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Research Article

Ovarian Hyperstimulation Syndrome and Pregnancy Outcome

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Abstract

Objective: To compare pregnancy outcome in IVF pregnant women with and without ovarian hyperstimulation syndrome.

Methods: One hundred and forty pregnant women after IVF were recruited in this case control study. Seventy patients in case group with OHSS and seventy patients in control group without OHSS who referred to two referral university based hospital between January 2009 - September 2014 were evaluated. Obstetrics outcome like abortion, pregnancy induced hypertension, gestational diabetes and preterm labor, LBW and multiple pregnancies were evaluated.

Results: The case group were younger than control group (P = 0.001). BMI was similar in both groups. Primary infertility in case group was 40% versus 70% in control group (p = 0.02). Male factor infertility was the most common cause in both group (44% in case group and 51.4% in control, p = 0.495). 30% of patients in the case group had PCOS versus 25% in control group. Early OHSS was more common than late OHSS (84.3% versus 14.3%). PIH, LBW, multiple gestation, GDM and abortion was the same in both group but preterm labor was higher in OHSS group.

Conclusion: It seems that preterm labor was more common in the OHSS group (p = 0.05) but other pregnancy complications like pregnancy loss, pregnancy induced hypertension and gestational diabetes or low birth weight were similar in pregnant patients with and without OHSS.

Keywords: *OHSS; PIH; GDM; Infertility; Multiple Pregnancy*

Introduction

Ovarian hyperstimulation syndrome is an iatrogenic complication of ovulation induction protocols that its incidence is higher in assisted reproductive techniques [1]. The cause of OHSS in ART cycles is the use of GnRH agonist, higher dose of gonadotropins and the younger age of patients who are candidate for ART [2].

The etiology of OHSS is still unknown, but hCG is assumed the cardinal factor in susceptible patients [3]. The hCG causes maternal secretion of various mediators like vascular endothelial growth factor, and interleukins from granulose and theca lutein cells. These mediators increase capillary permeability and the shift of fluids from blood vessels to extravascular space and plural and pericardial effusion, hemoconcentration, acute renal failure, thrombosis and life threatening complications may occur [4].

The early OHSS that starts within eighth day following oocyte retrieval is due to exogenous hCG which is prescribed for ovulation triggering but late OHSS is caused by endogenous hCG that is secreted by early pregnancy [5].

The obstetrics outcome of OHSS is not clear [6]. The obstetrics complications like abortion, gestational diabetes mellitus, pregnancy induced hypertension and low birth weight are reported [7].

Aim of the Study

The aim of the present study was to evaluate the outcome of pregnancy in IVF patients who were pregnant without OHSS as control group and to compare their outcome with pregnant women with IVF who had OHSS as case group.

Methods

In a retrospective case control study in two teaching tertiary hospital data of pregnancy after IVF were evaluated from March 2007to April 2013. The study group consists of 70 pregnant patients with OHSS F and 70 pregnant patients without OHSS after IVF as control group. The institutional review board has approved the study and all the patients had signed informed consent for using their data in this study.

Severe OHSS was diagnose by Golan., *et al*. criteria [8] which consists of clinical ascites, hydrothorax with dyspnea, renal, hemodynamic and liver dysfunction. Critical OHSS was defined as the presence of thromboembolic events, acute renal failure, and adult respiratory distress [9]. Early OHSS was defined if the situation was occurred in 3 - 7 days after ovulation triggering and late if it appeared 12 - 17 days after ovulation triggering [10].

The data like age, BMI, the cause of infertility, primary or secondary infertility, gravidity, history of PCOS, IVF indication and history of vascular disease were evaluated. Pregnancy complications consisted of abortion, diabetes mellitus; pregnancy induced hypertension, preterm labor, multiple pregnancy and low birth weight. The laboratory parameters consisted of CBC (Hb, RBC, WBC) Na, K and liver function test (ALT, AST, ALK p), BUN, Cr.

Controlled ovarian stimulation was done with administration of 3.75mg triptorelin (Decapeptyl: Ferring, Malmo Sweden) two weeks prior the initiation of Gonal-F and in the third day of menstruation 150 - 225 IU recombinant FSH (Gonal-F) was started according to the number of antral follicle count on cycle day 2 - 3 for 5 days. After that doses were adjusted according to the ovarian response. Ovulation triggering was induced by 5000IU hCG (Pregnyl; Organon, Skovlunde, Denmark). Oocyte retrieval was performed under general anesthesia by the transvaginal guided sonography 36h following hCG administration. Luteal phase support was prescribed by vaginal progesterone (Cyclogest 400/BD). The luteal phase support continued until the menstruation or 8 weeks of gestation in case of a positive pregnancy test.

Statistical analysis was performed with SPSS16 statistical software (Chicago). Descriptive data were presented as mean ± SD, data were compared using x^2 test. $P < 0.05$ was considered statistically significant.

Results

Overall one hundred and frothy pregnant patients after IVF were registered for this study. Seventy patients in case group had OHSS and 70 patients without OHSS as control group were evaluated. The case group were younger than control group (P = 0.001). BMI was

similar in both groups. Primary infertility in case group was 40% versus 70% in control group (p = 0.02). Male factor infertility was the most common cause in both group (44% in case group and 51.4% in control, p = 0.495).

30% of patients in the case group had PCOS versus 25% in control group. The history of vascular disease before pregnancy was similar in both group, case group 15% versus control group 11% (Table 1).

Variable	Patients with OHSS (n = 70)	Patients without OHSS (n = 70)	P value
Age	28.3 ± 6.3	31.4 ± 5.2	p = 0/001
BMI	21.2 ± 1.3	20.9 ± 1.4	p = 0/63
Indication of IVF			
Male factor	49.3% (n = 34)	51.1% (n = 36)	P = 0/495
Tubal factor	32.9% (n = 22)	34.3% (n = 48)	P = 0/34
Endometriosis	4.7% (n = 3)	5.4% (n = 4)	P = 0/48
Unexplained	13.1% (n = 9)	9.1% (n = 6)	P = 0/82
PCOS	30% (n = 21)	5.7% (n = 4)	P = 0/33

Table 1: *Demographic characteristics of both groups.*

**P < 0.05 is significant.*

Pregnancy induced hypertension was occurred 10% (7) of case group and 11.4% (8) of control group (p = 0.785) and gestational diabetes was not different in both group (case group 3 and control group 2 patients, p = 0.5), and pregnancy loss was the same (case 7.1% and control 12%, p = 0.07), and low birth weight (12.9% case, 11.4% control, p = 0.793).

Preterm labor was occurred in 14 (20%) of OHSS group versus 6 (8.6%) of control group (p = 0.05). Twin pregnancy was 20% in OHSS group and 23% in control group, and triplet was 3% in both group, and singleton pregnancy was 77% and 74% respectively (p = 0.478).

Regarding the severity of OHSS 28.6% had moderate, 40% severe and 25.7% had critical form of the syndrome. Liver enzyme elevations was occurred in 12.9%, dyspnea 8.6%, pericardial effusion 8.6%, oliguria 20%, nausea and vomiting 55.7% of OHSS group. HCT > 45%, WBC > 15000 in 45% and abdominal distension in 92.5% was occurred (Table 2).

Variable	Patients with OHSS	Patients without OHSS	P-value*
Abortion	7.1% (n = 5)	12% (n = 8)	0.07
Pregnancy induced hypertension	10% (n = 7)	11.4% (n = 8)	0.785
Gestational diabetes	4.3% (n = 3)	2.9% (n = 2)	0.50
Preterm labor	20% (n = 14)	8.6% (n = 6)	0.05
Low birth weight	12.9% (n = 9)	11.4% (n = 8)	0.793

Table 2: *Pregnancy outcome in both groups.*

**P < 0.05 is significant.*

Early OHSS was more common than late OHSS (84.3% versus 14.3%). Thromboembolic disorder was occurred in 5.7% and ovarian torsion in 7.1% of patients was reported. 25.7% of them needed ICU admission.

Discussion

The results of this study showed that preterm labor was more common in the OHSS group (p = 0.05) but other pregnancy complications like pregnancy loss, pregnancy induced hypertension and gestational diabetes or low birth weight were similar in pregnant patients with and without OHSS.

The effects of OHSS on pregnancy outcomes is not clearly defined [11]. Increase of abortion rate was reported in a study of 60 patients with severe OHSS (38%) compared with an average miscarriage rate of 15% in patients without OHSS [7,12]. Chen., *et al*. four additional study also reported the higher miscarriage rate in OHSS patients [11] but others could not find increase risk of early pregnancy loss in 41 IVF/GIFT clinical pregnancy rate, complicated by moderate or severe OHSS in comparison with 501 clinical pregnancies without OHSS [13]. Another study showed that the miscarriage rate was similar for patients with and without OHSS after IVF, and it was similar to the general population (17.5% vs .16%) [13]. Also in present study the miscarriage rate in both groups was not statistically significant. The miscarriage rate in OHSS group is a challenging issue, because there are many confounding factor in different studies that have evaluated this issue, like multiple pregnancy. In a multicenter study which had reported a total miscarriage rate 29.8% in OHSS patients versus 15% in non OHSS patients, the multiple pregnancy rate was high and only 43% of patients had singleton pregnancy and it was assumed that the late miscarriage rate after twenty weeks of pregnancy Was due to the multiple pregnancy [14].

Preterm labor is a complication that was reported in many articles as a consequence of pregnancy in OHSS group. Authors reported 36% rate of preterm labor but they assumed that there were many biases and confounding factors like uterine malformations or underweight BMI [15]. The rate of preterm labor was reported 25% and 44.1% by others [15,16]. In present study preterm labor was 20% in OHSS group versus 8.6% in non OHSS group.

Preterm labor was linked to the OHSS via inflammation and placental dysfunction mechanism [16]. In recent study preterm labor was significantly higher in OHSS group than non OHSS group. It is supposed that placental development is altered in the OHSS and maybe it is a predisposing factor for some obstetrical complications like preterm labor and pregnancy induced hypertension and fetal growth restriction [17]. There is a cohort study with high incidence of multiple pregnancy in OHSS patients [17].

Multiple pregnancy rates was reported higher in patients with OHSS versus patients without OHSS (45.5% and 40% respectively) [5]. But results of the present study showed that multiple pregnancies in both group had no significant difference. These results is similar to the others that reported the same rate of multiple pregnancy in patients with and without OHSS [15].

Pregnancy induced hypertension in some studies are correlated to the OHSS [17]. They reported a high rate of pregnancy induced hypertension in the OHSS group (21.2% vs.9.2%). They reported higher PIH in both group regarding to general obstetrical population, also they reported the placental dysfunction due to systemic vascular dysfunction and association between hemoconcentration, hypoxemia, and electrolyte disorder as possible predisposing factor for higher prevalence of PIH [18], they believed that many confounding factor like primiparity, older age, preexisting vascular disorder and maybe unknown underlying thrombophilia were present in their study population [18].

Conclusion

In the present study GDM had not significant different between both group like others [17,19] that reported GDM in 2.5% of their patients, the similar rate like general population. They believed that their study group was low risk for GDM, because of low BMI and lower rates of PCOS patients. Also they criticized that authors who reported higher rate of GDM, the BMI were not reported in their patients [14].

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Conflict of Interest

Authors declare that there is no conflict of interest.

Bibliography

1. Delvigne A and Rozenberg S. "Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review". *Human Reproduction Update* 8 (2002): 559-577.

2. Fiedler K and Ezcurra D. "Predicting and preventing ovarian hyperstimulation syndrome (OHSS): the need for individualized not standardized treatment". *Reproductive Biology and Endocrinology* 10 (2012): 32.

3. Abdalla HI., *et al*. "The effect of the dose of human chorionic gonadotropin and the type of gonadotropin stimulation on oocyte recovery rates in an *invitro* fertilization program". *Fertility and Sterility 4*8 (1987): 958-963.

4. Babayof R., *et al*. "Serum inhibin A, VEGF and TNFalpha levels after triggering oocyte maturation with GnRH agonist compared with HCG in women with polycystic ovaries undergoing IVF treatment: a prospective randomized trial". *Human Reproduction* 21 (2006): 1260-1265.

5. Papanikolaou EG., *et al*. "Early and late hyperstimulation syndrome: early pregnancy outcome and profile". *Human Reproduction* 20 (2005): 636-641.

6. Wiser A., *et al*. "Outcome of pregnancies complicated by severe ovarian hyperstimulation syndrome (OHSS): a follow-up beyond the second trimester". *Human Reproduction* 20 (2005): 910-914.

7. Mathur RS and Jenkins JM. "Is ovarian hyperstimulation syndrome associated with a poor obstetric outcome?" *British Journal of Obstetrics and Gynaecology* 107 (2000): 943-946.

8. Golan A., *et al*. "Ovarian hyperstimulation syndrome: an update review". *Obstetrical and Gynecological Survey* 44 (1989): 430-440.

9. Navot D., *et al*. "Ovarian hyperstimulation syndrome in novel reproductive technologies: prevention and treatment". *Fertility and Sterility* 58 (1992): 249-261.

10. Lyons CA., *et al*. "Early and late presentation of ovarian hyperstimulation syndrome: two distinct entities with different risk factor". *Human Reproduction* (1994): 792-799.

11. Chen CD., *et al*. "Serum estradiol level and oocyte number in predicting severe ovarian hyperstimulation syndrome". *Journal of the Formosan Medical Association* 96 (1997): 829-834.

12. Raziel A., *et al*. "Increased early pregnancy loss in IVF patients with severe ovarian hyperstimulation syndrome". *Human Reproduction* 17.1 (2002): 107-110.

13. Simon C., *et al*. "Increasing uterine receptivity by decreasing estradiol levels during the preimplantation period in high responders with the use of follicle stimulating hormone step down regimen". *Fertility and Sterility* 70 (1989): 234-239.

14. Mac Dougall MJ., *et al*. "*In vitro* fertilization and the ovarian hyperstimulation syndrome". *Human Reproduction* 7 (1992): 597-600.

15. Courbiere Blandine., *et al*. "Gamerre Marc, obstetric outcome of women with *in vitro* fertilization pregnancies hospitalized for ovarian hyperstimulation syndrome: a case control study". *Fertility Sterility* 95.5 (2011).

16. Abramov Y., *et al*. "Obstetric outcome of *in vitro* fertilized pregnancies complicated by sever ovarian hyperstimulation syndrome: a multicenter study". *Fertility Sterility* 70 (1998): 1070-1076.

17. Mathur RS and Jenkins JM. "Is ovarian hyperstimulation syndrome associated with a poor obstetric outcome?" *British Journal of Obstetrics and Gynaecology* 107 (2000): 943-946.

18. Bastek JA., *et al*. "Biomarker of inflammation and placental dysfunction are associated with subsequent preterm birth". *Journal of Maternal-Fetal and Neonatal Medicine* (2010).

19. Rizk B., *et al*. "The role of vascular endothelial growth factor and interleukins in the pathogenesis of severe ovarian hyperstimulation syndrome". *Human Reproduction Update* 3 (1997): 255-266.

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