

THYROID HORMONES PROFILE INDICES FOR THE MEASUREMENT OF INFERTILITY IN NIGERIAN WOMEN

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SUMMARY: The levels of thyroid hormones; thyroxine (T_4), triiodothyronine (T_3), and thyroid-stimulating hormone (TSH) were determined in non-pregnant women (NPW), pregnant women (PW) and infertile women (IW). The levels of T_4 (nmol/L) in NPW, PW and IW were 70.8 ± 10.6 , 79.0 ± 15.0 and 53.3 ± 13.0 respectively. The levels of T_3 (nmol/L) were 19.5 ± 3.0 , 9.2 ± 2.0 and 9.8 ± 3.0 respectively, while that of TSH (μ U/L) values were 3.4, 2.4 and 1.8 respectively. The result showed that T_4 in IW is significantly ($P < 0.05$) lower than in NPW and PW. The T_3 in NPW is significantly ($P < 0.05$) higher than PW and IW. The TSH values did not change much in the three groups of women.

From this study low values of T_4 , T_3 and TSH hormones could be used as indices in the assessment of infertility in women.

Keywords: Indices, Infertility, Thyroid dysfunction, Hypothyroidism.

Introduction

The thyroid is situated in the neck and consists of two lateral lobes, one on each side of the trachea immediately below the larynx. Three hormones are produced and released into the blood. They are tri-iodothyronine (T_3), thyroxine (T_4) and calcitonin (CT). The T_4 and T_3 increase metabolic rate in most cells by stimulating oxidative process. These hormones are essential for normal physical growth, sexual maturation, and mental development. The production and release of the thyroid hormones are controlled by thyroid stimulating hormone (TSH) secreted by the anterior pituitary.

Infertility is a common problem facing about 14% of couples (Emsile *et al.*, 1993). Examination of women should aim at detecting any underlying endocrine disorder such as T_3 , T_4 and TSH, because impairment of ovarian function which interrupts ovulation creates infertility. This may be caused by normal imbalance or be may be due to some intrinsic defects in the ovaries themselves Donna (1994). Apart from the above, other reasons for the measurement of these hormones are: their usefulness in the assessment of thyroid function in pregnancy (Burrow, 1990), diagnosis of postpartum thyroiditis (Ramsey, 1986), because about 9% of patients could develop thyroid dysfunction in postpartum period (Walfish and Chan 1985). The clinical features are not pronounced and indeed fatigue, and palpitations are the only two symptoms, which are common (Ramsey, 1986). It is also important to note that primary hypothyroidism could be associated with multicystic ovaries (Voorhis *et al.*, 1994), while secondary hypothyroidism could be associated with hypothalamus dysfunction with deficient TSH secretion leading to infertility, (Bolarin, 1997).

Materials and Methods

Seventy women participated in this study. They were interviewed to make sure that those

taking drugs like propylthiouracil, lithium carbonate and oral contraceptives were excluded. Twenty pregnant women were those attending the antenatal clinic of the University of Calabar Teaching Hospital (UCTH). The other twenty women were attending the gynaecology clinic of the UCTH for infertility problems. Thirty women were non-pregnant females with evidence of regular menstrual periods with normal flow (3-5) days served as control.

Sample collection and Competitive Enzyme immunoassay.

Three mls of venous blood was collected, allowed to clot and then centrifuged at 3000rpm for 5mins. The serum was stored at -20°C . The batch method was used in these analyses.

The Medix Biotech kit California USA, was used for all these assays. Antibody for T_4 was coated on a solid phase well plate. The plates were then secured in the holder and 50 μ l of standards, samples and controls were dispensed into appropriate wells and mixed for 30 seconds. Then 100 μ l of enzyme conjugate reagent (T_4 conjugated to horseradish peroxidase Bovine Serum albumin (BSA), 8 - Anilino - 1 - Naphthalene sulphonic (ANS) blue dye and preservatives in trisbuffer, was dispensed into each well and thoroughly mixed for 10 seconds. The wells were incubated for 45 minutes at room temperature. After incubation, the wells contents were flickered into a waste container, and then washed with running tap water, then absorbent paper used to remove the residual water droplets. After that, 200 μ l of tetramethyl benzedine (TMB) was then put into each well and incubated for 15 minutes at room temperature in the dark. The reaction stopped with addition of 50 μ l of 2M HCL. This was followed by gently mixing for 5 seconds and absorbance read at 450nm in a micro well reader spectrophotometer.

(Mini Readers, catalog NO 011 – 930 – 0500). The same assay procedures were used for T_3 and TSH with minor modifications. The statistical analysis used was the ANOVA and the level of significance was taken as $P < 0.05$.

Result

The T_4 levels for NPW, PW and IW were 70.8 ± 10.6 , 79 ± 15 and 53.3 ± 13.5 respectively. For T_3 they were 19.5 ± 3.0 , 9.2 ± 2.0 and 9.8 ± 3.0 respectively, while for TSH they were 3.4, 2.81 and 1.80 respectively, Table 1. The T_4 value for IW Table 1 was significantly lower ($P < 0.05$) than in NPW and PW.

For T_3 , the level in NPW is within the normal range and is significantly higher ($P < 0.05$) than in PW and IW, Table 1. The TSH values PW and IW are significantly lower ($P < 0.05$) than in NPW.

Discussion

The normal range for T_4 in NPW and PW are (62.5 – 150) and (70 – 120) respectively. The T_4 values for NPW and PW are within the normal range. The T_4 value in PW is greater than in NPW and is in agreement with the observation of others (Hoffenberg 1985 and Redman, 1985) that mild

hyperthyroidism is associated with conception and pregnancy.

The T_4 in IW is low and well out of the normal ranges hence it reflects hypothyroidism, which is associated with infertility (Crooks, *et al*, 1964). Generally the T_3 level changes in the direction of T_4 but there are instances in which the two hormones are inconsistent; (Hoffenberg 1985), and this is the case here. The decrease in the levels of T_3 in IW is a further proof of infertility because under this condition, T_3 is reduced as shown in Table 1.

The TSH values in NPW, PW and IW Table 1 are within the normal range but those of PW and IW are lower, which agrees with the observation of Burtis and Ashwood (1996). This low value of TSH in IW supports the view that hypothyroidism is present in IW. Another valuable information deduced from low TSH in IW, apart from sensitivity to hypothyroidism is that it is used in distinguishing between primary and secondary hypothyroidism, in which the latter is the case seen in this study (Whitby *et al*, 1980, Mayne, 1999).

From this work, the values of T_4 , T_3 and TSH are lower in IW compared with those of NPW and PW, hence they may serve as additional indices of infertility in women.

Table 1: Showing T_4 , T_3 and TSH in Non-pregnant, Pregnant and Infertile women

	Non-pregnant (NPW) n = 30	Pregnant women (PW) n = 20	Infertile women (IW) n = 20
T_4 nmol/L	70.8 ± 10.6	79 ± 15.0	53.3 ± 13.5
Normal Range*	(62.5 – 150)	(70 – 210)*	-
T_3 nmol/L	19.5 ± 3.0	9.2 ± 2.0	9.8 ± 2.0
Normal Range*	(18 – 29.3)	(8 – 52)	-
TSH mu/L	3.40	2.40	1.80
Normal Range*	(0.51 – 5.75)	Unchanged*	-

* Burtis and Ashwood 1996, n = no subjects.

References

- Bolarin, D. M. (1997) In: *A handbook of Clinical Chemistry* 1st Edition. Nelson Publishers Ltd., Lagos.
- Burrow, G. N. (1990) Thyroid Function in Pregnancy *Clinical Parientology*. 12, 420 – 425.
- Burtis, C. A. and Ashwood, E. R. (1996) Clinical Chemistry of Pregnancy. In: Tietz, N. W. (ed), *Fundamentals of Clinical Chemistry*. W. B. Sanders Coy., London, pp 745 – 760.
- Crooks, J., Aboul-Khair, S. A. and Turnbull A. C. (1964). The incidence of goiter during pregnancy. *Lancet*. 2. 334 – 336.
- Donna, S (1994) *Watson's surgical and Nursing Physiology*: ELBS, Butler and Tanner Ltd, London, pp 562-616
- Emslie, C., Grismshaw, J. and Templeton, A (1993) Do Clinical guidelines improve general practice management and referral of infertile couples? *Br. Med. J.* 306, 1728 – 1731.

- Hoffenberg, R. (1985) Thyroid Disorders. In: Weatherall, D. J., Ledingham, J. G. G. and Warrell, D. A. (eds), *Oxford Textbook of Medicine*. Oxford University Press, pp 10.24 – 10.41.
- Mayne, P. D. (1999) Thyroid Function. In: *Clinical Chemistry in Diagnosis and Treatment*. ELST with Arnold, London. pp 158 – 165.
- Ramsay, I. (1986) Post partum thyroiditis. *Brit. J. Obstet. and Gynaecol.* 93, 1121 – 1123.
- Redman, C. W. G. (1985) Thyroid Diseases in Pregnancy. In: Weatherall, D. J., Ledingham, J. G. G. and Warrell, D. A. (eds) Oxford University Press, 11.6 – 11.23.
- Vorhies, B. J. V., Neff, T. W., Syrop, C. H and Chapler F. K. (1994) Primary hypothyroidism associated with multicystic ovaries and ovarian Torsion in an adult. *Obstet Gynecol* 83, 885 – 887.
- Walfish, L. G. and Chan, J. Y. C. (1985) Partum hyperthyroidism *Clin. Endocrinol. Metab.* 14, 417 – 447.
- Whitby, L. G. Percy-Robb I. W. and Smith, A. F. (1980) Thyroid Hormones. In: *Lecture Notes on Clinical Chemistry*. Blackwell Scientific Publication, Edinburg. Pp 322–342.

Received: April 4, 2002

Accepted: October 4, 2002