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Assessment of Thyroid Function in Infertile Iraqi Females

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Abstract
Infertility is one of the medical, social and psychological burdens in Iraqi society. Thyroid dysfunction can lead to menstrual disturbance, anovulatory cycle and decreased fertility. The study was designed to evaluate the role of thyroid disorders in infertility with emphasis on autoimmunity by Measuring T3, T4, TSH, & anti Thyroid peroxidase antibody in infertile females comparing the results with matching fertile controls. The study was conducted during the period from March 2015 to September 2015 at Karbala Maternity Hospital, infertility unit, and some private clinics. This study included a total number of 143 women in the reproductive age; ranging between (15- 43) years; divided into: The patients group included 92 infertile females; while controls were 51fertile females. The following parameters were measured for all study groups: T3, T4, TSH, &anti-TPO using ELISA device. The results showed that there were 60.8% of patients with primary infertility (n =56) while 38.2% were with secondary infertility (n= 36). There was a significant difference in T3, and Anti-TPO between patients and controls being higher in patients; (p-value <0.05). In addition; Anti-TPO level was significantly higher in secondary infertile patients compared to primary infertile patients. In conclusion; Thyroid disorders are closely related to infertility in Iraqi females; and Anti-TPO may be used as a biochemical indicator of subclinical thyroid disorders and may help in assessment of thyroid function as a cause of infertility whether primary or secondary.
Keywords: Infertility, Thyroid disease, T3, T4, Anti-TPO

1. Introduction

Infertility is defined as failure to achieve a clinical pregnancy or inability of a couple to conceive naturally after 12 months or more of regular unprotected sexual intercourse (Gurunath *et al* 2011). It is classified into:
1. Primary infertility: in women whose pregnancy spontaneously miscarries, or whose pregnancy results in a still born child, without ever having had a live birth (Zegers-Hochschild *et al* 2009)
2. Secondary infertility: in those who repeatedly spontaneously miscarry or whose pregnancy results in a stillbirth following either a previous pregnancy or a previous ability to carry a pregnancy to a live birth (Cousineau *et al* 2007).

There are many causes of female infertility; Endocrine disorders and hormonal disturbances represent important ones affecting female reproduction and ovulation (Masoumi *et al* 2015).

Disorder of thyroid gland can cause infertility (Krassas *et al* 2010). Thyroid diseases are the most common endocrine disease in females at reproductive age. Thus, evaluation of thyroid functions during both pregnancy and treatment of infertility and treating relevant pathologies became important (Davis *et al* 2007, Van den Boogaard *et al* 2011). Autoimmune mechanisms are involved in the etiology of numerous thyroid diseases. The antibodies against thyroid tissues may exert negative effects on fertility due to immune dysfunction, cellular damage and decrease in thyroid hormones (Andreeva P. 2014).

Autoimmune thyroid diseases are the most common autoimmune conditions encountered in females in reproductive age characterized by presence of antibodies against some structures of thyroid gland such as thyroid peroxsidase (TPO), thyroglobulin, and thyroid microsomes (Abalovich *et al* 2007).

TPO is the key thyroid enzyme catalyzing both the iodination and coupling reaction for the synthesis of thyroid hormone (McLachlan *et al* 1992). Anti-TPO autoantibodies are present in approximately 90% of patients with autoimmune thyroid diseases and they are mainly of the IgG class (Silva *et al* 2003). Anti-TPO autoantibodies in pregnancy are markers for postpartum and long-term thyroid dysfunction (Premawardhana *et al* 2004).

The aim of this study was to evaluate the role of thyroid disorders in infertility with emphasis on autoimmunity by Measuring T3, T4, TSH, & Anti-TPO autoantibodies in infertile Iraqi females.

2. Material & Methods

Study design: The study is case-control based study designed to determine thyroid disorders in infertile female. The study was conducted during the period from March 2015 to September 2015 at Karbala Maternity Hospital ,

infertility unit, and some private clinics.

The study consisted of a total number of 143 women in the reproductive age, the age range was between (15- 43) years. The patients were 92 infertile females and 51fertile females. Control samples were collected from the community and some of the staff in the hospital and the university.

Diagnosis of infertility and patient selection were done by gynecologist present in infertility unit at Karbala Maternity Hospital.

Blood samples were collected from all participants; sera were separated and frozen for measurement of T3, T4, TSH, & Anti-TPO using ELISA device in Imam Hussein Teaching Hospital.

3. Results

Among the 92 patients included in the study; 56 females were with primary infertility (60.8%) while 36 females were with secondary infertility (38.2%) (Figure 1).

There was a significant difference between patients and control groups in levels of T3 and Anti-TPO; being higher in patients. Whereas there was no significant difference in both T4 and TSH between the two aforementioned groups (table 1).

The study also showed a significantly higher levels of Anti-TPO in secondary infertile patients compared to primary infertile females, no significant differences were found in T3, T4, or TSH levels ; respectively. (Table 2).

4. Discussion

Infertility is one of the medical, social and psychological burdens in Iraqi society (Frayyehl *et al* 2014). Most of patients in this study were with primary infertility; this agrees with previous studies (Al-Turki 2015, Kazemijaliseh *et al* 2015). Most newly married couples seek pregnancy and attend health services more frequently than those who already have a child. Moreover; Iraqi families take primary infertility much more seriously than secondary infertility.

Thyroid dysfunction can lead to menstrual disturbance, an ovulatory cycle, and decreased fertility (Rijal *et al* 2011). In women of reproductive age, the most prevalent cause of thyroid dysfunction is thyroid autoimmunity (Basal and Hayman *et al* 2009).

Results of the present study showed that serum Triiodothyronine T3 was significantly higher in infertility patients compared with control group, while no significant difference was found in total thyroxin; our results are consistent with a previous study done by (Omar *et al* 2015). Regarding the relation between T3, T4 levels and the type of infertility (primary or secondary), the result revealed no significant difference and this is consistent with (Maysaloun *et al* 2012). This could be explained by the variable expression of thyroid hormone receptors in female reproductive system as stated by López *et al* (2015) who found that thyroid hormone receptors were differently expressed in granulosa and cervical cells of infertile females and concluded that the expression of different markers of intracellular thyroid function is linked to fertility status. Resistance of these receptors will cause a reciprocal increase of the active thyroid hormone T3.

Results showed that the serum TSH level was neither significantly different in infertile patients group compared with control group, nor in primary compared to secondary groups; which agrees with other studies (Sharma *et al* 2013, Bhavna *et al* 2013). TSH significantly up regulates growth factors expression in endometrial cell cultures, suggesting a potential role of TSH in the implantation process (Aghajanova et al 2011). Some researchers also emphasized on the relation between levels of TSH and hyperprolactenemia in causing infertility status (Shapla *et al* 2014). Nevertheless, TSH levels were a little bit higher in patients group compared to control; suggesting a state of subclinical thyroid disease, known as Sub-Clinical hypothyroidism; which is defined as an increase in serum TSH concentrations with normal free thyroxine levels. The prevalence of Sub-Clinical hypothyroidism in infertile women has been reported to vary from 0.7% to 43% .The wide range of prevalence is due to the differences in sensitivity of serum TSH measurement. (Poppe *et al* 2007)

Our results show significantly higher Anti-TPO levels in serum of infertility group compared to that of control group, this agrees with (Maha *et al* 2014). Thyroid autoantibodies that react with key proteins in the thyroid, such as thyroid peroxidase can induce a chronic lymphocytic thyroiditis that ultimately results in destruction and loss of thyroid function; ultimately affecting fertility. Regarding the type or cause of infertility, data of the current study found that there is a significant difference in serum levels of Anti-TPO between primary and secondary infertility. These results might be explained by age variation between women with primary and secondary infertility. Nevertheless, there is a paucity of researches in this field.

5. Conclusion

Thyroid disorders are closely related to subfertility and infertility in Iraqi females especially autoimmune thyroid diseases. Also Anti-TPO may be used as a biochemical indicator of subclinical thyroid disorders and may help in assessment of thyroid function as a cause of infertility whether primary or secondary.

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Table 1: Serum levels of TPO, TSH ,T3 and T4 in patients and control groups

Parameters	Group	Mean ± SEM	Range	p- Value
TPO IU/ml	*Patient*	60.59± 13.42	0.001- 840	<0.05
	Control	29.33 ± 2.776	0.002-78	
TSH mIu/l	*Patient*	2.466 ± 0.2069	0.004-11.8	>0.05
	Control	2.445± 0.2753	0.02-8.870	
T3 ng/ml	*Patient*	1.909± 0.0489	0.65-2.683	<0.05
	Control	1.629± 0.0524	0.63- 2.040	
T4 ng/ml	*Patient*	8.863± 0.364	0.105-22.99	>0.05
	Control	8.690± 0.3482	3.49- 13.42	

TPO=Anti-thyroid peroxidase , TSH=thyrotropine ,T3= Triiodothyronine , T4=thyroxin
SEM=Stander error mean , IU =international unite ,ml =milliliter , ng =Nano gram

Table 2: Serum levels of TPO, TSH ,T3 and T4 in primary and secondary infertile females

Parameters	Type of Group	Mean ± SEM	Range	p-value
TPO IU/ml	Primary	50.99± 13.37	0.001-548.2	<0.05
	Secondary	75.54± 27.39	0.264-840.7	
TSH mIU/ml	Primary	2.250 ± 0.2097	0.004-8.801	>0.05
	Secondary	2.801± 0.4141	0.02-11.8	
T3 ng/ml	Primary	1.862± 0.0689	0.6500-2.683	>0.05
	Secondary	1.983± 0.0636	0.870-2.649	
T4 ng/ml	Primary	8.871 ± 0.4933	0.105- 22.99	>0.05
	Secondary	8.850± 0.5385	1.665- 20.11	

TPO=thyroid peroxidase, TSH=thyrotropine, T3= Triiodothyronine, T4=thyroxin
SEM=Stander error mean, IU =international unite, ml =milliliter, ng =Nano gram

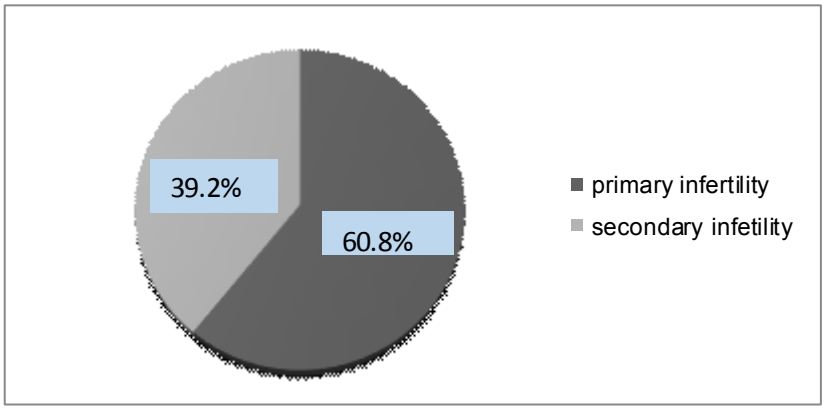

Figure 1. Type of infertility in patients' group