



RESEARCH ARTICLE

ASSESSMENT OF SERUM PROLACTIN IN HYPOTHYROIDISM INFERTILE FEMALES, IN WHITENILESTATE, SUDAN

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Abstract

Background: Thyroid dysfunction is a public health problem in White Nile State in Sudan. It is majorly caused by iodine deficiency. Hyperprolactinemia, the clinical condition associated with infertility is resulted from a number of causes.

Objectives: This study aimed to assess the relationship between thyroid hormone and prolactin serum level in Sudanese hypothyroidism infertile females.

Material and Method: One hundred Sudanese females with hypothyroidism were compared with eighty's healthy control. Blood samples were collected after an overnight fasting. Serum TSH, T₃, T₄ were analyzed using fully automated immunoassay analyzer system (AIA)TOSOH BIOSCINCEAIA360. Prolactin is measured using i-CHROMA™.

Results: Hypothyroidism patients showed increased prolactin levels. Prolactin is increased in 40% of hypothyroidism patients. Also, TSH levels were significantly positively correlated with prolactin levels.

Conclusion: The serum prolactin levels were increased in hypothyroidism infertile patients.

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Introduction:-

Human require iodine, the essential component for thyroid hormone; T₃ and T₄ synthesis. According to the Food and Nutrition Board of the National Research Council (1970); the optimum requirement for adult is in the range of 150–300microgram/day, the requirement for iodine by the mother during pregnancy is 250–300microgram /day during lactation the requirement is 225– 350microgram /day.⁽¹⁾

The fetus is totally dependent in early pregnancy on maternal thyroxin for mental brain development. Adequate maternal dietary intake of iodine during pregnancy is essential for maternal thyroxin production and later for thyroid function in the fetus.⁽²⁾ A safe supply is estimated to be 50 - 1000 microgram /day, failure to have adequate iodine

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leads to insufficient production of these hormones which affect many different part of the body, particularly heart, liver, kidney, and developing brain. Globally 2.2 billion people worldwide live in area with iodine deficiency IDD (38% of the world's population).⁽³⁾

World health organization (WHO) in 1993, reported that IDD affect 320million people mainly in developing countries. These effects include individually goiter, and hypothyroidism. In children hypothyroidism causes impaired mental and physical development.⁽⁴⁾ Hypothyroidism and deficiencies of iodine are most important nutritional problems in most developing countries.⁽⁵⁾ More than one billion persons are at risk of iodine deficiency worldwide and 200million have goiter. In Africa, goiter is endemic in many countries for example notably Congo, Uganda, Kenya, and Sudan.⁽⁶⁾ In Sudan hypothyroidism and iodine deficiency disorders are a causes of serious health problems in many areas. The prevalence of goiter was estimated to be 87% in Darfur states in western Sudan, 13.5% in Port Sudan in eastern Sudan, and 17% in the capital, Khartoum. However, in White Nile State 74%,⁽⁶⁾ and 43.3% were reported.⁽⁷⁾

A high level of TSH stimulate prolactin secretion and causes ovulatory dysfunction and leading to infertility. In hypothyroidism (underactive thyroid gland), a portion of the brain called the hypothalamus will secrete hormones to try to stimulate the thyroid gland (TSH). This same hormone may also causes excess prolactin to be produced from the pituitary.⁽⁸⁾ Prolactin hormone (PRL) is a lactogenic hormone secreted from the anterior pituitary gland in both men and women. It is a single chain polypeptide hormone made of 199 amino acids.⁽⁹⁾ Women normally have slightly higher levels than men. Normal level of prolactin in males (≥ 18 years) is 4.0-15.2ng/mL, however, in females (≥ 18 years) it is 5-35ng/ml.⁽⁹⁾ During pregnancy, PRL levels increase progressively to become 10 to 20 times the normal values. PRL levels are associated with galactorrhea and amenorrhea. PRL concentrations have been shown to be increased by estrogens, thyrotropin-releasing hormone (TRH), and several drugs affecting dopaminergic mechanism. PRL levels are elevated in renal disease, hypothyroidism and in some situations of stress and exercise.⁽¹⁰⁾ The release of PRL is episodic and demonstrates diurnal variation. Biological actions of prolactin are mostly related to lactation and reproduction and exerts multiple effects regulating both differentiation and proliferation in diverse tissues.⁽¹⁰⁾

Hyperprolactinemia was observed in 39 % of the patients with untreated primary hypothyroidism.⁽¹¹⁾ The prolactin level was elevated greater than 14.0ng/dl.⁽¹¹⁾ According to Adele, et al, in 2011, increase level of serum prolactin has been reported in 30% of patients with primary hypothyroidism due to the stimulatory effect of TRH on lactotrophs.⁽¹²⁾ Kamal, et al, in 2016, reported, hyperprolactinemia and hypothyroidism are important and widely prevalent causes of infertility.⁽¹³⁾ Intisar Reehem, in 2016, found that there is a positive correlation between hypothyroidism and hyperprolactinemia. There is a high incidence of hyperprolactinemia in infertile women.⁽¹⁴⁾ In areas with thyroid dysfunction in White Nile State, the major cause of hypothyroidism is the dietary iodine insufficiency. Decreased thyroid hormone level was of a high incidence. TSH production is increased, and there is positive correlation between hypothyroidism and hyperprolactinemia.⁽¹⁵⁾

This study aimed to assess the relationship between thyroid hormone and serum prolactin in Sudanese hypothyroidism infertile females.

Materials & Methods:-

This descriptive-cross-sectional study is carried out in White Nile State's three major cities; Kosti, Rabak and Kenana, in the period from April 2017 to May 2020. The study population include a 100 diagnosed and confirmed hypothyroidism females patients, their age range (20-40 years) and having TSH level above 4.0mIU/dl, with complains of weight gain, muscle cramps, generalized weakness. Eighty females were considered as control group, their age range (18-50 years). They are having TSH in the normal level (0.4-4.3mIU/dl) and having no signs or symptoms of acute or chronic illness. All patients whom they were with pregnancy, lactation, hypertension, diabetes, cardiovascular disease, liver disease and renal failure, and those who are taking any vitamins or minerals were excluded, they are not participate in this study.

Before beginning of this study the permission to conduct the research was obtained from the ministry of health and El Imam El Mahdi committee. Verbal and written consent were obtained from all patients, controls group, their families and health officials.

Samples and laboratory work:

Five milliliters of fasting blood sample obtained from each participant of study population in the morning of day three of the menstrual cycle for serum biochemical analysis. Serum was separated and stored for further analysis. All thyroid hormones including serum TSH, T₃, and T₄ were estimated using automated immunoassay analyzer (AIA) system, TOSOH BIOSCINCE AIA 390. And the using of i-CHROMATM PRL test for measurement of serum prolactin hormone in Kosti Hospital, Renal Dialysis unit's laboratory.

Statistical analysis:

Data obtained from patients and control group were analyzed using SPSS (Statistical Package for Social Sciences) Software for windows, version 20, and Microsoft excel 2007. Results were presented as means and standard deviations, Pearson's correlation was applied with the significant p-value being set at 0.05.

Results:-

This study includes (100) females, diagnosed and confirmed as hypothyroidism patients. Their mean age is 34 years (range 20-45 years) and other (80) females as a control group their mean age is 32.6 years (18-50 years). The statistical analysis for the tested parameters are presented in tables and figures.

Out of the 100 females patients, 40 (40%) have increased prolactin level.

There is a significant higher variation in means of prolactin (PRL) and thyroid stimulating hormone (TSH) levels of patients when compared to those of controls. Mean values of T₃, and T₄ of patients are lower than those of controls, Table, 1.

There is 32 (80%) infertile women their results show positive correlation between infertility and hyperprolactinemia, Table, 2.

There is a positive correlation between prolactin and TSH levels ($r = 0.371$), figure, 1.

T₃ and T₄ show negative correlation with prolactin ($r = -0.397$, $r = -0.090$), these results are shown in figures, 2, and 3, respectively.

Clinical symptoms were slightly different in hypothyroidism patients with and without hyperprolactinemia. However, the percentage increased in normal prolactin levels, Table, 3.

Menstrual dysfunction were reported in about (60) 60% hypothyroidism females while it was only (16) 20% in (80) of controls.

Table 1:- Mean values and standard deviation of Prolactin, T₃, T₄ and TSH of patients and control.

Subjects n=(180)	PRL	T ₃	T ₄	TSH
Patients n= (100)	42.9±20.3	0.90± 0.6	0.82± 0.67	7.05± 3.00
Control n = (80)	16.7± 16.9	1.12± 0.99	1.20± 0.82	01.90± 2.47
Normal Range	(2–25 ng/ml)	0.25–0.6 ng/dl	1.0– 3.0 ng/dl	0.5 – 4.7 mIU/ml
P – value	≤ 0.05	≤ 0.05	≤ 0.05	≤ 0.05

Table 2:- Prevalence of infertility among hyperprolactinemic females.

Hyperprolactinemic females	No.	Percentage (%)
Fertile women	8	20 %
Infertile women	32	80 %
Total	40	100%

Table 3:- Clinical symptoms in hypothyroidism female patients with or without hyperprolactinemia.

Normal prolactin levels n = 60 (60%)	High prolactin levels n= 40 (40%)	Symptoms

35 (58%)	22 (55%)	Fatigue
18 (30%)	8 (20%)	Dry skin
20 (33.3%)	12 (30%)	Cold intolerance
35 (58%)	18 (45%)	Muscle cramp
8 (13%)	2 (5%)	Weight gain

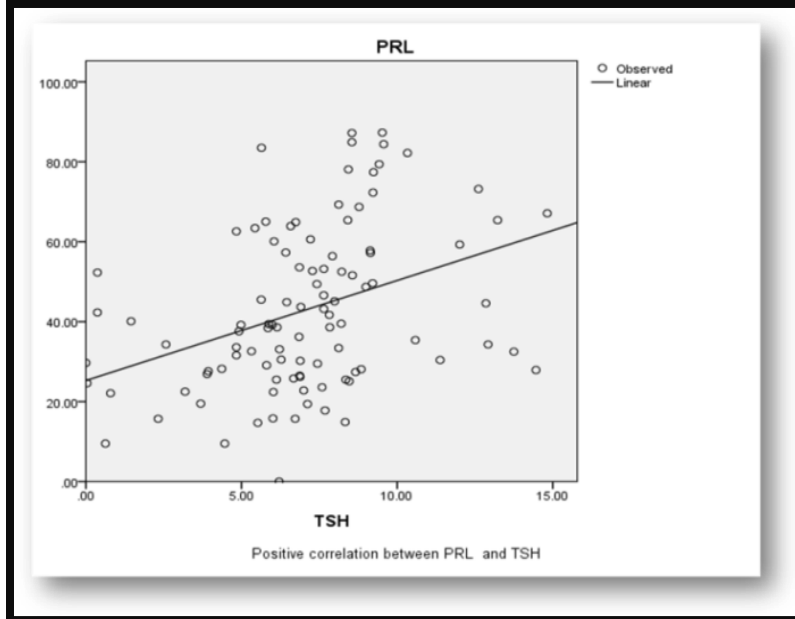


Figure 1:- Correlation between PRL levels and TSH among hypothyroid females patients (r= 0.371).

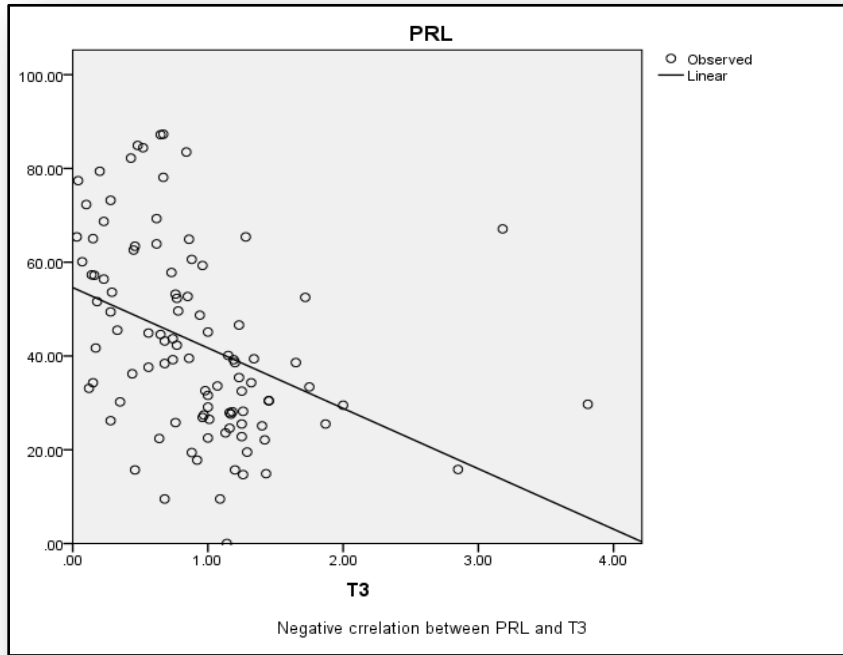


Figure 2:- Correlation between PRL levels and T₃ among hypothyroid females' patients (r = -0.397).

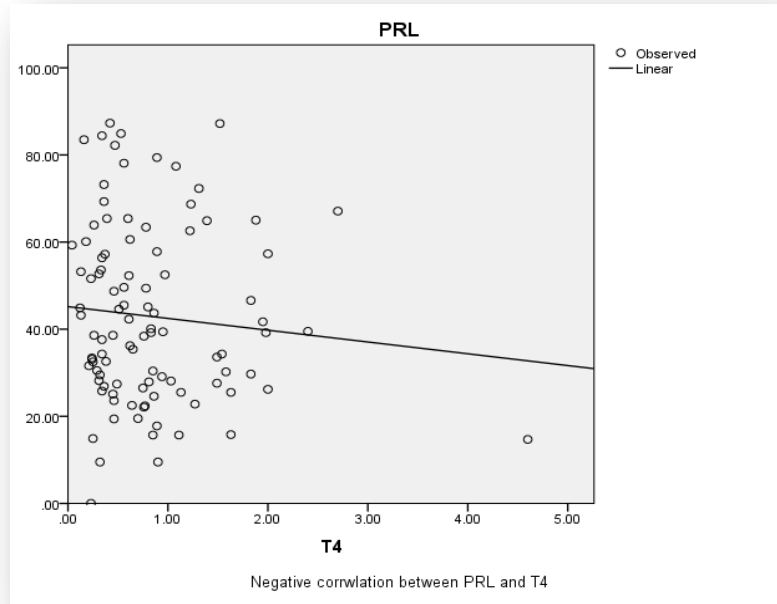


Figure 3:- Correlation between PRL levels and T_4 among hypothyroid female patients ($r = -0.090$).

Discussion:-

In this study we found higher prevalence of hyperprolactinemia in hypothyroidism female their age in the range of (20–45 years). There is an elevation of prolactin in 40% (40%) of women that are confirmed as hypothyroidism patients. The mean prolactin level in hypothyroidism females in this study is (42 ± 20.3) . Similar results are reported by Avasthi, in 2006 and Pratigya, in 2019. A positive correlation is found between hyperprolactinemia and infertility.

Significant positive correlation ($p \leq 0.05$) between thyroid stimulating hormone (TSH) and prolactin (PRL) levels in hypothyroidism patients ($r = 0.371$) was observed. This finding is agreed with finding of Deepali, in 2018. In this study, means of T_3 and T_4 in hyperprolactinemic women are significantly lower than those of controls ($P \leq 0.05$). Similar findings are reported by Adele, et al, in 2011. In this study, thyroid stimulating hormone levels are correlated negatively and significantly with both T_3 , T_4 in all study group. Significant negative correlation between prolactin and T_3 , T_4 in all patients with hypothyroidism is also observed ($P \leq 0.05$). Similar findings are conducted in study of Kamal, et al, in 2016.

Also this study revealed that 40% of the participated patients are having high prolactin level. These results are similar to results of Honbo, et al, 1978. Honbo, et al, in 1978, reported that hyperprolactinemia is found in 39% of patients with untreated primary hypothyroidism. ⁽¹¹⁾ Our result of prolactin level is greater than 40 ng/dl. The prolactin level is elevated greater than 14.0 ng/dl. ⁽¹¹⁾ Also, Adele, et al, in 2011 reported an increased level of serum prolactin in 30% of patients with primary hypothyroidism. Adele, et al, in 2011, conclude that the increased level of prolactin in patients with primary hypothyroidism is due to the stimulatory effect of TRH on lactotrophs. ⁽¹²⁾ In this study we found that there is an association between hypothyroidism, hyperprolactinemia, and infertility.

Conclusions:-

Prolactin (PRL) and thyroid stimulating hormone (TSH) are found to be elevated in patients when compared to control group. However, thyroxine (T_4) and triiodothyronine (T_3) levels are reduced in patients than in control group. TSH is positively correlated with PRL and negatively correlated with T_4 and T_3 . In nearly, half of the hypothyroidism female patients, the PRL levels are elevated. Increased levels of prolactin in hypothyroid cases, menstrual irregularities and altered gonadotropin patterns were observed in this study. Alteration in thyroid hormone levels may have considerable role in hyperprolactinemia. Thyroid hormone altered levels may play an important role in reproductive physiology abnormality and leading to infertility.

Recommendations:-

More studies are needed in Sudan, particularly in White Nile state, to identify the effect of iodine deficiency on women at reproductive age and its relationship to infertility. Extended studies are needed to set base line data for thyroid dysfunction and hyperprolactinemia in White Nile State, Sudan.

References:-

- 1- National Research Council, Committee to Assess the Health Implication. Washington, DC: The National Academies Press, 2005.
- 2- Institute of Medicine, Food and Nutrition Board. Washington, DC: The National Academies Press, 2001.
- 3- Patrick, L. Iodine deficiency and therapeutic consideration. *Altern Med Rev*, 2008, 13(2): 116 – 127.
- 4- World Health Organization, United Nations Children's Fund & International Council for the Control of Iodine Deficiency Disorders.
- 5- Ekpechi, O. L., Iodine deficiency disorders in Africa. In: Hetzel BS, Dunn JT, Stanbury JB, eds. *The prevention and control of iodine deficiency disorders*. Amsterdam: Elsevier, 1987:219–36.
- 6- Eltom, M. A., Endemic goiter in the Sudan. PhD thesis. University of Uppsala, Uppsala, Sweden, 1984.
- 7- Dawelbiet, A. Y, Biochemical evaluation of endemic goiter in White Nile State, PhD (Thesis) University of Khartoum, Khartoum Sudan, 2001.
- 8- Vassart, G. and Dumont J, E. The thyrotropin receptor and the regulation of function and growth. *Endocrine Reviews*, 1992: 13; 596-611.
- 9- Bole Feysot C.H, Goffin, V., Edery, M, Binart, N, Kelly, P. A. Prolactin (PRL) and its receptor: action, signal, transductions, pathways and phenotypes observed in PRL receptor knockout. *Endocrine Rev* 1998:19:225-268.
- 10- Freeman ME, Kanyicska B, Lenart A, Nagy G. Prolactin: structure, function and regulation of secretion, *Physiol Rev* 2000: 80 : 1523 – 1631.
- 11- K.S. Honbo, A. J. Van Herle, K. A. Kellet; Serum prolactin levels in untreated primary hypothyroidism, *The American Journal of Medicine*, 1978: 64 (5), 782-787.
- 12- Adele B, Ozera A, Zahra K and Zakiie V, Hyperprolactinemia associated with hypothyroidism. *Caspian J Intern Med*, 2011: 2(2): 224-238.
- 13- Kamal. A. Ahmed, Salah. A. Elmahadi, Alneil M. Hamza and Abdalla. E. Ali. Assessment of thyroid function test among hyperprolactinemia Sudanese infertility female. *Health Science Journal* 2016.
- 14- Intisar ReehemAlsultance, The Study Effect on Serum Prolactin Level in Women with Hypothyroidism Disorder, *International Journal of Pharm Tech Research CODEN (USA)*: 2016: 9 (3); 460-465.
- 15- Deepali Mehra, HP Gupta, Shivani Singh, Uma Gupta, Anu Chandra, Evaluation of thyroid and prolactin levels and its correlation in patients with Infertility, *International Journal of Medical and Health Research*, 4 (12); 2018; 126-128.