Evaluation of the Oocyte Quality Versus ICSI Outcomes in Sub Fertile Iraqi Women with Polycystic Ovary Syndrome

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Abstract---Background: Polycystic ovarian syndrome (PCOS) is a common endocrine condition, occurs in about 5% to 10% of women and is thought to be caused by a hypothalamic disorder, In some women with PCOS especially obese one has hyper secretion of insulin with insulin resistance, the aim of study: To determine oocyte number and quality and ICSI outcome in infertile patient with PCOS. All patient fit with diagnostic criteria of PCOS where undergoes stimulation by antagonistic protocol and ICSI procedure is done under a control condition. The result of pickup (number and quality of oocyte) and result of ICSI (number of 2 pronclea), was compared with result of oocyte pick up and ICSI of tubal factor. Result and Discussion: In this study characteristic clinical feature of PCOS like acne, hirsuitism, irregular cycle not found in tubal factor group. Also some hormones like LH, Testosterone and prolactin levels in PCOS higher than tubal factors group with normal ovaries As a result of ovarian stimulation and ICSI procedure shows there is good number of oocytes and good quality (M2), with higher fertilization rate in patient with PCOS undergoes ICSI than patient with normal ovaries.

Keywords---fertilization rate, ICSI, oocyte quality, ovary syndrome, PCOS.
Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrine condition, occurs in about 5% to 10% of women and is thought to be caused by a hypothalamic disorder(1), PCOS is clinically defined as a chronic anovulation associated with hyperandrogenism without any cause in pituitary gonadal axis, half of those affected characterized by infertility, hirsutism, obesity and various menstrual disturbances range from amenorrhea to irregular vaginal bleeding (2). There is increase in the incidence of obesity, hyperandrogenism and insulin resistance hyperandrogenism in PCOS.(3) PCOS is the one of the causes of subfertility and irregular menstruation, incidence between 16% -33% in normal adult women (4), (5). The etiology: May be genetic causes as there is cluster of syndrome in families but the scientific explanation of PCOS ,there is an elevated level of LH which lead to increase cytochrome P450 activity which lead to increase level of androstenadion and testosterone which lead to increase production of estrogen in big amount and increase the sensitivity of ovarian follicle to normal level of FSH hormone leading to development of many small follicle in both ovaries or one ovary and high estrogen level (6),(7).

In some women with PCOS especially obese one has hyper secretion of insulin with insulin resistance, her the insulin augment theca cell production of androgen in response of LH and granulose cell production of estrogen in response to FSH (8). In PCOS patient there is wide spared of vascular endothelial growth factor that stimulate vascular (VEGF) permeability ,in normal ovaries VEGF cause diversion of blood flow from non-dominant ovary to dominant ovary and from the cohort follicle causes diversion of FSH hormone from cohort follicle and permit them to atresia and the development of dominant follicle .In PCOS patient VEGF prevent the diversion of blood flow substantial number of follicle to respond to gonadotropin stimulation which lead to incomplete maturation of many follicle in ovary (9),(10). Inappropriate release of LH effect the egg maturation and the release egg either unable to fertilize or if fertilized will end with miscarriage we have to demonstrate that women with PCOS requires management to achieve follicular maturation in an environment free of levated Level to achieve egg fertilization and pregnancy (11),(12).

The diagnosis of PCOS: women with PCOS may have presented with symptom of endocrine and metabolic disturbance prior to seeking assisting conception or diagnose first at fertility clinic mostly the diagnosis done by ultrasound 12 or more follicle of 29mm in diameter or ovarian volume of more than 10 cubic centimeter, if one or both ovaries have one of these criteria it is enough for diagnosis (13), (14). Clinically obesity sign of hyperandrogenism (hirsuitism of score 8 or more on modify Ferryman Gallewy score. Menstrual disturbance (oligomenorrhæ 8 or less cycle per year), stromal echogenicity and volume of ovary specific for PCOS (15). PCOS could be detected as early as age of 6 year, it is necessary to differ polycystic ovary than PCOS .PCO disciple only morphological appearance of ovary and PCOS mean morphological appearance of ovary and metabolic disturbance and endocrine disturbance and obesity (16).

Endocrine disturbance it is an alteration in concentration of LH hormone and estrogen and prolactin and androgen hyperprolactinemia it is not due to pituitary
defect but because of high estrogen production although the pathogenesis is unknown but it is believe it is happen because of interaction between genetic and multiple environmental factor, so it is multifactorial disease and the understanding the pathogenesis of this disease and diagnosis and treatment may allow prevention of PCOS associated morbidity (17), (18). Even by most developed ultrasound there is some difficulty in doing anteral follicle count specially in obese and virgin women, serum AMH (antimullerian hormone) can be used for diagnosis, AMH is number of transforming growth factor beta (TGF β) superfamily secreted by granulose cell of small anteral and preanteral follicle to regulate early follicle development (19). AMH expression start at 25 week of embryo and continue until menopause level of AMH it is closely correlated with number of follicle in both healthy and PCOS women so, AMH can be replace AFC in PCOS diagnosis as it is level independent on hypothalamic pituitary axis (20).

Material and Methods

A retrospective study for PCOS patient from January 2016 _ August 2019 patient fit with diagnostic criteria of PCOS .All patients were stimulated by antagonist protocol patient given gonadotropins recumbent FSH (follisurge) for 7 days when oocyte reach size of 14 mm antagonist given in multiple dose protocol which called lubeck protocol, antagonist are injected in flexible region depend on size of follicle which is more suitable for PCOS patient because of profound ovarian response. Antagonist used is cetrorilax 0.1 mg this protocol is simple and well tolerated by patient and there is no stimulatory phase and no symptom of estrogen deprivation as in agonist protocol and reduce the risk of OHSS and reduce dose of gonadotrophen needed also endometrium development in this protocol mimic the natural endometrium. When the follicle reach the size of 18mm_20mm the ovarian trigger given by HCG Pregnasurge given 10000iu unit after 36hrs from injection of ovarian trigger oocyte collection is done which is the process of oocyte aspirated from stimulated ovary, here patient under general anesthesia, vaginal ultrasound guided needle aspiration is done for all follicle in both ovaries, follicular fluid which aspirated contain oocyte cumulus complex is collected in tube of 14mm in size given to embryologist scan for complex is dissecting microscope under low power magnification and the complex put in culture media (aspiration media) and put in incubator for 2hrs for rest and final maturation of oocyte, incubator is setting to 37°C and 5%CO2 after that denudation is done which is the process of removing cumulus cells from the oocyte by putting the complex in hyaluronidase media this permit for us to correct visualization to detect which one contain polar body or not before doing ICSI.

A sample of seminal fluid was taken from male partner and prepared by wash and swim up technique to get most motile and normal morphology sperms from seminal fluid sample than oocyte and prepared sample of seminal fluid put in incubator for another 2hrs for rest and then transfer them to ICS I dish, ICSI was done for oocyte in metaphase 2 stage only. (ICSI) is the injection of one motile normal sperm in each oocyte by use of inverted microscope, 18_20hrs later we checked the oocyte for fertilization only 2 pronouns oocyte was taken for culture embryo is graded from 1to 3 and 1-2 embryo transfer to patient (21). All patients
not gave oral contraceptive pills or any complementary therapy before stimulation.

**Result**

A total of 73 PCOS patients were identified, these data were compared to 37 tubal factor patients during the same period Table (1). There were no differences in FSH and female age but showed difference between PCOS and Tubal factor in duration of infertility, LH, testosterone, prolactine, TSH and AMH shown in table (1), when compare between PCOS and tubal factor undergoes ICSI shows significant in number of oocyte, GV (Germinal vesicle oocytes), M1 (Metaphase I oocytes), M2 (Metaphase II oocytes) and 2p (two pronuclea) shown in the table (2). Clinical characteristics of PCOS patients such as Hirsutism, Acne, irregular of cycle and type of infertility shown in the table (3) with percent of each between PCOS and tubal factor.

<table>
<thead>
<tr>
<th>Variable</th>
<th>PCOS</th>
<th>Tubal factor</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>31±4.327</td>
<td>31.16±3.465</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of infertility</td>
<td>7.56±3.2</td>
<td>10.26±4.816</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LH</td>
<td>8.99±5.56</td>
<td>4.47±1.69</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>FSH</td>
<td>4.10±1.62</td>
<td>4.57±1.34</td>
<td>NS</td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.48±0.756</td>
<td>0.43±0.471</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Prolactine</td>
<td>29.46±7.56</td>
<td>23.21±8.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TSH</td>
<td>2.73±1.49</td>
<td>2.83±0.829</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>AMH</td>
<td>8.34±3.93</td>
<td>3.83±3.37</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid stimulating hormone (TSH), antimullarian hormone (AMH).

<table>
<thead>
<tr>
<th>Variable</th>
<th>PCOS</th>
<th>Tubal factor</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GV</td>
<td>3.062±2.062</td>
<td>3.94±3.206</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>M1</td>
<td>2.75±1.75</td>
<td>2.41±1.32</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>M2</td>
<td>14.1±7.62</td>
<td>8.29±4.49</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Number of oocyte</td>
<td>17.81±8.45</td>
<td>12.92±5.55</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2PN</td>
<td>11.4± 1.002</td>
<td>7.22±0.612</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

(GV) Germinal vesicle oocytes. M1 (Metaphase I oocytes) and M2 (Metaphase II oocytes), 2p (two pronuclear)
Table 3
Clinical characteristics of polycystic ovarian syndrome (PCOS) Patients and Tubal factor

<table>
<thead>
<tr>
<th></th>
<th>PCOS</th>
<th>Tubal factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary infertility</td>
<td>95.89%</td>
<td>97.2%</td>
</tr>
<tr>
<td>Secondary infertility</td>
<td>4.1%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>58.9%</td>
<td>0%</td>
</tr>
<tr>
<td>Acne</td>
<td>45.2%</td>
<td>0%</td>
</tr>
<tr>
<td>Increase body weight</td>
<td>84.9%</td>
<td>0%</td>
</tr>
<tr>
<td>Irregular cycle</td>
<td>46.5%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Discussion

PCOS is clinically defined by chronic anovulation, hyperandrogenism with in women without causes related to pituitary gonadal axis. This syndrome is characterized by obesity and approximately half of those affected had infertility, hirsutism and various menstrual disturbance range irregular vaginal bleeding to amenorrhea (22,23). Tubal factor infertility is female infertility caused by diseases such as scarring, congenital malformations or obstructions, damage and other factors which interfere with descent of a fertilized ovum or unfertilized ovum into the uterine cavity through the Fallopian tubes and interfere with normal pregnancy and full term delivery (24). Results of the present study shows no significant difference in level of FSH between PCOS and tubal factor patients, our results are agreed with a previous study done by (Sigala, J., et al 2015)(25), but shown difference between PCOS and Tubal factor in duration of infertility this result not agreement with our research (M.Ludwig et al 1999), (Banchhita Sahu et al 2008) (25,24). Because the researchers did not use the comparison between PCOS and tubal factor, they used the comparison between PCOS and PCO-only. When comparing PCOS and tubal factor with LH, a significant difference was found these findings correspond with (Banchhita Sahu et al 2008) (25), but not agreement with (Sigala, J., Sifer et al 2015), When comparing PCOS and tubal factor with AMH, a significant difference was found these findings correspond with (Sigala, J., Sifer et al 2015) (23). When study Oocyte quality and number of oocyte between PCOS and tubal factor shows a significant in number of oocyte, GV (Germinal vesicle oocytes), M1 (Metaphase I oocytes), M2 (Metaphase II oocytes) Studies oocyte quality in women with PCOS have been frequent. The results confirm that Studies of egg quality in women with recurrent PCOS have confirmed this, but some research matches results such as (Ibrahim Esinler, M.D., et al 2005) (M.Ludwig et al 1999), (22,25).

Conclusion

Patient with PCOS shows a higher number of embryos mainly due to the higher number of oocyte pickup and a higher number of 2PN when compared with tubal factor groups.
References


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