Prevalence rate of Sudanese Hyperprolactinemic Infertile Females with High thyroid stimulating hormone / high Luteinizing hormone Attended Reproductive Health Care Center –Khartoum (2005-2010).

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ABSTRACT

This was a retrospective study conducted at Reproductive Health Care Center in Khartoum State during the period from 2005 to 2010 to determine prevalence rate of infertile women with hyperprolacinemia and high thyroid stimulating hormone (hypothyroidism) or high luteinizing hormone. A total of 1685 infertile women with high TSH attended the center 1388 (79.4%) with prolacin level within the normal range and 347 (20.6%) women with hyperprolacinemia and high TSH. It was noted that the prevalence rate gradually increased throughout the screening period particularly in the last three years. The prevalence rate increased from 10.5% in 2007 to 21.2% in 2009, with overall prevalence rate =20.6%. Total number of infertile females with high LH and normal prolactin was found to be 1887 (76.2%) and those with high LH and high prolactin were 449 (23.8%). Prevalence rate of women with hyperprolactinemia associated with high LH ranged between 20.1 % to 24.5% but no clear pattern was observed.

KEYWORDS: Thyroid gland, infertility, prolactin, hypothyroidism, luteinizing hormone.
INTRODUCTION
Thyroid function and prolactin are closely interrelated. Long-standing, untreated hypothyroidism is associated with ovulatory dysfunction (1). Measurement of prolactin and thyroid hormones, especially thyroid stimulating hormone (TSH), has been considered as an important component of infertility work up in women (2). Thyroid dysfunctions interfere with numerous aspects of reproduction and pregnancy. Some women with glactorrhea and hyperprolactinemia might have primary hypothyroidism (3). This is characterized by low serum level of thyroxin and decreased negative feedback on the hypothalmo-pituitary axis (4). The resulting increased secretion of thyrotropin – releasing hormone (TRH) stimulates thyrotrophs and lactotrophs , thereby increasing the levels of both TSH and prolactin (5). Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production that may block secretion and action of gonadotrophins (6). Even in the absence of hyperprolactinemia, hypothyroidism itself may contribute to infertility since thyroid hormones may be necessary for the maximum production of both estradiol and progesterone (7). In areas with endemic goiter, the major contributor of thyroid dysfunction is iodine deficiency. Infertility associated with thyroid dysfunction in these areas is common (8). Prolonged untreated hypothyroidism has been reported to cause hyperprolactinemia and increased levels of gonadotrophins mainly follicle stimulating hormone (FSH) (9). According to Adele, et al (10) different increase level of serum prolactin has been reported in 30% of patients with primary hypothyroidism. They concluded that prevalence of hyperprolactinemia in subclinical hypothyroidism is notable and this disorder is more common in females than in males. There is a high incidence of hyperprolactinemia with a positive correlation of 1:4 between hyperprolactinemia and hypothyroidism (11). One of the hormones which increases in infertility is Luteinizing hormone (LH) which is a glycoprotein gonadotropin composed of alpha and beta subunits. LH binds to receptors in the ovary and testis and regulates gonadal function. LH secretion is controlled by gonadotropin releasing hormone (GnRH). High LH indicates failure of feedback mechanism from the ovary indicating infertility (12). Number of infertile females at reproductive age (18-39 years) visited Reproductive Health Care Center in 2005 was 2307 and the number increased to 2570 in 2010. 1685 of them with high TSH and 1887 with high LH. Investigation of causes of infertility beside hyperprolactinemia is highly recommended particularly TSH and LH which interfere with gonadal functions.

MATERIAL and METHODS
This is a retrospective study conducted at Reproductive Health Care Center – Khartoum during the period 2005-2010.

Inclusion criteria:
Infertile hyperprolactinemic females with high thyroid stimulating hormone / high lutenizing hormone.

Exclusion criteria:
Infertile hyperprolactinemic females with normal thyroid stimulating hormone / normal lutenizing hormone.

Data collection:
Clinical and demographic data of the participants was obtained from Statistical Department of
Prevalence rate of infertile women visiting Reproductive Health Care Center during the period from January 2005 to December 2010 was calculated according to the Kars et al (13) using period prevalence rate which is calculated according to the following formula:

\[
\text{Period prevalence rate} = \frac{\text{Every instance of the investigated disease within a defined time period}}{\text{Average (At risk) population during the time period}}
\]

Thyroid stimulating hormone (TSH) was determined by Immunoradiometric assay (IRMA). Luteinizing hormone was determined by Enzymatic immnosorbance assay (EIA).

RESULTS

The total number of females with high TSH was 1685. 1338 (76.4%) were with normal prolactin level, while 347 (20.6 %) were with high prolactin level. Prevalence rate of infertile women with hypothyroidism gradually increased throughout the screening period. 11.3% prevalence rate of study group was recorded in 2005 which increased to 21.2% in 2009, with overall prevalence rate = 20.6%. Frequency of infertile women with hypothyroidism and normal prolactin serum level ranged between 60.1% and 90.4% of study population. Prevalence rate of infertile women with hypothyroidism and hyperprolactinemia gradually increased from 11.3% to 39.9 % in 2005 and 2008 respectively (table 1).

Table 1 Prevalence rate of Sudanese Infertile Women with Hyperprolactinemia and TSH > 4.5 U/L (2005-2010)

<table>
<thead>
<tr>
<th>Year</th>
<th>No of women with PRL ≤ 400 IU/L</th>
<th>No of women with PRL &gt; 400 IU/L</th>
<th>Total No of study group</th>
<th>Prevalence Rate / 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>227</td>
<td>88.7%</td>
<td>29</td>
<td>11.3%</td>
</tr>
<tr>
<td>2006</td>
<td>206</td>
<td>90.4%</td>
<td>22</td>
<td>9.6%</td>
</tr>
<tr>
<td>2007</td>
<td>234</td>
<td>86.7%</td>
<td>27</td>
<td>10.3%</td>
</tr>
<tr>
<td>2008</td>
<td>223</td>
<td>60.1%</td>
<td>148</td>
<td>39.9%</td>
</tr>
<tr>
<td>2009</td>
<td>232</td>
<td>75.3%</td>
<td>76</td>
<td>24.7%</td>
</tr>
<tr>
<td>2010</td>
<td>216</td>
<td>82%</td>
<td>45</td>
<td>17.2%</td>
</tr>
<tr>
<td>Total</td>
<td>1338</td>
<td>79.4%</td>
<td>347</td>
<td>20.6%</td>
</tr>
</tbody>
</table>

Prevalence rate of infertile women with high LH ranged between 21.3% and 24.5% (table 2). Frequency of infertile women with high LH and normal prolactin level increased from 78.7% in 2005 to 82.0 % in 2007 then decreased to 79.0 % in 2010.

Prevalence rate of infertile women with hyperprolactinemia and high LH = 21.3 % in 2005 and increased to 34.6% in 2008 with overall prevalence rate = 23.8%.
Table 2. Prevalence rate of Sudanese Infertile Women with Hyperprolactinemia and LH > 9.6 U/L (2005-2010)

<table>
<thead>
<tr>
<th>Year</th>
<th>No of women with PRL ≤ 400 IU/L</th>
<th>No of women with PRL &gt; 400 IU/L</th>
<th>Total No of study group</th>
<th>Prevalence rate / 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>218</td>
<td>59</td>
<td>277</td>
<td>21.3</td>
</tr>
<tr>
<td>2006</td>
<td>134</td>
<td>45</td>
<td>179</td>
<td>22.8</td>
</tr>
<tr>
<td>2007</td>
<td>445</td>
<td>97</td>
<td>542</td>
<td>20.1</td>
</tr>
<tr>
<td>2008</td>
<td>189</td>
<td>100</td>
<td>289</td>
<td>23.4</td>
</tr>
<tr>
<td>2009</td>
<td>179</td>
<td>77</td>
<td>256</td>
<td>24.5</td>
</tr>
<tr>
<td>2010</td>
<td>273</td>
<td>71</td>
<td>344</td>
<td>23.8</td>
</tr>
<tr>
<td>Total</td>
<td>1438</td>
<td>449</td>
<td>1887</td>
<td>23.8</td>
</tr>
</tbody>
</table>

DISCUSSION:
Most of the women with hypothyroidism having serum prolactin within the normal range. Prevalence rate of women with both hypothyroidism and hyperprolactinemia increased throughout the screening period. Vidal et al. (14) reported that higher prevalence of hypothyroidism and hyperprolactinemia in infertile women compared to fertile women, resulting in menstrual disorders which agreed with Goswami, et al., (15) who stated that hypothyroidism is commonly associated with hyperprolactinemia resulting in ovulatory failure, hence assessment of serum TSH and prolactin level are mandatory in the work of all infertile women specially with those with menstrual irregularities. Several mechanisms have been proposed for the increased serum prolactin level in primary hypothyroidism, of these mechanisms, attributed to increased prolactin secretion under the influence TRH which stimulates TSH as well PRL secretion (16-18). Thyroid hormones themselves may play an important role in the cause of hyperprolactinemia, Davis et al. (19) noticed that 3,5,3'-triiodothyronine reduces prolactin messenger RNA levels in rodents pituitary cells thus decreasing thyroid hormones levels resulting in increased prolactin synthesis. Thyroid releasing hormone (TRH) is considered as a stimulant factor for rising prolactin level, estrogen may cause increase prolactin response to TRH that causes higher prolactin level in women (10). Pituitary adenoma was observed among one third of patients with incidence of hypothyroidism in women with hyperprolactinemia = 25%, in other studies = 16.6% (11). The relatively high occurrence of abnormal TSH levels in women with ovulatory dysfunction and oligomenorrhea emphasizes the importance of TSH screening in these women. Other pathological factors leading to hyperprolactinemia in primary hypothyroidism might involve actions on prolactin receptors as well as on prolactin gene expression (18). The overall prevalence rate of infertile women with hyperprolactinemia and hypothyroidism in this study = 20.6%. Moreover, hyperprolactinemia is present in 36 to 57% of hypothyroidism patients. Greenspan and Gardner (12) reported that approximately 40% of patients with primary hypothyroidism present with a minimal increase in prolactin level (25-30 ng/ ml) and 10% with even...
higher Serum levels compared to (20.6%) in the present study. Since patients with primary hypothyroidism have an increase in thyroid releasing hormone (TRH) which stimulates TSH and prolactin release leading to hyperprolactinemia, the authors concluded that the prevalence of hyperprolactinemia in subclinical hypothyroidism patients is considerable, since hyperprolactinemia causes reproduction disorders in women, early diagnosis and treatment of this disease is important. In Sudan, Shabbo et al.\textsuperscript{(20)} reported that 13.6% of hyperprolactinemic patients were found to be hypothyroid, which showed clear association between hypothyroidism and hyperprolactinemia. High prevalence rate of infertile women with hyperprolactinemia and LH may be due to pituitary nonfunctioning tumors which synthesized glycoproteins such as LH. Moreover, LH secretion is episodic with secretory bursts mediated by GnRH. The amplitude of these bursts is greater in patients with primary hypogonadism.\textsuperscript{(12)}

**CONCLUSION**

Prevalence rate of infertile females with hyperprolactinemia associated with high TSH increased throughout the screening period particularly the last three years. Infertile females with hyperprolactinemia and high LH showed higher prevalence compared to infertile hyperprolactinemic females with high TSH. Prevalence rate of hyperprolactinemic infertile females visited the center during screening periods also increased.

**REFERENCES**


