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RESEARCH ARTICLE

A REVIEW AND CURRENT SITUATION OF PCOS WITH INFERTILITY

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Abstract

Polycystic ovary syndrome (PCOS) is a condition in which the ovaries produce an abnormal amount of androgens. PCOS causes an imbalance of androgen hormones and causes many of the symptoms of the disorder. It affects about 8-10% of all women of reproductive age and 22% in India. If lifestyle changes are not successful in controlling the symptoms of PCOS, then women may be advised to consider weight loss surgery.In some cases, the weight loss surgery may be combined with hormonal therapy.This treatment aims to achieve even greater weight loss, which may lead to the reduction of excessive facial and body hair. Too much testosterone can also interfere with the development of the follicles (the sacs in the ovaries where eggs develop) and prevents normal ovulation (the release of a mature egg). Hypothyroidism (low thyroid function) is common in women with PCOS. Excess androgens can be induced by insulin resistance and hyperinsulinemia, as they cause a reduction in sex hormone binding globulin levels, which lead to a subsequent increase in free androgens and unfavourable metabolic profiles. The ovarian PCOS morphological traits of enlarged, multi-cystic ovaries and theca interstitial hyperplasia are reported in women who are subjected to high levels of androgens as a result of endogenous adrenal androgen hyper secretion in congenital adrenal hyperplasia treatment in female-to-male transsexuals. Even if an egg is released, the uterus lining or the endometrial may not be ready for pregnancy Symptoms of PCOS The following symptoms will help you understand PCOS occurrence: Irregularity in menstrual cycles or lack of cycles Excessive body or facial hair is seen in teens and females in their 20s The condition worsens over the years with an increase in hair growth It is due to the surplus testosterone and androstenedione that results in high male hormone production in females in their blood. Reproductive age, approx 10% of women are affected by this syndrome, with common symptoms including weight gain, irregular periods, acne, an increase in body hair, and infertility due to ovulation failure.

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Introduction:-

Polycystic ovary syndrome (PCOS) is a condition in which the ovaries produce an abnormal amount of androgens, male sex hormones that are usually present in women in small amounts. The name polycystic ovary syndrome describes the numerous small cysts (fluid-filled sacs) that form in the ovaries. However, some women with this disorder do not have cysts, while some women without the disorder do develop cysts.[1][2]Ovulation occurs when a mature egg is released from an ovary. This happens so it can be fertilized by a male sperm. If the egg is not fertilized, it is sent out of the body during your period.[2]In some cases, a woman doesn't make enough of the hormones needed to ovulate. When ovulation doesn't happen, the ovaries can develop many small cysts. These cysts make hormones called androgens. Women with PCOS often have high levels of androgens. This can cause more problems with a woman's menstrual cycle. And it can cause many of the symptoms of PCOS.[3]This disorder causes an imbalance of hormones and is a "female hormone" problem. It is characterized by an imbalance of sex hormones such as estrogen and progesterone. These often referred to as "cysts," are caused by an excess of androgen hormones. These hormones naturally occur in both men and women.[4] Polycystic ovary syndrome (PCOS) is a complex hormonal disorder. "Polycystic" means "many cysts." It refers to a large number of partially developed follicles in ovary, each containing an egg cell. They rarely reach adulthood or produce eggs that can be fertilized. Women with PCOS often have elevated levels of ineffective insulin, or "androgens," or both. The cause is not known, but family history, genetics, hormones, and lifestyle all play a part. Insulin resistance is present in 4 of her 5 women with PCOS. A woman whose mother, aunt, or sister has her PCOS is 50% more likely to develop PCOS. The condition is also common among Asians, Aborigines, Torres Strait Islanders, and African women. PCOS is relatively common, especially in infertile women. It affects 8-13% of women of childbearing age (late puberty through menopause). Almost 70% of these cases go undetected. [5] However, an imbalance of these hormones can cause PCOS. The term "polycystic ovary syndrome" (PCOS) was first used in an article published in the journal "Teratology" in 1959. PCOS was initially confused with the condition called "polycystic ovary disease," which is caused by excess testosterone.[6] However, it is now understood that the two conditions are distinct and may even have different causes. PCOS is a complex endocrine-metabolic syndrome that is associated with multiple morphological or predominantly biochemical conditions. [7] PCOS is the most commonly diagnosed disorder among reproductive-age women is polycystic ovary syndrome (PCOS). It affects about 8-10% of all women of reproductive age, and its prevalence continues to grow.[8] In India, it is about 22%. The health of women is affected by numerous factors, including genetics, lifestyle, and environment. An ideal environment is characterized by a healthy balance between stress and rest. This balance is disrupted in individuals who have PCOS, which can lead to hormonal imbalances that cause a variety of health conditions.Treatment for PCOS is often done with medication. This can't cure PCOS, but it helps reduce symptoms and prevent some health problems.[9]

Sign And Symptoms

Not all women with PCOS will have all of the symptoms, and each symptom can vary from mild to severe. Some women only experience menstrual problems or are unable to conceive, or both. Common symptoms of PCOS include:

- Irregular periods or no periods at all/ Oligomenorrhea
- Difficulty getting pregnant (because of irregular ovulation or failure to ovulate)
- Excessive hair growth (hirsutism) – usually on the face, chest, back or buttocks
- weight gain/ Obesity
- Thinning hair and hair loss from the head
- Oily skin or acne
- Ovarian cysts
- Depression
- Low sex drive
- Heavy menstrual bleeding [10][11]

The clinical manifestations of PCOS are not just circumscribed around the gynaecological sphere but some of these are infertility, gestational diabetes or pregnancy-induced high blood pressure, miscarriage or premature birth, non-alcoholic steatohepatitis (a severe liver inflammation caused by fat accumulation in the liver), metabolic syndrome-a cluster of conditions including high blood pressure, high blood sugar, and abnormal cholesterol or triglyceride levels that significantly increase your risk of cardiovascular disease, type 2 diabetes or prediabetes, sleep apnea, depression, anxiety and eating disorders, abnormal uterine bleeding, cancer of the uterine lining (endometrial cancer), obesity, thyroid, hypertension, abnormal lipid profile, anemia liver infections, UTI which affected by PCOS come across the prevalence of several other co-morbidities associated with it.[13][14]

Etiology

PCOS is a type of illness in which the heterogeneous, clinical, and metabolic phenotype is determined by a combination of genetic and environmental factors. Even though the fact that the genetic etiology of PCOS is unknown. Formal segregation analysis is impossible due to a complete lack of phenotypic information.[15] PCOS tends to cluster in families related to an autosomal dominant pattern.Poor food habits and lack of physical activity can worsen external factors allegedly involved in PCOS (e.g., obesity); bacterial infections or toxicants may also play a significant role. PCOS associated with metabolic functions can sometimes be reversed with lifestyle modifications such as fat loss and workouts.[16]

The exact cause of PCOS is not clear. Many women with PCOS have insulin resistance. This means the body can't use insulin well. Insulin levels build up in the body and may cause higher androgen levels. Obesity can also increase insulin levels and make PCOS symptoms worse.[17]

PCOS may also run in families. It's common for sisters or a mother and daughter to have Factors that might play a role includingexcess insulin.[18] Insulin is the hormone produced in the pancreas that allows cells to use sugar. If cells become resistant to the action of insulin, then blood sugar levels can rise and the body might produce more insulin. Excess insulin might increase androgen production, causing difficulty with ovulation.Low-grade inflammation i.e.white blood cells' production of substances to fight infection. Research has shown that women with PCOS have a type of low-grade inflammation that stimulates polycystic ovaries to produce androgens, which can lead to heart and blood vessel problems. Factors also include heredity and excess androgen in which the ovaries produce abnormally high levels of androgen, resulting in hirsutism and acne.[19][20]

Pathophysiology

The exact etiology of PCOS is unknown, although it is known to be a metabolicdisorder that affects several hormones including insulin (hyperinsulinemia),androgen hormones (e.g. testosterone), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). There are no specific pain sensations that patients experience, although they do experiences more psychosocial factors such as interpersonal sensitivity, depression, and sexual dysfunction.[21] Normal ovaries produce a single dominant follicle that results in a single ovulation per menstrual cycle. This dominant follicle is responsible for estradiol synthesis during the follicular phase of the menstruation cycle; after ovulation, the dominant follicle forms into the corpus luteum, which secretes high levels of progesterone during the luteal phase of the menstrual cycle.[22] Then, estradiol and progesterone act on the uterus to prepare for the implantation of the human embryo.[23] Under normal circumstances, ovarian follicles contain egg cells that are released during ovulation. In polycystic ovary syndrome, the ovarian cycle and the folliculogenesis process are disrupted. Abnormal hormone levels prevent follicles from growing and maturing to release egg cells. Instead, these immature follicles accumulate in the ovaries.[24] Affected women can have 12 or more of these follicles.

In PCOS, elevated androgens, or hyperandrogenism, is a key feature. Androgens are considered male hormones that are made by the adrenal cortex, and in women are also produced by the ovaries.[25] In women, these hormones are further broken down into estrogen (in large amounts) and testosterone (in smaller amounts). All women have testosterone, and in small amounts, this serves a purpose, especially for reproduction, bone health, and libido. Androgen excess initiates premature luteinization, hindering ovulation by impairing the selection of dominant follicles. Excess androgen levels can also explain the excess hair growth and acne present in some PCOS cases. Excess androgens also reduce the synthesis of estradiol, growth hormones of tissues of the reproductive organs, which are required for the full development of antral follicles.[26] The “cysts” on the ovaries are antral follicles that are prematurely developed.[27] **Polycystic ovaries** are characterized by theca cell hyperplasia, ovarian cortical thickening, and the increase in antral follicles and ovarian stroma. The theca cells secrete higher levels of androgens – both basally and in response to LH and insulin. Polycystic ovaries are present in up to 33% of PCOS cases.

Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are made and secreted by a part of the brain called the pituitary gland. These hormones are essential to reproduction as they are necessary for the expression of gonadal steroidogenic enzymes and sex hormone secretion. The primary goal of LH is to stimulate and produce androgens. FSH is responsible for the stimulation and maturation of an egg before it is released during ovulation. In PCOS, these hormones are imbalanced. There is an increase in the production of LH, which produces too many androgens that convert to testosterone, and a decrease in FSH, which prevents the stimulation, maturation, and release of an egg during ovulation.[28][29]

It should be noted that though insulin resistance is not included in the diagnostic criteria for PCOS, it is highly prevalent among PCOS cases. Sixty to eighty percent of PCOS cases have insulin resistance. In insulin resistance, the body's cells are unable to use the hormone insulin to metabolize glucose for energy. When there is an excess amount of glucose in the body, it is stored in the body as fat.[30] This is what contributes to weight gain in some women with PCOS. Insulin is also a big factor in the secretion of androgen (male) hormones. When there is an excess amount of insulin in the body that is not being used, it stimulates the overproduction of androgens. Acanthosis nigricans is also present in some PCOS cases. This condition may create velvet-like skin lesions and correlate to insulin resistance, as insulin causes excess keratinocyte growth, leading to abnormal skin patches.[31]

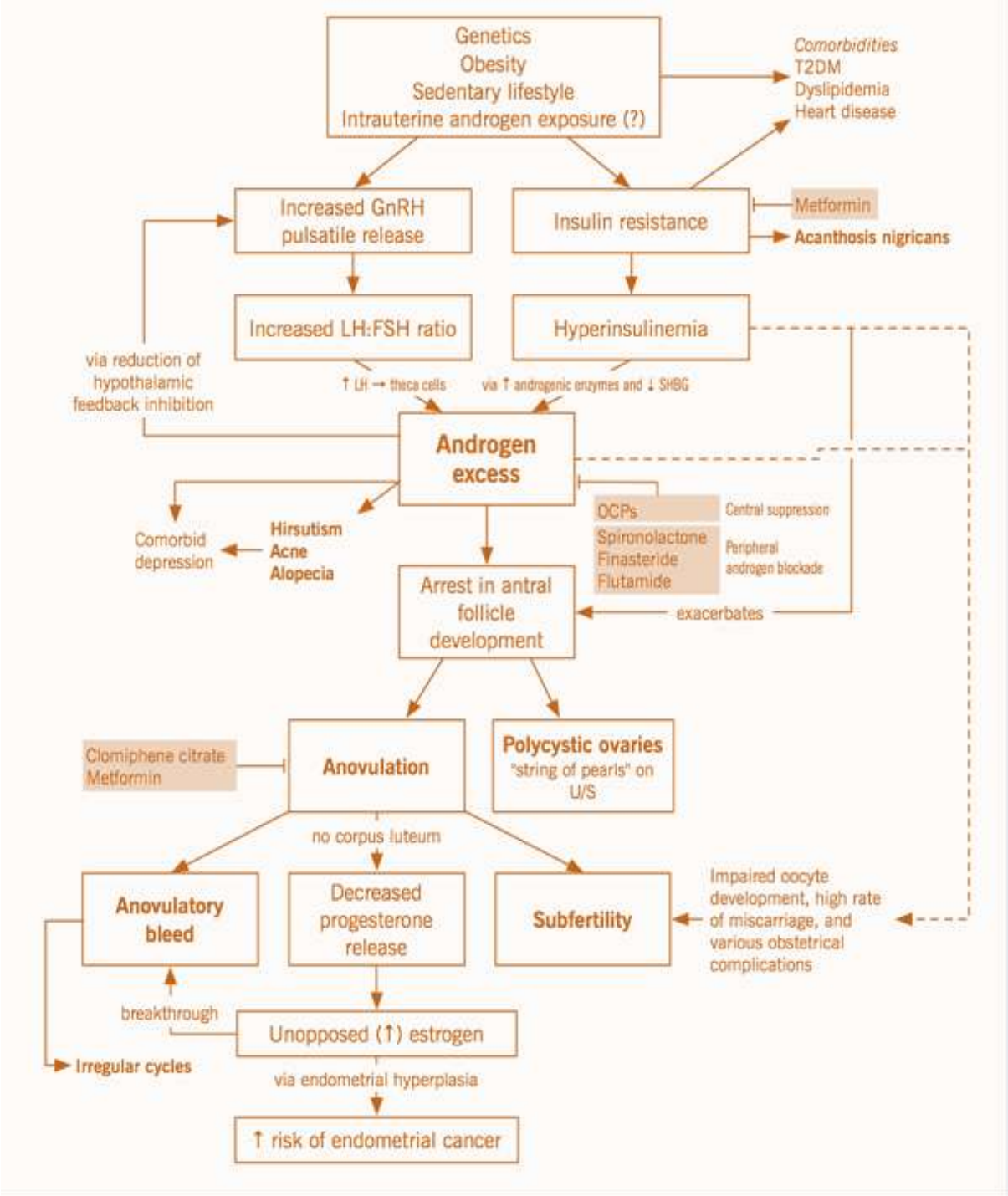

Figure no.1:- Pathophysiology of PCOS.

Importance And Role Of Hormones

Estrogen

Estrogen is an important hormone produced by the ovaries and in small quantities by the adrenal glands. It's responsible for the development of female sex characteristics. Estrogen is required for the development of female sexual organs, maintenance of the skeletal system, regulation of the menstrual cycle, and maintenance of pregnancy.[32]

Estrogen levels normally fluctuate throughout the menstrual cycle and throughout a lifetime.During the menstrual cycle, estrogen levels fluctuate throughout the month. Secreted by the developing egg follicle, this hormone aids in thickening the endometrium for ovulation and possible pregnancy.Also one of the major hormones of pregnancy, estrogen supports the production of fluid in the reproductive tract that enhances the survival of sperm by modifying cervical secretions.Toward the end of pregnancy, estrogen promotes the growth of milk ducts within the mother's breasts and enhances the effect of prolactin, the hormone responsible for lactation.[33][34]

Testosterone

If your body produces too much testosterone, you may have irregular or absent menstrual periods. You may also have more body hair than the average woman. Some women with high testosterone levels develop frontal balding. Other possible effects include acne, an enlarged clitoris, increased muscle mass, and deepening of the voice.[35]

High levels of testosterone can also lead to infertility and are commonly seen in polycystic ovarian syndrome (PCOS). PCOS is an endocrine condition that is sometimes seen in women of childbearing age who have difficulty getting pregnant. Women with PCOS have symptoms similar to those produced by high testosterone levels. they include obesity, an apple-shaped body, excessive or thinning hair, acne, and menstrual irregularity.[36]

By the time of menopause, women have experienced a decline in testosterone since their 20s that does not decrease further.[38] That decline may be correlated to reduced libido. Some findings indicate that testosterone replacement therapy may benefit sexual function in certain perimenopausal and postmenopausal women. Testosterone replacement is unadvised in women with breast or uterine cancer. It also may increase the chances of cardiovascular disease or liver disease.[39]

Progesterone

Progesterone is a key steroid hormone produced mainly by the ovaries, and its synthesis and secretion are primarily regulated by luteinizing hormone during the menstrual cycle and by human chorionic gonadotropin during pregnancy. Progesterone is absolutely required for uterine implantation, decidualization, and maintenance of pregnancy.[40] The uterine endometriums include epithelial cells, stromal cells, immune cells, and blood vessels, and both epithelial and stromal cells are exquisitely sensitive to steroid hormone stimulation in women during the menstrual cycle. For example, 17ß-estradiol (E2) drives epithelial cell proliferation whereas progesterone inhibits E2-stimulated epithelial cell proliferation. Progesterone resistance implies a decreased responsiveness of target tissue to bioavailable progesterone, and such an impaired progesterone response is seen in the endometriums of women with PCOS. Women with PCOS often present with an abnormal menstrual cycle and anovulation, and this results in minimal or absent P4 production as evidenced by the fact that the endometriums is thicker in women with PCOS than in healthy women. In the literature, progesterone resistance generally refers to women who suffer from endometriosis.[41] Endometriosis is an E2-dependent disease but it alters a subset of progesterone-regulated genes and pathways in the endometriums. Although gene expression analysis of PCOS endometriums reveals progesterone resistance and candidate susceptibility genes in women with PCOS, the molecular mechanisms underlying endometrial progesterone resistance or sensitivity in these patients are not completely understood.[42]

LH AND FSH

In PCOS the disturbed hypothalamic-pituitary-ovarian (HPO) axis has been extensively reviewed. The most evident neuro-endocrine feature regulating abnormal ovarian follicle development in PCOS is increased luteinizing hormone (LH) pulsatility regarding both frequency and amplitude, with relatively low FSH secretion. Increased LH pulse frequency increases theca cell production of androgens, while the lower FSH level impairs follicle maturation and consequently ovulation.[43]

The cause of LH hyper secretion in PCOS is probably due to enhanced pituitary sensitivity to gonadotropin releasing hormone (GnRH) or to changes in GnRH secretion patterns rather than increased GnRH secretion. It appears to be a

result of an acquired impaired sensitivity of the hypothalamic pulse generator to the negative feedback of estrogen and progesterone in PCOS, possibly by chronic estrogen exposure. Levels of follicle stimulating hormone (FSH) in PCOS appear to be low or within the lower follicular range, and response to GnRH is relatively similar to ovulatory controls. Altered sex steroid production, metabolic dysfunction, and obesity may all contribute to the changes in LH secretion pattern. Hyperandrogenemia itself may cause hypothalamic desensitization to progesterone/estrogen negative feedback that further increase gonadotropin secretion and hence ovarian androgen production, causing a self-driven viscous circle.[44] Although increased body mass index (BMI) has a blunting effect on LH secretion, hyperinsulinemia and insulin resistance may directly or indirectly (by enhancing ovarian gonadotropin stimulated sex steroid production) contribute to the abnormal gonadotropin secretion, although the mechanism is not clear. All these factors increase free androgen levels and contribute to anovulation.[45]

Ovarian Dysfunction in PCOS

The ovulatory dysfunction in PCOS can be ascribed to disturbed follicular development with excessive early follicular growth and abnormal later stages of arrested follicle growth well before expected maturation. This pattern of follicular growth with failure in the selection of a dominant follicle for ovulation results in one of the hallmarks of PCOS, PCO morphology. The ovarian dysfunction of PCOS involves both these morphological features of polycystic ovaries, described as an accumulation of small antral follicles of size 2–9 mm, as well as the clinical consequence of oligo-/anovulation.[46] The prevalence of menstrual irregularities oligo-/amenorrhea in PCOS depends on the used diagnostic criteria but is approximately 75% . The NIH criteria, of course all patients will experience menstrual irregularities. Ultimately, irregular ovulation can cause infertility due to difficulties conceiving and should be acknowledged.[47]

Moreover, there are several other follicle abnormalities where the most consistent feature is androgen hyper secretion. Ovarian steroid production is based on a close collaboration between theca and granulosa cells in the growing follicles and requires gonadotropin input.[48] Theca cells produce androstenedione from cholesterol, either by the Δ4 or Δ5 pathway, and the conversion to estrone and estradiol thereafter is exclusively acknowledged aromatase cytochrome P450 hydroxylase (CYP19) containing granulosa cells. Women with PCOS appear to have theca internal hyperplasia, a thicker layer of the theca cells, which seem to be responsible for their increased androgen steroidogenesis.[49]

Thyroid Stimulating Hormone

The underlying pathophysiology has been rise in thyrotropin-releasing hormone (TRH) in primary hypothyroidism leads to increased Prolactin and thyroid stimulating hormone (TSH). Prolactin contributes toward polycystic ovarian morphology by inhibiting ovulation as a result of the change in the ratio of follicle stimulating hormone (FSH) and luteinizing hormone and increased dehydroepiandrosterone from the adrenal gland. Increased TSH also contributes due to its spill-over effect on FSH receptors.[50] Increased collagen deposition in ovaries as a result of hypothyroidism has also been suggested. Pathophysiology of polycystic ovaries in patients with primary hypothyroidism. The severity of ovarian morphology also depends on duration and severity of underlying primary hypothyroidism. In most severe cases like long standing untreated cases of congenital hypothyroidism ovarian morphology can be very striking and can even be mistaken for ovarian malignancies.[51]

Hypothyroidism is known to affect the ovaries in a similar way as PCOS, causing the enlargement of the ovaries and the formation of cysts. Hypothyroidism tends to worsen PCOS symptoms, including an increased risk of insulin resistance (the inability of the body to utilize insulin to control blood sugar) and type 2 diabetes. Hypothyroidism can also increase the production of the male hormone testosterone (referred to as hyperandrogenism). Too much testosterone can also interfere with the development of the follicles (the sacs in the ovaries where eggs develop) and prevents normal ovulation (the release of a mature egg).[52] Hypothyroidism (low thyroid function) is common in women with PCOS. This includes an autoimmune form of the disease called Hashimoto's thyroiditis. Hypothyroidism can not only worsen the symptoms of PCOS (including weight gain, irregular periods, and increased insulin resistance) but it can cause symptoms not commonly seen with PCOS. These include goiters (an enlarged thyroid gland), facial mooning, and bradycardia (an abnormally slow heart rate).[53]

Insulin

The pancreas, a gland in the abdomen with a number of functions, produces insulin. Insulin is typically secreted in response to increased blood levels of glucose, a small sugar molecule. When we eat carbohydrates, the glucose molecules enter into our blood within about 15 minutes. Insulin allows cells throughout the body to take in the

glucose, which is later used for energy. When someone has insulin resistance, the body does not respond to insulin as efficiently or as quickly as it should, leading to high glucose levels in the blood, low energy, or both.2 With time, larger and larger amounts of insulin are required before glucose is taken into the body tissues. Eventually, the body begins to deal differently with sugar. Consistently high levels of glucose in the blood can lead to pre-diabetes, and then to diabetes.[54]

PCOS is recognized as a risk factor for developing diabetes. Despite the fact that the signs and symptoms of PCOS begin before the signs and symptoms of insulin resistance, it is believed that insulin resistance may play a role in causing PCOS, rather than the other way around. Elevated insulin levels may be a contributing factor to inflammation and other metabolic complications associated with PCOS.[55] While the connection is known, the cause of the relationship between the two conditions is not completely clear. Most importantly, insulin resistance does not affect everyone in exactly the same way, and some women with insulin resistance develop PCOS, while others do not. Some experts suggest that obesity-associated insulin resistance alters the function of the hypothalamus and the pituitary gland in the brain, increasing the production of androgenic hormones, which contribute to PCOS. Excessive production of androgenic hormones is an independent risk factor for female infertility and ovarian dysfunction, with or without PCOS. While each condition is associated with depression, the risk of depression is much stronger when the two conditions occur together.[56]

Similarly, insulin resistance and PCOS each contribute to infertility. The hormonal changes of PCOS interfere with proper implantation of the embryo, while insulin resistance can lead to miscarriage due to inadequate nutrition and support of the growing embryo. When PCOS and insulin resistance are combined, infertility and early miscarriage can make it difficult to carry a baby to term.[57] Insulin resistance or PCOS, also at risk of developing gestational diabetes during pregnancy. This is an independent risk factor for female infertility and ovarian dysfunction, with or without PCOS.[58]

Androgen

Hyperandrogenism represents a chief attribute of PCOS as elevated androgen levels are the most constant feature, with the majority (−60%) of patients exhibiting hyperandrogenism (Rotterdam definition).[59] Women with hyper androgenic PCOS present with elevated levels of various androgens, including testosterone (T) and the pro-androgens androstenedione (A4) and dehydroepiandrosterone sulphate (DHEAS), as well as the enzyme required to convert pro-androgens to bioactive androgens, 3β-hydroxysteroid dehydrogenase (3β-HSD) in serum. Excess androgens can be induced by insulin resistance and hyperinsulinemia, as they cause a reduction in sex hormone binding globulin levels, which lead to a subsequent increase in free androgens and unfavourable metabolic profiles.[60] The ovarian PCOS morphological traits of enlarged, multi-cystic ovaries and theca interstitial hyperplasia are reported in women who are subjected to high levels of androgens as a result of endogenous adrenal androgen hyper secretion in congenital adrenal hyperplasia, or exogenous testosterone treatment in female-to-male transsexuals. Additionally, cultured human theca interna cells removed from PCOS ovaries exhibit higher androgen secretion that continues during long-term culture. These observations corroborate a role for androgens in the acquisition of the PCOS ovarian features.[61]

Infertility With PCOS

PCOS is these days highly responsible for causing infertility in women. Even though this is yet another hormonal condition that is often causing abnormal production of androgens in the body, it sure is a matter of great concern.With this condition, the woman is not able to have normal ovulation which in some cases leads to lack of ovulation. Reason for PCOS It is sighted that Androgens or the male hormones as referred to in common term are the primary reason. These hormones are present in males that cause the production of muscle mass and hair growth in men. In women, too these are required to produce estrogen. However, with the PCOS condition, the level of these hormones shoots up beyond the normal range. With surplus Androgens, women suffer from physical conditions like acne and excessive hair growth on their bodies. It also leads to irregular and often absent ovulation that results in the irregularity of periods or even absent menstrual periods. With these, a woman encounters difficulty in conception. Any female suffering from PCOS suffers from changes in hormones that are responsible for the production of eggs and cause troubles in pregnancy. Women who have PCOS are not able to conceive due to three reasons.[62] The trouble with ovulation is Irregularity with periods as opposed to healthy women who can have normal cycles. Even if an egg is released, the uterus lining or the endometrium may not be ready for pregnancy Symptoms of PCOS The following symptoms will help you understand PCOS occurrence: Irregularity in menstrual cycles or lack of cycles Excessive body or facial hair is seen in teens and females in their 20s The condition worsens over the years with an

increase in hair growth It is due to the surplus testosterone and androstenedione that results in high male hormone production in females in their blood. Hirsutism is a condition that is marked by excessive body hair. Chances of PCOS This syndrome is common to women at early reproductive age.[63] An estimated 8-10% of women are said to suffer from this syndrome. PCOS and fertility Women suffering from PCOS are not able to produce a healthy egg that is required for fertilization by male sperm. With this disorder, the woman needs proper treatment to be able to conceive. Ovulation thus becomes a necessary change in the body that enables in preparation of mature eggs. Polycystic ovaries are associated with a high rate of infertility. These women are more likely to have problems obtaining pregnancy and will seek treatment to improve their chances. PCOS is treatable through medications, if it is an acute case then IVF is required to conceive. The treatments are determined by the case history and the medical condition of the patient. Consult a gynaecologist immediately if any PCOS symptoms are seen to avoid further trouble.[64]

Since in this disease, an excessive amount of male hormones are produced, ovulation may spontaneously stop, making pregnancy impossible. Its major symptom is an irregular menstrual cycle. If a woman has an irregular menstrual cycle, it could be possible that she is having PCOS. If you have undergone the appropriate tests and have proven that you have it, you need not fret because there are several treatments for PCOS and infertility. PCOs & infertility have a close relationship. Small cysts called antral follicles live in the ovaries and can be seen on most scans. The cysts can be clearly shown with help of ultrasound. Generally, the diameters of the cysts are 2 to 9 millimetres in diameter. Some of these structures are generally linked to the ovaries.[65]

Generally, it is caused by an imbalance of hormones - not enough estrogen and too much androgen. The high amounts of androgens are responsible for the more distressing PCOS symptoms like acne and anomalous hair growth. It is also caused due to genetic disorders. However, medication, lifestyle changes, and a combination of therapies can often help to alleviate symptoms and manage the condition. There are various drug treatments available for PCOs and infertility issues. The best treatment for PCOS is weight loss. If a woman is overweight, this can influence hormonal balance.[66]

Losing weight can restore these imbalances and result in normal menstruation. Fertility medicines also can be used to stimulate follicle production and ovulation. This is done in two ways. **IVF** may also be considered the best way to achieve a successful pregnancy. IVF offers good results and can minimize the risks of multiples. IVF gives women the best chance of becoming pregnant if fertility medication is not effective. It is also an option if all else fails.[67]

If a patient is diagnosed with PCOS, they will be probably aware of the fertility issues. They have tried to conceive with the aid of fertility pills but have been unable to do so. However, if such fertility medications do not work, the patient wants to consider another option. Ovarian drilling may be a viable option.[68]

Ovarian Drilling is a type of surgery that doctors frequently suggest for PCOS. The treatment is very similar to OWR (ovarian wedge resection), in that the ovarian tissue is destructed and the production of androgen is reduced. Symptoms of this syndrome can be managed in this manner. At reproductive age, approx 10% of women are affected by this syndrome, with common symptoms including weight gain, irregular periods, acne, an increase in body hair, and infertility due to ovulation failure. PCOS has been related to other issues such as insulin resistance (IR) and diabetes. Women who have PCOS produce a lot of testosterone and insulin, which causes fertility problems.[69]

The care is frequently performed using the laparoscopic method, in which a surgeon makes a small cut in the abdomen and then inserts a tube to enlarge the abdomen with a small amount of CO2 gas so he or she can embed the laparoscope without harming the inner organs. The surgeon can easily examine the inner organs using a laparoscope. Because this is a less invasive surgery, the doctor will most likely recommend discharge on the same day of surgery, and the patient will be able to resume normal daily activities within 24 hrs. Typically, recovery from surgery takes two to four weeks. The treatment is generally recommended for women who have PCOS, are not ovulating after trying fertility drugs, or are trying to lose weight.The treatment is customized to each individual's needs. Women who are unable to conceive using medications and undergo ovarian drilling may be able to conceive in 50% of cases after the surgery. Laparoscopic ovarian drilling surgery, like any other medical procedure, carries risks such as internal bleeding, infection or bleeding from the incision inserted during the procedure, accidental injury to the internal organs, and, in rare cases, issues caused by anesthesia.[70]

2.3.3 Diagnostic Criteria

Some sets of criteria for diagnosis have been proposed for PCOS: National Institutes of Health Criteria (NIH), defined in 1990 and include only presence of clinical and/or biochemical hyperandrogenism and oligo/amenorrhea anovulation. Later in 2003 the Rotterdam Criteria used polycystic ovarian morphology on ultrasound as a new criterion to be added to the two previous criteria of NIH. The European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine Rotterdam consensus (ESHRE/ASRM) developed and enlarged the diagnosis of PCOS, requiring two of three features: anovulation or oligo-ovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology (PCOM) seen on ultrasound. Finally the Androgen Excess Society defined PCOS as hyperandrogenism with ovarian dysfunction or polycystic ovaries. Thus the Androgen Excess Society (AES) considered that androgen excess is a central event in the development and pathogenesis of polycystic ovary syndrome, and established that androgen excess should be present and accompanied by oligomenorrhea or PCOM or both of them.[71]

Exclusion of other androgen excess disorders should be excluded such as non-classical congenital adrenal hyperplasia (NC-CAH), Cushing's syndrome, androgen-secreting tumors, hyperprolactinemia, thyroid diseases, drug-induced androgen excess, as well as other causes of oligomenorrhea or anovulation.[72]

In November 2015, the American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE), and Androgen Excess and PCOS Society (AES) released new guidelines in the evaluation and treatment of PCOS. Among their opinions and recommendations are the following:

- The diagnostic criteria for PCOS should include two of the following three criteria: Chronic anovulation, Hyperandrogenism (clinical/biologic), and Polycystic ovaries
- In addition to clinical findings, obtain levels of serum 17-hydroxyprogesterone and anti-Müllerian hormone to aid the diagnosis of PCOS.
- Free testosterone levels are more sensitive for determining androgen excess than total T levels and should be obtained with equilibrium dialysis techniques
- Women with PCOS should also be evaluated and/or treated for reproductive function, hirsutism, alopecia, and acne.[73][74]

2.3.4 Diagnosis

PCOS requires accurate diagnosis and management because it can lead to a variety of biochemical and cardiovascular-vascular- vascular risks if not treated properly. The underlying pathophysiology of PCOS is not fully understood. As a result, treatment is frequently focused on individual symptoms rather than the syndrome as a whole. However, as knowledge of the pathophysiology of PCOS grows, so does treatment. Although treatment should be tailored to the individual, it should also focus on minimizing future complications and all metabolic consequences.[75] More study and knowledge of the path biology of PCOS will enhance medication adherence and patient management.

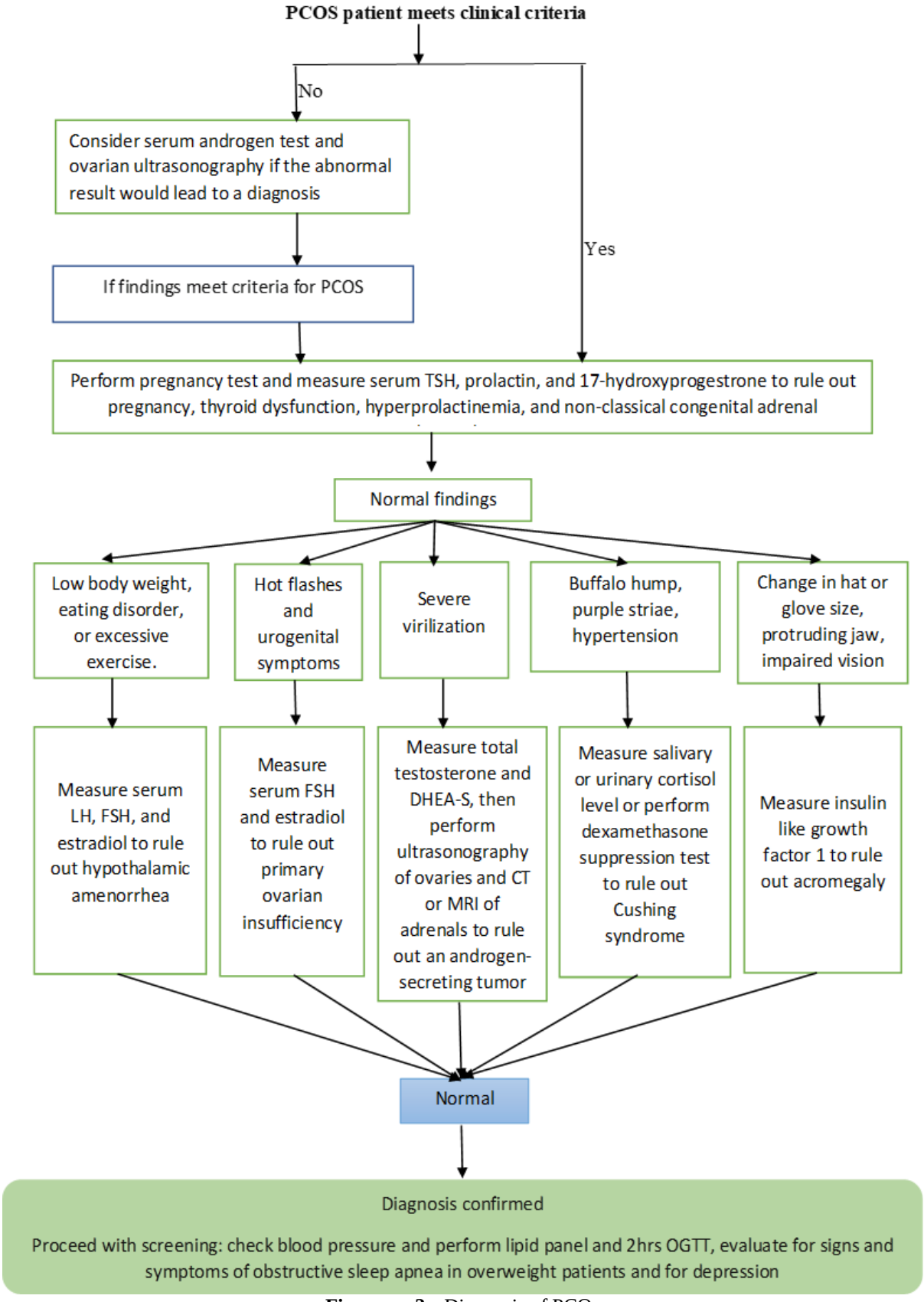

Figure no.2:- Diagnosis of PCO.

2.3.5 Treatment

The treatment options available for PCOS are a combination of lifestyle changes, medications, and surgery.

- **Lifestyle changes:** Several lifestyle changes can help to control and reduce the symptoms of PCOS. These include: - Regular exercise - Losing weight if you are overweight - Living a healthy lifestyle, without smoking and drinking alcohol excessively - Eating a balanced diet, which is low in saturated fats.[76]
- **Medications:** In addition, medications can be used to address the root cause of the increased amount of androgens in a woman's body. This can be achieved by blocking the activity of certain hormones; or by reducing the number of androgens in the body through medication.
- **Insulin sensitizers:** These are medications that increase the sensitivity of the body's cells to the hormone insulin. When insulin is released, it plays a vital role in regulating how cells use glucose, a type of sugar, for energy. Insulin sensitizers can help to restore the balance of hormones in the body, by controlling the level of insulin in the body.[77]
- **Anti-androgens:** Anti-androgens are medications that block the activity of certain hormones. These can reduce the number of androgens in the body, which can help to restore the balance of hormones in the body.
- **Weight loss surgery:** If lifestyle changes are not successful in controlling the symptoms of PCOS, then women may be advised to consider weight loss surgery. In some cases, the weight loss surgery may be combined with hormonal therapy. This treatment aims to achieve even greater weight loss, which may lead to the reduction of excessive facial and body hair.[78][79]

2 .3.5.1 NCBI – Guidelines

Table 1:- STG (Standard Treatment guidelines) for Infertility with PCOS.

Clinical Symptoms	**First Line Treatment**
1.Menstrual abnormality 2.Hirsutism 3.Acne	Hormonal contraceptives (HCs): oral contraceptives, patches or vaginal ring.
1.Obesity 2.Weight gain 3.Reproductive / metabolic dysfunctions 4.Risk factors- cardiovascular disorder, Diabetes	Lifestyle therapy; Weight loss, exercise, dietary intervention.
1.Cutaneous manifestations 2.Pregnancy complications	Metformin
Anovulatory Infertility	Clomiphene citrate, Letrozole
Clinical Symptoms	**Second Line Treatment**
1.T2DM/IGT 2.Menstrual irregularity 3.Infertility	Metformin

Current situation of PCOS:

Studies show that 5-13% of women of childbearing age have PCOS. Anovulatory infertility is a common consequence of PCOS, and the incidence of PCOS in women with anovulatory infertility is higher, at 70% to 80%. Therefore, there is a options for anovulatory infertility treatment. However, PCOS often have other co-morbidities such as increased BMI, cardiac metabolic syndrome, psychiatric disorders, and poor health-related quality of life. Drug treatments and lifestyle interventions are recommended to improve fertility and other reproductive outcomes. These evaluations and treatments begin in primary care, with referral to other relevant specialties as needed.

Conclusion:-

PCOS is a condition that affects women and their hormonal balance. It is a complex disorder that has no known cause. It is estimated that 1 in 10 women of reproductive age have PCOS. However, this number changes over time so it is difficult to know how many women have the condition. PCOS is a complex disorder that requires a variety of therapeutic techniques and psychological reasons a doctor aims to diagnose. Antidiabetics can be used to treat the long-term effects of PCOS, such as t2dm and cardiovascular disease. PCOS is a condition in which the hormone levels in the body are disrupted. Causes the ovaries to become enlarged and develop small cysts which look like small sacs. It genrally occurs in women who are aged between 15 and 35, but it can also develop in women who are older than this. It can also affect men. One in ten women of reproductive age i.e. between the ages of 15 and 44 has PCOS. Around 1 in every 25 women of reproductive age has it, but this number is likely even higher. PCOS can

cause a range of health problems for women, which can have a serious effect on their quality of life. PCOS is highly responsible for causing infertility in women. Androgens or the male hormones are referred as primary reason. Women who have PCOS are not able to conceive due to three reasons, irregularity in menstrual cycles, lack of ovulation, and hair growth are some of them. PCOS is treatable through medications, if it is an acute case, IVF may be required.

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