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Overview of Ovarian Disease in Pregnancy

[1]Saad Abdullah S Shaiban, [2]Saleh Y Alhedyan, [3]Abdullah Mohammed H Kafy

Abstract: **Polycystic ovary syndrome (PCOS) is a set of symptoms due to raised androgens (male hormonal agents) in women. Signs and symptoms of POCS include irregular or no menstrual durations, heavy durations, excess body and facial hair, acne, pelvic pain, trouble getting pregnant, and spots of thick, darker, silky skin. Associated conditions consist of type 2 diabetes, weight problems, obstructive sleep apnea, heart disease, mood disorders, and endometrial cancer. Ovarian disorders that are a specific effect of the hormone milieu of pregnancy such as pregnancy luteoma (PL) and Hyperreactio Luteinalis (HL) are uncommon. Nevertheless, they have essential ramifications for both the mother and the fetus considering that they can be puzzled with ovarian malignancy leading to unneeded surgery. This evaluation concentrates on the significant aspects of management of these ovarian conditions during pregnancy.**

Keywords: **pregnancy luteoma (PL), Hyperreactio Luteinalis (HL).**

1. STRUCTURE OF THE OVARY

The ovary consists of three main cell types: theca cells, granulosa cells, bacterium cells as well as assistance structures. The ovarian cortex is comprised of ovarian hair follicles surrounded by stroma. The ovarian follicles in turn consist of granulosa cells and cumulus oophorus which surround the primary oocyte. Ovarian roots are more numerous below the capsule of the ovary and end up being increasingly sparse to the ovarian medulla. Each roots is surrounded by theca cells that are the source of androgens which in turn are the substrate for follicular oestrogen production moderated by aromatisation within the granulosa cells.

2. REVIEW OF OVARIAN FUNCTION IN PREGNANCY

The primary function of the ovary during pregnancy is to supply endocrine support over the very first trimester until the placenta ends up being self-sufficient. This function is mediated by the corpus luteum.

- ***Corpus luteum:***

The corpus luteum is essential for establishing and maintaining pregnancy through the secretion of progesterone which is responsible for decidualization of the endometrium under the influence of luteinising hormone and subsequently chorionic gonadotrophin from the trophoblast.

This short-term endocrine gland also makes substantial amounts of androgen and oestradiol. Approximately one-third of the cells of the corpus luteum are steroidogenic and secreting 17 hydroxy- progesterone, androstenedione and oestradiol in addition to progesterone. These cells are derived from theca interna and granulosa lutein cells. Endothelial cells comprise another third of the cells within the corpus luteum and these are stemmed from extreme vascular expansion which leads to an abundant capillary network under the influence of vascular endothelial development element. More cell types include immune cells, fibroblasts and macrophages. In a fertile cycle the corpus luteum is rescued from regression by the action of hCG produced by the trophoblast. Serum hCG is noticeable from approximately 8 days after ovulation increasing gradually over the very first 12 weeks of pregnancy.

The corpus luteum likewise produces the peptide hormone relaxin from the time of ovulation through the first trimester of pregnancy. The degree of dependence of the human pregnancy on this hormone is uncertain. Females who achieve pregnancy without a corpus luteum utilizing ovum donation have low flowing relaxin concentrations with no apparent negative impacts. In women, laxity of the joints of the pelvis leads to separation of the pubis by approximately 10 mm and

this process has actually been credited to the action of relaxin; an action inferred from the function of relaxin in rodents. Raised serum relaxin concentrations are found in pregnant females with type 1 diabetes mellitus but this may be represented by cross-reacting proteins [1].

Table 1: A summary of the types of ovarian malignancy in 68 pregnancies[11,54,55].

Tumour type	Percent
Germ cell tumour	35.3
Borderline malignancy	27.9
Invasive epithelial	25
Sex cord	11.8

- ***Pre-existing ovarian pathology and pregnancy:***

Polycystic ovary syndrome (PCOS):

There is a lot of info mentioning the possibility that ladies who have PCOS appear to have actually an increased threat of miscarriage, pregnancy-induced hypertension, gestational diabetes (GDM), and premature delivery [2]. For the most part, these dangers are related to weight problems rather than PCOS per se and there is no good data that recognizes an increased threat of any event related to pregnancy as soon as obese has been managed for.

There is no doubt nevertheless, that the environmental and genetic background of women with PCOS leads to an increased threat of gestational diabetes [3]. A background of PCOS for that reason must trigger more strict security for GDM in pregnancy and early suggestions on lifestyle modifications as a preventative procedure. Management of hypertension and GDM in the context of PCOS should follow standard guidelines. Some retrospective studies have investigated the possibility that the administration of metformin in pregnancy may lower the prevalence of GDM or miscarriage [4] however there is no good quality proof to support this idea. Way of life procedures stay the mainstay of reducing the danger of GDM in ladies with PCOS. While pre-treatment with metformin has been shown to result in a somewhat higher pregnancy rate in females with PCOS compared with controls, using the more rigid end point of live birth rate, there is no evidence of a beneficial effect from this drug[5]. In the context of In vitro fertilisation (IVF) however, the use of metformin into early pregnancy appears to reduce the incidence of ovarian hyperstimulation syndrome (OHSS)[6].

- ***Premature ovarian insufficiency (POI):***

The variety of females with POI who use up the alternative of pregnancy with ovum donation is increasing[7,8]. All pregnancies from helped reproductive innovations carry a greater danger of unfavorable events especially of miscarriage. It has frequently been believed that ovum donation pregnancies carry an especially high danger[9]. Just recently the rate of pregnancy-induced high blood pressure (PIH) has been quantified in a meta-analysis. In 2308 shipments 22.6 women had PIH. The calculated odds ratio for PIH after oocyte contribution, compared to traditional reproductive treatment, was 2.57 (95% CI, 1.91-3.47), and compared to ladies with non-assisted pregnancies was 6.60 (95% CI, 4.55-9.57).10 In contrast, some systems report no excess pregnancy risk [7] and a few of the identified excess risk might be connected to innovative maternal age and the danger of multiple pregnancy.

Ovum contribution pregnancies by their very nature are valuable and subjected to more cautious monitoring and this typically causes a higher danger of caesarean area.

- ***Ovarian pathology presenting in pregnancy:***

Ovarian malignancy:

Deadly ovarian cancers are an uncommon problem of pregnancy with an incidence estimated to be one in 12,000 shipments[11]. Ovarian malignancy is typically discovered during evaluation of the pregnancy with ultrasonography but they can also provide at Caesarean section[12]. The spectrum of malignancies explained in pregnancy exists in Table 1. Three quarters of cases are identified at stage 1 and in these, total remission can be expected.

In advanced or aggressive disease, chemotherapy, surgery and radiotherapy need to be considered. In some circumstances chemotherapy can be administered throughout the third or second trimester of pregnancy. Most of the times, conservative debulking is possible and conclusive treatment can be postponed until after delivery depending upon the prognostic features of the tumour. Because of the early detection of a lot of tumours the general survival rate is much better than that for ovarian cancer that provides beyond pregnancy.

Ovarian hyperandrogenism in pregnancy:

The two most common ovarian pathologies that provide in pregnancy are characterised by their presentation with maternal virilisation. The most frequent reason for hyperandrogenic states during a pregnancy are pregnancy luteoma (PL) and hyperreactio luteinalis (HL). Table 2 reveals the key features of these conditions.

The mother is relatively secured against virilisation by a high flowing concentrations of sex hormone-binding globulin (SHBG), progesterone and oestradiol and by placental aromatase[13]. The foetus is secured from maternal ovarian androgen excess by placental aromatase that changes the androgens into oestrogens. It is just when the practical capability of placental aromatase is totally overwhelmed that maternal or foetal virilisation occurs[14,15]. Foetal masculinisation happens more frequently with PL compared to HL[16]. In this condition, foetal dehydroepiandrosterone (DHEA) gets away aromatisation by the placenta which would typically secure the mother from androgen impacts.

Clinical features of androgen excess consist of hirsutism, acne, bitemporal and scattered alopecia and in more extreme cases cliteromegaly and a deepening of the voice. The more serious symptoms might not be completely reversible depending on the period of direct exposure. The differential diagnosis of maternal virilisation in pregnancy consists of aromatase shortage whereby foetal dehydroepiandrosterone (DHEA) is the source of androgen.

Pregnancy luteoma:

Over 200 cases of pregnancy luteoma (PL) have been described and these probably represent an extreme virilised end of a spectrum with much more asymptomatic versions which secrete little or no excess androgen, remaining unreported[17].

Pregnancy luteomas typically look like a strong ovarian mass most regularly between 5 and 10 cm but adenoma up to 20 cm are also reported[18]. They are benign and in approximately 50% bilateral[15]. Threat elements for the advancement of PL include advanced maternal age, multiparity, pre-existing PCOS and Afro- Caribbean ethnic subgroup[19]. Macroscopic appearance is of a multi-nodular brownish-yellow mass typically with internal hemorrhagic deposits. The microscopic description is of lutein cells, the development of which is promoted by of human chorionic gonadotropin (hCG)[20].

Many cases of PL are normally found incidentally during pregnancy ultrasound and are asymptomatic[21]. Clinical functions of androgen excess take place in just one-third of mothers with a luteoma and most commonly this appears in the 2nd half of pregnancy. Just two-thirds of mothers who experience virilisation bring to life a virilised female foetus. In addition to their discussion with features of androgen excess, PL can present acutely with haemorrhage, torsion or mass impact[20]. A late feature of androgen excess consists of suppression of lactation which may be delayed for up to one week.

As a rule, PL regress spontaneously after childbirth with androgen levels returning to regular over 2 weeks and clinical functions regressing over three months[22]. Surgical intervention is only needed for those with an acute presentation when differentiation from malignancy is not possible based on imaging. Surgical elimination of PL should be postponed till the second trimester to prevent an increased risk of miscarriage. Surgery in the third trimester must be prevented since of the threat of early birth. There is little released data on the result of female foetal virilisation. In general it appears the result depends upon the intensity of virilisation. As androgen levels go back to regular quickly after birth, signs of virilisation can likewise fall back. For those with more severe virilisation, feminizing genital surgery might be required at a later date[21,23].

Reoccurrence in subsequent pregnancies is observed [24] and because of this it might be possible for pre-implantation genetic diagnosis to be considered for the choice of a male embryo in order to avoid virilisation of a female fetus[25].

3. HYPERREACTIO LUTEINALIS

Hyperreactio luteinalis (HL) refers to significant bilateral cystic enhancement of the ovaries and extreme production of ovarian androgens during pregnancy. It is a reasonably rare condition with roughly 100 cases reported in the literature with the majority of reports remaining in multiparous ladies in their 20's[19]. Although benign, HL can mimic an ovarian neoplasm and therefore needs cautious evaluation to avoid unnecessary surgery. Approximately 20% of females with HL experience hyperandrogenism.

The cause is unidentified, the mechanism is believed to consist of increased ovarian level of sensitivity to HCG leading to extreme development of ovarian theca lutein cysts and increased androgen production [26]. It is associated with conditions in which exceedingly elevated levels of HCG are discovered such as several pregnancy and trophoblastic disease (molar pregnancy and choriocarcinoma) and has actually been explained in chronic kidney disease, presumably due to decreased

clearance of HCGb[27,28]. In spite of the association with elevated HCG, 60% of reported cases were discovered in uncomplicated singleton pregnancies. It can simulate ovarian hyperstimulation syndrome (OHSS) [29] which is a complication of fertility treatments but can be distinguished by occurring in spontaneously developed pregnancies and somewhat behind OHSS which generally takes place early in the very first trimester. New start virilisation suggests HL, whereas huge fluid shift which is a trademark of OHSS, is unusual in HL.

While many commonly impacting both ovaries, unilateral disease has been explained.30 It is frequently asymptomatic and is most frequently an incidental finding at the time of ultrasound scanning or caesarean section. It might present throughout any trimester with abdominal pain or an acute abdomen due to ovarian torsion [31] or haemorrhage[32]. In many cases it might be related to ascites and/or pleural effusions[27,33-35]. Though maternal virilisation can happen due to hyperandrogenaemia, foetal masculinisation has actually not been explained in HL. This is in contrast to PL and the mechanism surrounding the distinction in foetal action to similar levels of androgen excess in both conditions remains unusual[16]. In uncommon cases, HL can be related to hyperthyroidism,[36,37] pre-eclampsia [36,38-41] or haemolysis, elevated liver enzymes and low platelets (HELLP).[42,43].

On ultrasound examination, HL is characterised by large adnexal masses that include numerous thin- walled theca lutein cysts, providing it the appearance of a 'spoke wheel'[44]. Microscopic findings are of significant hypertrophy and luteinisation of the theca interna layer.

The natural history of HL is post-partum resolution with ovarian volume and androgen concentrations going back to typical by 3 months post-partum in the vast majority of cases. The spectrum of period of androgen excess extends from those that fall back during pregnancy in parallel with the decrease in hCG concentrations from 12 to 16 weeks gestation,45 to unusual cases of consistent cliteromegaly[46]. The association with serum hCG concentrations is not continuous however as in the 3rd trimester resolution has been reported in spite of reasonably constant hCG levels[47,48]. Recurrence in subsequent pregnancies is uncommon[49,50].

As with PL, the essential of treatment is conservative and surgery ought to be limited to the management of complications such as ovarian torsion or haemorrhage or to omit malignancy.

Table 2: Key features distinguishing pregnancy luteoma and hyperreactio luteinalis.

	Pregnancy luteoma	**Hyperreactio luteinalis**
Clinical features		
Incidence	w200 cases described	w100 cases described
Presentation	Multiparous women in 20's and 30's Usually incidental	Multiparous women in 20's Usually incidental
Risk factors	Advanced maternal age Multiparity PCOS Afro-Caribbean ethnic subgroup	Multiple pregnancy trophoblastic disease
Bilateral disease	50%	>90%
Hyperandrogenism	60%	20%
Foetal virilisation	2/3 of virilised mothers	No reported cases

4. OVARIAN DISORDERS OF PREGNANCY WITHOUT ENDOCRINOPATHY

Singular cysts of pregnancy are categorized as either luteinised follicular cysts or corpus luteal cysts which do not produce or modify circulating hormone concentrations. Large luteinised follicular cysts are thin-walled unilocular collections raving up to 30 cm in size[51]. They are rare and generally solitary although bilateral cysts have actually been reported in a twin pregnancy[52].

Corpus luteal cysts are smaller with one series pricing quote sizes as much as 3 cm with a characteristic hyperdense rim found in the majority[53]. Rupture of a corpus luteal cyst is a rare cause of acute lower abdominal pain sometimes leading to a haemoperitoneium.

5. SUMMARY

The majority of ovarian disease in pregnancy associates with pre-existing ovarian conditions. The most common ovarian disorder of women of reproductive age is PCOS. While females with PCOS are at increased threat of gestational diabetes, pregnancy-induced hypertension and miscarriage; these dangers appear to be connected to weight problems which is

common in this condition rather than PCOS per se. Pre- conceptual recommendations about lifestyle interventions to reduce these threats need to form the pillar of treatment. Women with POI who conceive via ovum donation have an increased danger of pregnancy issues but additional research is needed to clarify mechanism of this. New ovarian pathology presenting in pregnancy although rare, can have essential clinical repercussions. In particular, the hyperandrogenic disorders PL and HL can masquerade as an ovarian malignancy and require careful assessment to prevent unnecessary surgery which can have terrible consequences. In general the treatment for these conditions is conservative unless problems such as ovarian torsion or haemorrhage take place. If surgery is needed to omit malignancy, then a frozen area biopsy is the very best choice and proceeding to more comprehensive surgery only if malignancy is verified.

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