBC indices including (MCV, MCH, MCHC and RDW), affects coagulation system such as PT and APTT. This prospective cross-sectional, descriptive, hospital – based study, conducted at Almek Nimir University Hospital in females at reproductive age with noncancerous thyroid disorders during the period from 2014 to 2017 to evaluate the effect of noncancerous thyroid disorders on haematological parameters and coagulation profile. The study includes (150) females (60) with hypothyroidism, (40) with hyperthyroidism and (50) healthy females as control group. The range of ages was (18 - 48) years. The investigation were performed on venous blood samples (1.25 ml) drawn in EDTA container for complete blood count by using auto haematology analyzer ((Mindray BC-5000), (2.25 ml) drawn in trisodium citrate for***

***coagulation profile by using Coagulyzer (Clot 2S). Regarding to study result the level of haemoglobin , PCV and PT (12g/dL,37% and 13.2 second) in hypothyroidism show significant variation with P-value <0.05, in hyperthyroidism the haemoglobin,PCV and PT (12.1g/dL,36% and 13.1 second) respectively also show significant variation with p-value <0.05. The study concluded that haemoglobin was low, Platelet count was slightly decreased, minor coagulation abnormalities were observed in noncancerous thyroid disorders compared with control .So the study recommended to screening the female patients with hypothyroidism and hyperthyroidism for haematological changes to avoid the anaemia, coagulation defect, to decrease the risk of such complications (bleeding tendency, thrombosis) to avoid the problems of reproduction.***

***Key Words: Hypothyroidism, Hyperthyroidism, PT, PTT and Sudan.***

## INTRODUCTION

The thyroid is a small gland located below the skin and muscles at the front of the neck. *Thyroid Stimulating Hormone* (*TSH*) controls the thyroid gland by inducing the transport of iodine into the gland, and then the subsequent secretion of thyroxine (*T4*) and *Triiodothyronine* (*T3*) into circulation. (*T3*) is the most active metabolite, followed by (*T4*) and then the *inactive reverse* (*rT*3). The thyroid affects nearly every organ system in the body and appears to be a major regulator of metabolism. Low (*T3*) is seen with malnutrition, anorexia, severe burns, and febrile illnesses. The thyroid produces hormones that play key roles in growth and development, changes in thyroid function can have a major effect on reproductive function before, during and after conception. Thyroid disease is a common endocrinopathy found in (1%) of women of reproductive age. The prevalence of hypothyroidism in women in the reproductive age (20-40 years) varies between (2 and 4 %) (Wang and Crapo 1997, Bjoro et al., 2000). In this age group, *autoimmune thyroid disease* (*AITD)* is the most common cause of hypothyroidism (Vanderpump et al., 1995, Hollowell et al., 2000). *Hypothyroidism* is associated with a broad spectrum of reproductive disorders ranging from abnormal sexual development through menstrual irregularities to infertility (Bercovici, 2000, Vaquero et al., 2000).

## MATERIALS AND METHODS

This is a prospective cross-sectional, descriptive, hospital – based study, conducted at Almek Nimir University Hospital in females at reproductive age (18-48 years) with noncancerous thyroid diseases during the period from 2014 to 2017 to evaluate the haematological parameters and coagulation profile , Included 150 participant females (100 with thyroid diseases at reproductive age, 60 with hypothyroidism and 40 with hyperthyroidism) and (50) healthy females as control group after they agreed to sign the consent form and to fill questionnaire, Females with thyroid disorders at ages less than 18 or above 48 years, or under treatment (on warfarin, on corticosteroid) were excluded from the study. The consent of the selected individuals to the study was taken after being informed with all detailed objectives of the study and its health benefit in future. Data were collected using self-administered pre-coded questionnaire which was specifically designed to obtain information. (3.5) ml of venous blood was collected from each member (2.25 ml in trisodium citrate for coagulation study and (1.25 ml) in *EDTA* container for *CBC*) by Haematology analyzer (Mindray BC-5000). Blood in

trisodium citrate centrifuged immediately for (15 min) at (3000 rpm) to obtain plasma for estimating levels of *PT* and *PTT* by Coagulyzer (Clot 2S). The entire sample collected for study population takes ethically after information about the study and ethical approvals, letter of the faculty (Faculty of Graduates Studies and Scientific Research, Shendi University), letter of the hospital and patient acceptance form.

The gathered data was analyzed with Statistical Packages for Social Sciences (SPSS) software version (20), Independent T-test was used for calculating degree of variation. P. value<0.05 was considered significant variation.

## RESULT

The study included (150) females (60) of them with hypothyroidism (40%), (40) with hyperthyroidism (27%) and (50) as control (33%) as shown in **Table 1**.

**Table 1. Distribution of Patients and controls (%).**

| Category | NO | Percentage |
|---|---|---|
| Hypothyroidism | 60 | 40% |
| Hyperthyroidism | 40 | 27% |
| Control | 50 | 33% |

The age of the studied groups range from (18-48 years) in the age group (18-27 years),(17,7,30) females with hypothyroidism, hyperthyroidism and control respectively, in the age group (28-37 years) (16,8,8) females with hypothyroidism, hyperthyroidism and control respectively and in the age group (38-48 years) (27,25,12) females with hypothyroidism, hyperthyroidism and control respectively **Figure1**.

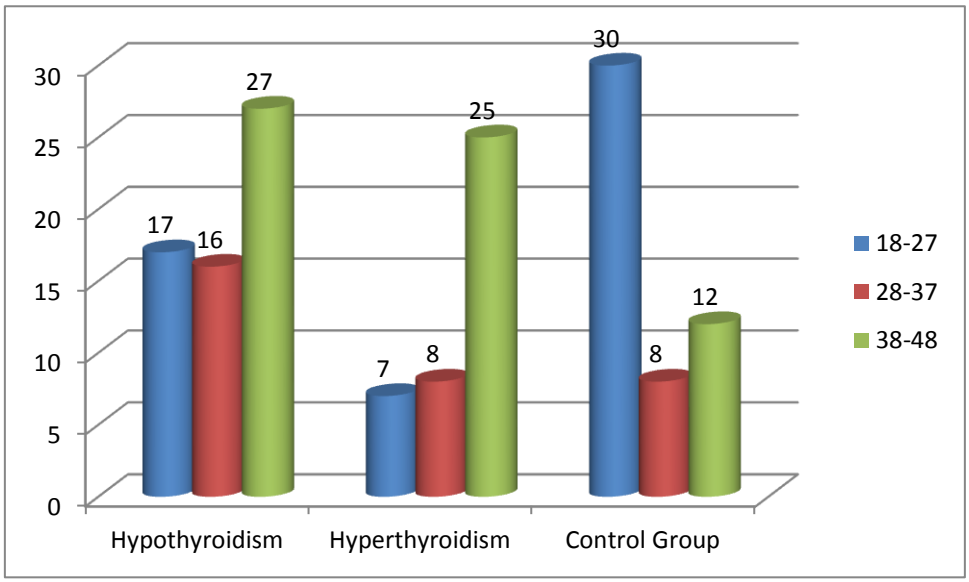


**Figure 1. Age of patients and control.**

**Table 2. Mean of RBCs parameters in female with hypothyroidism and control group.**

| | Hypothyroidism | Control | P-value |
|---|---|---|---|
| RBCs $x10^{12}$ /L | 4.2 | 4.3 | 0.19 |
| Hb g/dl | 12 | 12.9 | 0.002 |
| PCV % | 37 | 38 | 0.02 |
| MCV /fl | 87 | 89 | 0.28 |
| MCH/pg | 29 | 30 | 0.054 |
| MCHC g/dl | 33 | 34 | 0.06 |
| RDW % | 14.8 | 13.9 | 0.01 |

Fl: Femtoliter, pg: picogram, g/dl: gram per deciliter

As demonstrated in above table the haemoglobin, packed cell volume and RDW were low in female with hypothyroidism

**Table 3. Mean of RBCs parameters in female with hyperthyroidism and control group.**

| | Hyperthyroidism | Control | P-Value |
|---|---|---|---|
| RBCs $x10^{12}$ /L | 4.3 | 4.3 | 0.5 |
| Hb g/dl | 12.1 | 12.9 | 0.002 |
| PCV % | 36 | 38 | 0.007 |
| MCV /fl | 84 | 89 | 0.002 |
| MCH/pg | 28 | 30 | 0.002 |
| MCHCg/dl | 33 | 34 | 0.06 |
| RDW % | 14.9 | 13.9 | 0.02 |

As illustrated in table 3 the haemoglobin, packed cell volume .mean cell haemoglobin and RCW were low in females with hyperthyroidism

**Table 4. Mean of Hb level (g/dL) according to Age groups.**

| Age group | Hypothyroidism | Hyperthyroidism | Control Group |
|---|---|---|---|
| 18-27 | 12.1 | 11.9 | 12.8 |
| 28-37 | 12.4 | 12.8 | 12.9 |
| 38-48 | 11.9 | 11.8 | 13.3 |

As demonstrated in table above the haemoglobin level was low in the age group (38-48) years in case study.

**Table 5. Mean of TWBCs and differential count in female with hypothyroidism and control.**

| | Hypothyroidism | Control | P-Value |
|---|---|---|---|
| TWBCs $x10^{9}$ /L | 5.8 | 5.4 | 0.23 |
| Neutrophil % | 47 | 46 | 0.3 |
| Lymphocyte % | 40 | 40 | 0.8 |
| Monocyte % | 9 | 11 | 0.01 |
| Eosinophil % | 2.8 | 2.9 | 0.7 |
| Basophil % | 0.9 | 1.1 | 0.03 |

**Table 6. Mean of TWBCs and differential count in female with hyperthyroidism and control.**

| | Hyperthyroidism | Control | P-Value |
|---|---|---|---|
| TWBCs x$10^9$ /L | 5.9 | 5.4 | 0.2 |
| Neutrophil % | 50 | 46 | 0.02 |
| Lymphocyte % | 36 | 40 | 0.05 |
| Monocyte % | 10 | 11 | 0.18 |
| Eosinophil % | 2.9 | 2.9 | 0.9 |
| Basophil % | 0.9 | 1.1 | 0.004 |

**Table 7. Mean of Platelet count and MPV in female with hypothyroidism and control.**

| | Hypothyroidism | Control | P-Value |
|---|---|---|---|
| Platelet ×$10^9$/L | 240 | 253 | 0.3 |
| MPV | 10.3 | 11 | 0.01 |

**Table 8. Mean of Platelet count and MPV in female with hyperthyroidism and control.**

| | Hyperthyroidism | Control | P- Value |
|---|---|---|---|
| Platelet×$10^9$/L | 248 | 253 | 0.7 |
| MPV | 10.5 | 11 | 0.07 |

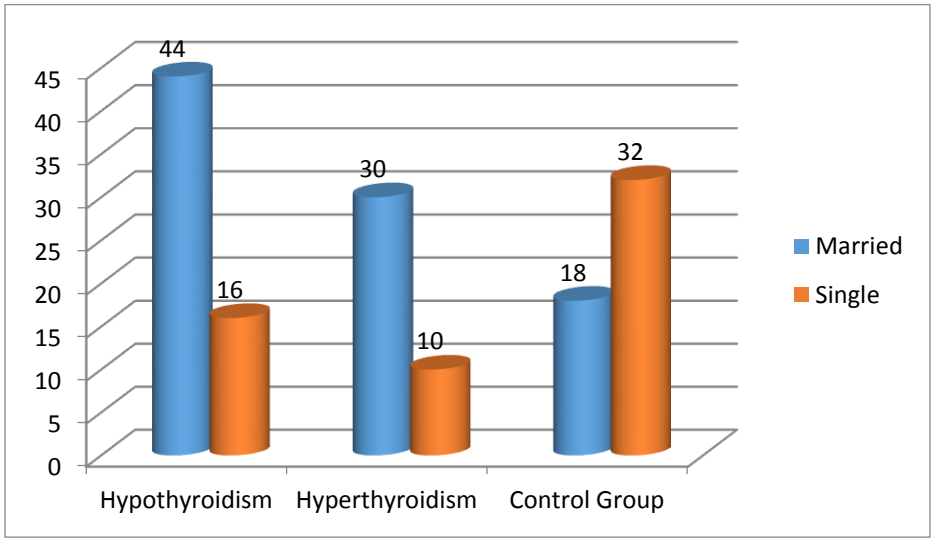


**Figure 2. Marital status of the patients and control.**

**Table 9. Mean of PT, INR and PTT in female with hypothyroidism and control.**

| | Hypothyroidism | Control | P-Value |
|---|---|---|---|
| PT/second | 13.2 | 13.8 | 0.000 |
| INR | 1 | 1.1 | 0.002 |
| PTT/second | 33.3 | 35.5 | 0.06 |

**Table 10. Mean of PT, INR and PTT in female with hyperthyroidism and control.**

| | Hyperthyroidism | Control | P-Value |
|---|---|---|---|
| PT/second | 13.1 | 13.8 | 0.001 |
| INR | 1 | 1.1 | 0.003 |
| PTT/second | 33.4 | 35.5 | 0.12 |

**Table 11. Past history of bleeding and thrombotic complications in female with hypothyroidism.**

| Complication | Frequency | Percent % |
|---|---|---|
| Abortion | 22 | 36.7 |
| No complications | 38 | 63.3 |
| Total | 60 | 100 |

**Table 12. Past history of bleeding and thrombotic complications in female with hyperthyroidism.**

| Complication | Frequency | Percent% |
|---|---|---|
| Abortion | 13 | 32.5 |
| Thrombosis | 1 | 2.5 |
| Menorrhagia | 1 | 2.5 |
| No Complications | 25 | 62.5 |
| Total | 40 | 100 |

**Table 13. Mean of PT, PTT and platelet count in female with hypothyroidism with past history of bleeding and thrombotic complications.**

| Category | No | PT/sec | PTT/sec | Platelet×$10^9$/L |
|---|---|---|---|---|
| Female with hypothyroidism and abortion | 22 | 13 | 32.3 | 244 |
| Female with hypothyroidism and without bleeding disorders | 38 | 13.7 | 33.9 | 238 |
| Control | 50 | 13.8 | 35.5 | 253 |

**Table 14. Mean of PT, PTT and platelet count in female with hyperthyroidism with past history of bleeding and thrombotic complications.**

| Category | NO | PT/sec | PTT/sec | Platelet×$10^9$/L |
|---|---|---|---|---|
| Female with hyperthyroidism and history of abortion | 13 | 12.9 | 31.5 | 215 |
| Female with hyperthyroidism and history of thrombosis | 1 | 12.5 | 34.8 | 286 |
| Female with hyperthyroidism and history of menorrhagia | 1 | 13.9 | 21.8 | 194 |
| Female with hyperthyroidism and without bleeding or coagulation disorder | 25 | 13.4 | 34.8 | 266 |
| Control | 50 | 13.8 | 35.5 | 253 |

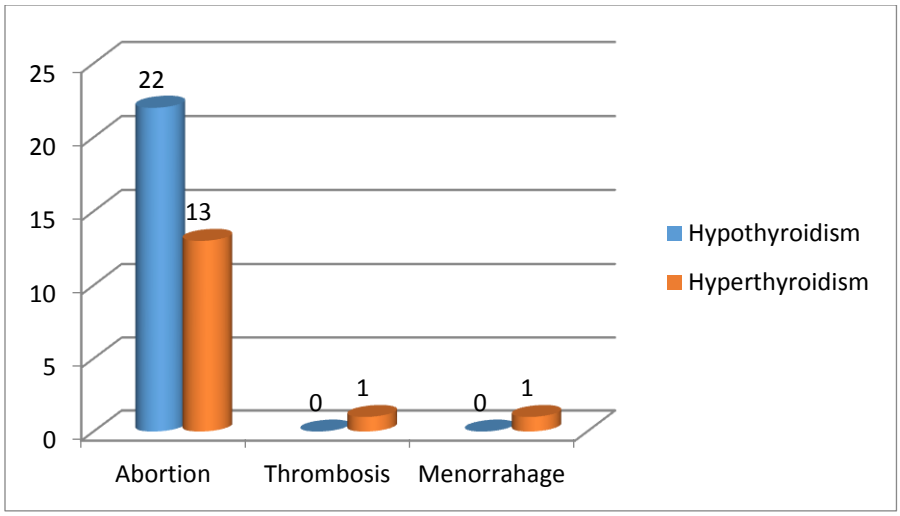


**Figure 3. Frequency of bleeding tendency and Coagulation disorders in female with thyroid disorders.**

## DISCUSSION

Thyroid gland as the largest and the most important endocrine gland of human body with the secretion of two hormones, *T3* and *T4*, has a major role in metabolism of cells and organs. Thyroid gland also has a crucial effect on erythropoiesis by induction of erythropoietin secretion and also proliferation of erythroid progenitors (Fujita, 1975, Golde et al., 1977, Das et al., 1975).

The most common thyroid dysfunctions, hypothyroidism and hyperthyroidism affect blood cells and cause anaemia with different severity. These thyroid disorders also cause thrombocytopaenia, leukopaenia and even in rare cases cause pancytopaenia (in hypothyroidism). Other blood indices including *MCV, MCH, MCHC, Hb* also could change during thyroid dysfunction (Kawa et al., 2010).

According to data obtained in patients with hypothyroidism, although all parameters were decreased except *RDW* which increased, only *Hb, PCV* and *RDW* showed statistically significant difference between female with hypothyroidism compared to the control group (*P-value <0.05*). High *RDW* with the decreased MCV can be due to the slight anaemia seen in some groups (anaemia of chronic disorder). The study agree with the study of Kawa MP and et al in 2010 who reported that *RBC, HB, MCH and MCHC were* decreased in hypothyroidism, while differ in *HCT and MCV* when they stated that they were increased (Kawa et al., 2010, Dorgalaleh, and Mahmoodi, 2013).

In females with hyperthyroidism although all parameters were decreased except *RDW* which increased, only *Hb, PCV, MCV, MCH* and *RDW* when compared with the control group showed statistically significant difference (*P-value <0.05*) but the *RBCs* count and *MCHC* had no significant difference, Also *high RDW* with the *decreased MCV* can be due to the slight anaemia seen in some groups (anaemia of chronic disorder). This study didn't coincide with the study of Kawa MP and et al in 2010 who reported that *RBC, HB and HCT* in patients with hyperthyroidism were significantly higher than control groups & this looks strange and may be due to the good medical supervision in those patients which was not available to the patients while they concluded that *MCH and MCHC* were lower in their study which agreed with the findings.

*Hb* was low in females with these disorders in all age groups compared with control group. The *Hb* in age (18-27) were (12.1, 11.9 and 12.8 g/dL) and in age (28-37) were (12.4, 12.8 and 12.9g/dL) and in age (38-48) were (11.9, 11.8 and 13.3g/dL) in hypothyroidism, hyperthyroidism and control groups, these results indicated that these disorders lead to decrease in *Hb level* and anaemia was seen in some patients.

**In hypothyroidism** the results showed statistically significant difference in monocyte and basophil count (*P-value <0.05*) but did not show statistically significant difference in *WBC, neutrophil, lymphocyte* and *eosinophil count* (*P-value>0.05*),

**In hyperthyroidism** the *neutrophil and basophil* showed statistically significant difference compared with control group (*P-value<0.05*) but the *WBC*, *lymphocyte, monocyte and eosinophil counts* didn't show significant difference (*P-value >0.05*).

Regarding to the result there no significant difference in *PLT* count in two groups of females and control (*P-value >0.05*), whereas; *MPV* had significant difference in hypothyroidism (*P-value <0.05*).

In a study by Geetha J and Srikrishna R in 2012, red blood cell indices were compared with patients with hypothyroidism and hyperthyroidism revealed that *RDW and MCV* in these two groups of patients in comparison to euthyroid individuals were statistically significant difference but other *RBC parameters* like *HB and HCT* did not show any significant difference in comparison with euthyroid status but in this performed study, *HB, PCV and RDW* were statistically different between patients with hypothyroidism and hyperthyroidism and control group but *RBCs and MCHC* showed no difference and *MCV and MCH* were significantly different in hyperthyroidism (Geetha and Srikrishna, 2012).

Lima C.S and et al in 2006 described four patients with Graves' disease who had severe pancytopaenia. Finally they concluded that thyroid evaluation for all patients with pancytopenia should be performed even though no related symptoms are found (Lima et al., 2006).

**The results revealed that** *PT, PTT and INR* were decreased in the patients but it was statistically significant in *PT and INR* only (*P-value <0.05*) and not statistically significant in *PTT*.

To the study conducted by Mohamed-Ali MS, Ahmed RO (A significantly decrease in *PT* was observed in hypothyroid patients, and hyperthyroid patients compared with the control group, *PTT* was significantly decreased only in hyperthyroid patients compared to the control group.[(10)] But in this study the *APTT* were decreased in the two groups compared with control groups but they were not statistically significant as mentioned above.

**The study revealed that**, (22, 13) females had abortion in hypothyroidism and hyperthyroidism respectively and one female with *DVT* and other one with menorrhagia in female with hyperthyroidism.

In this study; (60) females with hypothyroidism (22) of them had a bleeding tendency (36.7%) such as abortion and (38) did not show bleeding tendency (63.3%) **The hyperthyroidism status** included (40) females (13) of them had abortion (32.5%), one female had *DVT* (2.5%), also another one female had menorrhagia (2.5%) and other (25) females did not show any disorders (62.5%) as mentioned.

**Regarding the results obtained**; this study correlated between history of complications of pregnancy (bleeding tendency and coagulation disorders) by estimation of *PT, PTT* and platelet count our result show that *PT* (13, 13.7 and 13.8), *PTT* (32.3, 33.9 and 35.5) and platelet count

was (244, 238 and 253) in females with abortion, without abortion in hypothyroidism and control respectively. The above results showed that *PT and PTT* in abortion was less than without abortion due to the disturbance in coagulation factor, but the Platelet count was more in the case of abortion because the bleeding induces bone marrow to produce more platelets, and there were low in *PT, PTT* and Platelet count compared with control groups.

The above calculated results showed that the *PT* (12.9, 12.5, 13.9, 13.4 and 13.8), *PTT* (31.5, 34.8, 21.8, 33.8 and 35.5) platelet count (215, 286, 194, 266 and 253) in female with abortion, *DVT*, menorrhagia and had no disorders in hyperthyroidism and control respectively, this result showed *PT and Platelets* were less in menorrhagia.

The study concluded that haemoglobin was low, Platelet count was slightly decreased, minor coagulation abnormalities were observed in noncancerous thyroid disorders compared with control.

**According to the cumulative data obtained**; the study recommended to screening the female patients with hypothyroidism and hyperthyroidism for haematological changes to avoid the anaemia, coagulation defect and to decrease the risk of such complications (bleeding tendency, thrombosis) to avoid the problems of reproduction.

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