



Recent Updates on Female Reproductive Physiology: A Review

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Abstract: The human sex organs, which comprise the male and female reproductive systems, are part of the entire reproductive process. Having offspring that have the same characteristics as their parents is the ultimate objective of reproduction. It is necessary for humans to have a male and a female reproductive system for sexual reproduction. The female reproductive system is mostly concerned with ovulation. In most anisogamous species, female reproductive cell or gamete is the egg cell or ovum (Plural ova) (organisms that reproduce sexually with a larger, female gamete and a smaller, male one). To describe a situation in which the female gamete is unable to migrate, the word (non-motile). Exogamous sexual reproduction occurs when a male gamete (sperm) may migrate independently of the female gamete.

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INTRODUCTION

Females' reproductive systems (or female reproductive systems) are made up of internal genitalia and external genitalia, both of which play a significant part in the creation of new progeny, female reproductive systems in humans are underdeveloped at birth, but they grow throughout time to become fully functional adult reproductive systems.

The uterus, fallopian tubes and ovaries are the three internal female genital organs that play a major part in the female reproductive system's capacity to produce gametes and carry embryos to full term, vaginal and

uterine secretions play a significant role in sperm transport to the fallopian tube. Oocytes (cells in the egg) are produced by the ovaries. Anatomy of the external genitalia: labia, clitoris and vaginal aperture. And cervix, an important muscular tube connecting the vagina to the uterus.

External genitalia: The term "vulva" refers to the external female reproductive system as a whole.

Vulva: Among the most important vulva features are the mons pubis, the clitoral hood and glans, the urinary

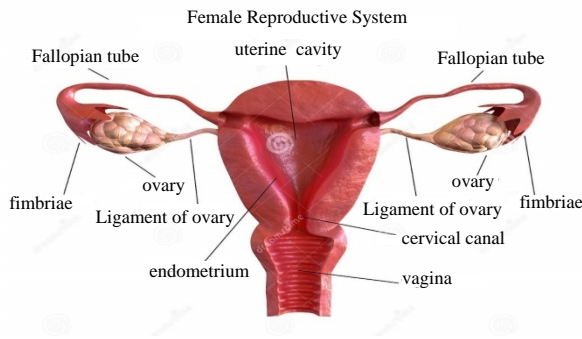


Fig. 1: Female reproductive system^[1]

meatus, the vaginal entrance and the hymen and the vestibular glands of Bartholin and Skene. Also included are pubic hair, sebaceous glands, the valvular vestibular area and other parts of the urogenital triangle.

Internal organs: The vagina, uterus, Fallopian tubes and ovaries are considered as the main structure of the female internal reproductive organs.

A-Vagina: The Latin word for "sheath" or "sheath" is vagina and the combination of the vagina is either vagina or vaginas in the context of pregnancy and delivery^[2]. Anatomical meaning of the word vagina relates only to the internal anatomy, whereas colloquial refers to the vulva or both the vagina and the vaginal canals^[3]. The human vagina is a flexible muscle canal extending from the vulva to the cervix pink color, which connects between the vulva and the cervix. The cervix surrounding the vaginal part is called fornix^[4].

Perineum between the urethra and anus, the vaginal canal goes to the top and back as well as between urethra and rectum in the front and rear, respectively, the uterus, cervix and vaginal epithelium are important as they are the first place in the vaginal secretions as well as the Bartholyn gland which is important in small vaginal lubrication when sexual arousal^[5].

To moisten the vagina, it just takes a little amount of vaginal discharge During sexual arousal, the midst of a woman's menstrual cycle, the days leading up to menstruation and even during pregnancy, excretions might rise. "period" or "monthly menstruation" refers to the time period when the uterus's internal lining begins to the orderly discharge of blood and mucus tissue (known as menstruation) through the vagina.

To create an alkaline and fruitful environment in the vaginal canal, the cervix's cervix mucous glands release distinct mucus differences before to and during

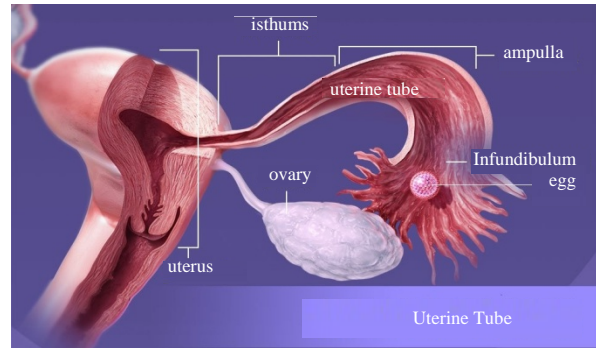


Fig. 2: Uterine tube structure^[8]

ovulation. Be a suitable place for sperm survival, vaginal lubrication decreases after menopause naturally^[6].

B-Uterus: In the female reproductive system of humans and the majority of other animals, the uterus or womb is regarded as a secondary genitalia. A woman's uterus is placed in the pelvic region, behind and almost covering the bladder and in front of the sigmoid colon. The uterus of a woman, shaped like a pear^[7].

C-Ovary: In women, the ovary is a reproductive organ that releases an ovum, which travels via the fallopian tube to the uterus, where it may be fertilized by either sperm or egg^[9].

Both the left and right sides of the body include an ovary, which is derived from the Latin ovarium and means "egg, nut." Menstrual cycle and fertility are both influenced by hormones produced by the ovaries^[10].

The ovary undergoes a series of changes from conception until menopause. Endocrine gland due to the many hormones that it produces^[11].

Structure of ovary: The female gonads include the ovaries. The ovarian fossa, where each ovary is positioned next to the uterine lateral wall, is a white zone. This is the area of the uterus that is limited by the iliac artery and the ureter in front of the internal iliac artery, as well as by the external iliac^[12]. The ovaries are encircled by a capsule and have an outer cortex and an inner medulla. This region is about 4 cm x 3 cm x 2 cm in size. If one of the two ovaries is missing or malfunctioning throughout the menstrual cycle, the remaining ovaries will continue to produce eggs, resulting in no change in the duration or frequency of the monthly cycle. One end of the ovary points downward

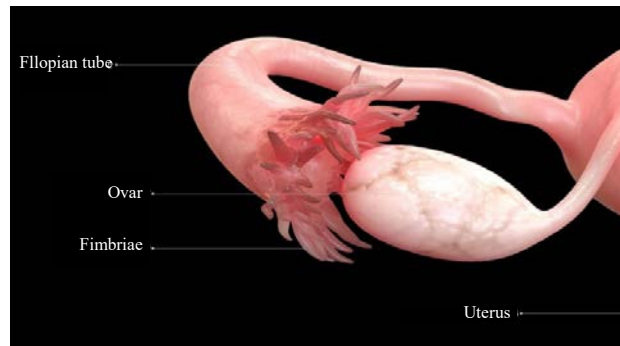


Fig. 3: Image of ovary 3D

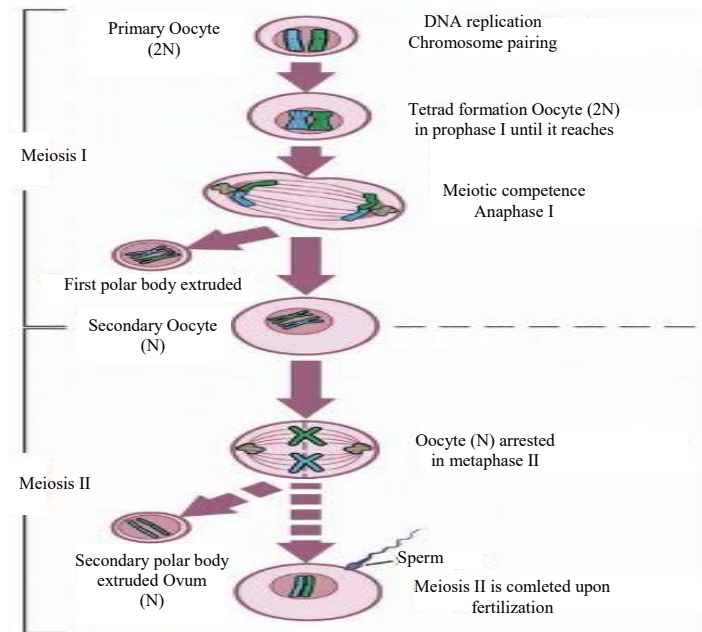


Fig. 4: Oogenesis process^[20]

and is joined to the uterus by the ovarian ligament, while the other end is attached to the fallopian tube by the infundibulo pelvic ligament^[13].

Function: The ovary starts to release more hormones during puberty. In reaction to the hormones, secondary sex traits begin to emerge. Reproductive capacity grows. At puberty, the ovary undergoes major structural and functional changes^[14].

gamete production: The ovaries produce and release egg cells, the female gametes, on a regular basis. Follicles, which are filled with fluid, contain the developing egg cells (oocytes). Typically, one oocyte matures at a time, but many oocytes might mature at the same

time^[15]. According to the stage of oocyte development, follicles are made up of various kinds and numbers of cells and their size is a good indicator of the oocyte's maturity^[16].

Ovulation occurs when the pituitary gland secretes a large amount of luteinizing hormone, which causes the follicle to burst and release the mature oocyte^[17]. To ensure that the uterus is ready for the implantation of the embryo, progesterone is secreted by the follicle, which continues to function^[18].

Fertilized eggs undergo a process known as oogenesis, which transforms the ovum (egg cell) into a differentiated cell capable of continued development. The main oocyte is matured by the process of Oogenesis, which begins in the embryonic stage^[19].

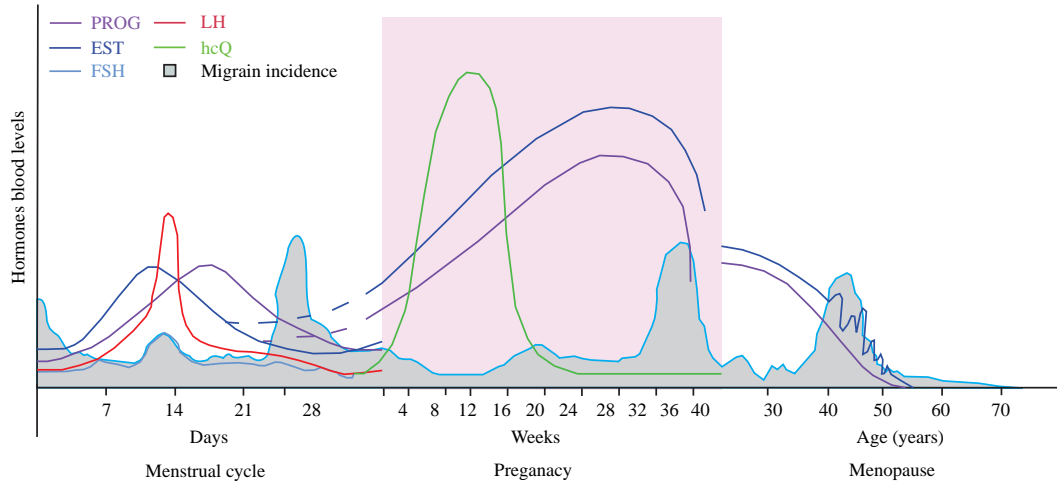


Fig. 5: Female hormone secretion regulation^[26]

Ovulation: Ovulation in women happens after the follicular phase, roughly halfway through the menstrual cycle in humans. Days 10 to 18 of a 28-day menstrual cycle are the most fertile period, which is when a woman is at her most reproductively active^[21]. The brain's hypothalamus regulates ovulation, as do chemicals generated by the pituitary gland's anterior lobe, including as luteinizing hormone (LH) and follicle-stimulating hormone (FSH)^[22].

FSH stimulates the ovarian follicle to undergo a series of changes known as cumulus expansion, which results in a hole in the follicle known as the stigma, through which the secondary oocyte exits the follicle. This process occurs during the preovulatory phase of the menstrual cycle. An increase in the pituitary gland's secretion of FSH and LH signals ovulation. The secondary oocyte travels to the uterus via the fallopian tubes during the luteal (post-ovulatory) phase. Within 6-12 days of being incubated by an egg, the fertilized secondary oocyte or ovum might get implanted there^[24].

Hormone secretion: Women's ovaries and adrenal glands create 50% of the body's testosterone, which is then delivered into the bloodstream through the gonads and progesterone^[25]. As a female enters puberty, estrogen is important for the development of secondary sexual characteristics and for keeping reproductive organs in a fully developed and functioning form. The uterus and the mammary glands are prepared for pregnancy and breast feeding by progesterone. Estrogen and progesterone work together to regulate the menstrual cycle in the endometrium.

From embryonic stem cells, the development of human female reproductive tract epithelium: Emerging from the primitive stripe, mesoderm gives birth to the coelomic epithelium during development. During fetal development, invagination of the coelomic epithelium results in the formation of the Mullerian Duct (MD). It is from here that the ovary, uterus and the upper vaginal canal develop into the human Female Reproductive Tract (FRT). Uterine mucosa is well-known for its extraordinary ability to regenerate itself throughout the reproductive years of females^[27].

The ability of the endometrium to regenerate itself has been linked to a tiny number of stem/progenitor cells that exist inside the tissue. To track and identify adult stem/progenitor cells, the smooth muscle differentiation of the stromal cells may be traced back to embryonic stem cells (ESCs) according to a study published in the journal development^[28].

Female Genital Tract Embryology: Embryo genesis at an early stage In around 4 days, a morula of 12 to 16 cells containing the fertilized ovum enters the uterine cavity. Approximately six days after conception, A blastocoel develops and loses its zona pellucida. During the eighth day, the blastocyst is made up of an embryonic disk that separates the amniotic and yolk sac chambers inside the chorionic membrane. Chorion membrane's trophoblastic section begins to differentiate around the 11th or 12th day into cytotrophoblast, intermediate trophoblast and syncytiotrophoblast. This is the first stage of embryonic development.

Seven Second-week embryos are oval disks of 0.2 mm in diameter and they have two sets of cells on each

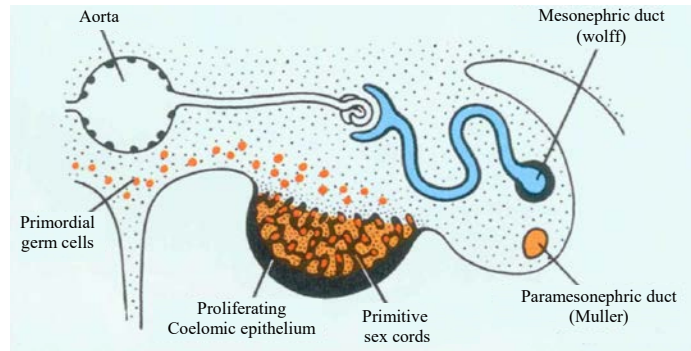


Fig. 6: Creation of the feminine reproductive tract in the human race^[29]

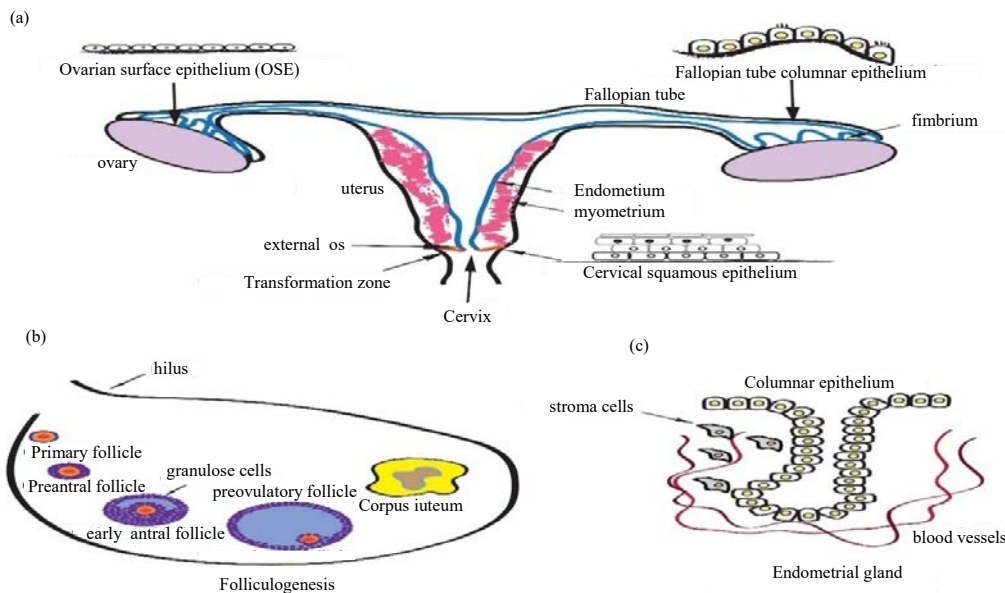


Fig. 7: Embryonic of human female reproductive tract

side. The first two germ layers are represented by the two laminae. It is the ectoderm that covers the top and the endoderm that covers the bottom^[30].

The developing female genital tract: from genetics: The ovary, the hypothalamus-pituitary-gonadal (HPG) axis and the reproductive tract, which includes the uterus and oviduct, must all operate together harmoniously in order for female reproductive function to be successful. Because of this, exposure to any one of these components may have an effect on the others as well.

Understanding ovarian development and function, as well as the involvement of many variables that influence these processes. Studied steroid hormones and their receptors, as well as select transcription methylation, A process that is thought to be sensitive to

the impacts of hormones^[31]. Normally, the germ cell genome is pre-methylated in rats before migration to the vSaginal ridge, but following migration, the genome is post-methylated, even at imprinted loci. When somatic and germ cells interact, re-methylation happens at distinct developmental stages in a sex-specific way. The re-methylation of female germ cells begins in the postnatal period PND 1-5 and continues throughout oocyte development until the prenatal follicle stage^[32].

The Müllerian ducts of the mammalian female reproductive system differentiate into oviducts, uterine horns, the cervix and the anterior vaginal ducts in a cranial to caudal orientation^[33].

Members of the genital track female's hox gene families, Which regulate critical developmental genes, Are a subset of home box genes, A collection of related

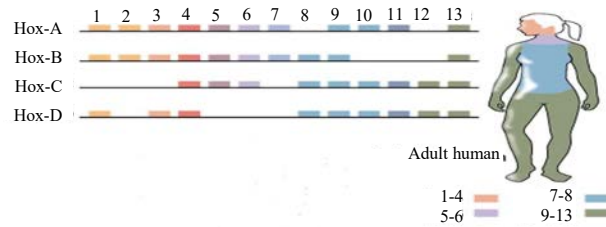


Fig. 8: Hox proteins encode and specify 'position'^[36]

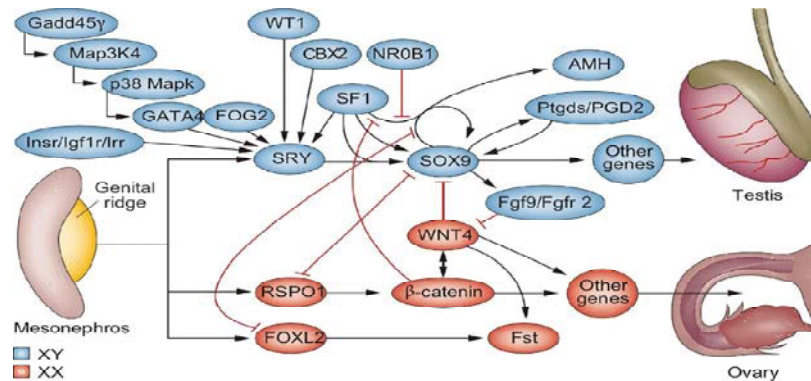


Fig. 9: Gonadal differentiation is shown in this diagram of genes involved in the process

genes that designate parts of an embryo's body plan along the head-tail axis of animals throughout this organogenesis^[34].

To ensure that the proper structures develop in the correct parts of the body, Hox proteins in vertebrates encode and define aspects of 'position.' Hox proteins impart segmental or positional identity to segmented animals, But they do not actually produce the segments. Steroid hormones have a role in the female vaginal tract's subsequent development as well. Therefore, steroid-like chemicals may function as agonists or antagonists on fetuses when exposed^[35].

Müllerian duct regression and development are regulated by certain genes. Male and female reproductive duct primordials coexist in the so-called sexually indifferent stage (bipotential gonad). It is possible to differentiate male and female reproductive organs based on the embryonic gender, which is determined by the genetic sex of the embryo. Without particular male hormones, in female embryos, female reproductive system generate ducts develop embryos.

Differentiation of primordial germ cells and gonads: Somatic cells and germ cells are the two major cell types in the mammalian ovary. Originating from extra gonadal

tissues around embryonic day, the sexually undifferentiated primordial germ cells migrate into the indifferent gonad, where they quickly multiply. During mitotic arrest, growing germ cells in the male (XY) gonad create seminiferous cords and enter meiosis, whereas in the female (XX) gonad, proliferating germ cells form oocyte nests and enter meiosis^[37]. The embryonic testis or ovary develops from the cells of the indifferent gonad, which is derived from the genital ridge. In an XY embryo, an ovary develops instead of a testis when the SRY gene is deleted or mutated (the sex-determining region of the Y chromosome). As gonadal differentiation proceeds down the male route, many additional elements that are downstream of SRY are required to create a testis rather than an ovary if SRY is expressed in a XX embryo^[38].

Oocyte and early follicular genetic: Somatic pre granulosa cells surround meiotic female germ cells known as oocytes during the early diplotene phase of meiotic prophase I. The ovary's primordial follicle count is increased by deleting the pro-apoptotic molecule, since most of these germ cells are destroyed by apoptosis^[39].

One layer of flattened pregranulosa cells covers the rest of the remaining oocytes and this layer is what eventually develops into primordial follicles. These first

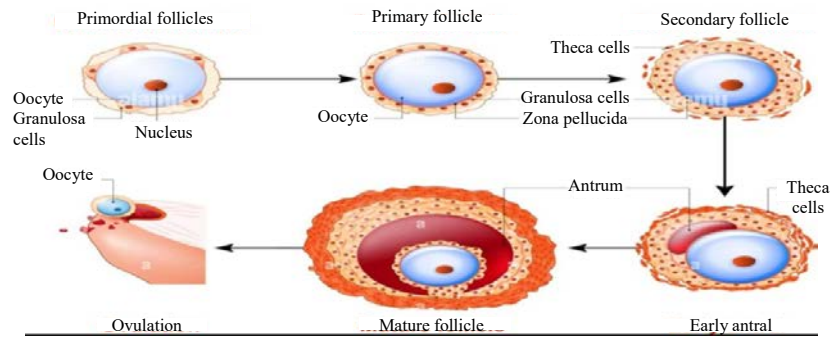


Fig. 10: Maturation of a follicle. Diagram of folliculogenesis^[41]



Fig. 11: Polycystic ovary syndrome(PCOS)^[44]

form after birth and the process is nearly complete. Most primordial follicles remain dormant, but some begin to grow and develop into primary follicles. Profoundly, as the success of female reproduction is dependent on these early processes, the disruption of these interactions might lead to early depletion of follicles that can result in an early reproductive senescence^[40].

The most prevalent kind of birth abnormalities in women genetic Poly cystic ovary syndrome (PCOS): Based on clustering instances within families, it seems that PCOS has a hereditary component. In family instances, hyperandrogenemia seems to be the most strongly inherited trait. PCOS genetics research has been hindered by a number of issues. To do linkage analysis, big pedigrees are difficult to come by since PCOS is connected with infertility^[42].

Due to the fact that PCOS is a diverse disorder one, it is difficult to compare family studies that employ various diagnostic criteria. The phenotype of PCOS in men has not been thoroughly established. Accordingly, a dominantly inherited characteristic with poor

penetrance and variable expression has been found in the majority of research. This manner of inheritance is in line with the wide range of clinical symptoms seen in PCOS patients. Since genetic variability is polygenic and complex, however^[43].

Candidate, genes: As several genes display aberrant expression patterns, this shows that PCOS impacts signal transduction pathways regulating the expression of a family of genes, rather than the abnormal expression of a single steroidogenic enzyme gene in the PCOS gene pool. According to this, cytogenetic investigations have been unable to detect frequent karyotypic anomalies^[45].

A particular breakpoint in an observed aberration would suggest the presence of a causal gene. Researchers have long investigated links or connections between PCOS and the many genes involved in the androgen biosynthetic pathway or metabolic pathways involved in insulin action since anomalies in steroidogenesis are a hallmark characteristic of PCOS. It is possible to utilize linkage analysis to show that a genetic variation and a disease locus co-segregate^[46].

Studies of genetic variation and illness are known as association studies. The family-based linkage disequilibrium test (TDT) examines whether or not parents heterozygous for a disease allele transmit that allele to their afflicted offspring more often than they transmit the non-disease allele to them. Numerous research looking at potential PCOS-related genes' linkage and association have come up empty-handed. 31-39 Below, we'll go into further depth about studies that had favorable or mixed outcomes^[47].

CYP17 (cytochrome P450 17-hydroxylase/17, 20-desmolase): PCOS has been linked to the 17-hydroxylase/17, 20-lyase cytochrome CYP17 gene, however subsequent research has failed to substantiate this discovery, making this gene an unlikely candidate for a PCOS gene^[48].

CYP11A (cytochrome P450 side-chain cleavage enzyme): Hyperandrogenemia in women with PCOS may be linked to the cytochrome P450 11A gene, which codes for the cholesterol side-chain cleavage enzyme. The CYP11A pent nucleotide repeat polymorphism was shown to be strongly associated with total serum testosterone levels in women with PCOS^[49]. There are further limitations to these early studies due to insufficient statistical corrections for multiple testing, as discussed above in this section. A pent nucleotide repeat in the CYP11A gene was shown to be associated with PCOS in another investigation^[50].

CYP21 (cytochrome P450 21-hydroxylase): Most instances of congenital adrenal hyperplasia are caused by a protein encoded by CYP21 called 21-hydroxylase (CAH). Many PCOS women with a normal 17-hydroxyprogesterone response to adrenocorticotrophic hormone (ACTH) stimulation had CYP21 mutations, which raises doubts about the diagnostic difference between PCOS and CAH, according to a recent study^[51].

Androgen receptor: The CAG repeat polymorphism in the X-linked androgen receptor gene has been associated to the development of polycystic ovary syndrome (PCOS). However, it has been shown that a low CAG repeat length is negatively related to androgen concentrations. 48 Exon 1 of the androgen receptor has biallelic means that are substantially more common in PCOS women than normal women, according to a study of those women. established a correlation between the CAG repeat polymorphism in the androgen receptor gene and premature puberties.

Sex hormone binding globulin (SHBG): In 4 of 482 women with PCOS, hirsutism, or ovarian dysfunction, they discovered a polymorphism in the SHBG coding area that encodes a missense mutation, P156L. They found a relationship between the (TAAAA)_n polymorphism in the SHBG and PCOS. There was a higher frequency of longer (TAAAA)_n alleles in women with PCOS (more than eight repetitions) than in individuals who had shorter alleles.

Insulin receptor: Insulin receptor gene sequence has been studied in a number of investigations for substantial alterations of sequence. 50 percent of women with PCOS had elevated insulin receptor serine phosphorylation in skeletal muscle and fibroblasts, which shows that insulin action is disrupted in PCOS and that this is the mechanism at work. The insulin receptor's tyrosine auto phosphorylation was also discovered to be reduced in the ovaries of women with PCOS in a recent research. Polycystic ovary syndrome 713 is associated with a C/T single nucleotide polymorphism in the tyrosine kinase region of the insulin receptor gene and a higher risk of developing PCOS^[52]. PCOS and a marker (D19S884 at chr 19p13.3) Near the insulin receptor gene have been linked in two distinct studies. 34,57 Researchers from. The strongest connection evidence was found at the D19S884 marker^[53]. In Caucasians, there is a statistically significant relationship between an area on chromosome 19p13.3 and levels of androgen, indicating that the region may play a substantial role in PCOS. A family of genes involved in steroidogenesis and insulin action is likely to be affected by the presence of the insulin gene 50 VNTR (variable number tandem repeats), which is strongly linked and associated with PCOS, despite the fact that the PCOS gene in this region has not yet been identified. The class III allele of the insulin VNTR has not been linked to hyperandrogenemia or PCOS and the INS VNTR polymorphism has not been linked to hyperandrogenemia^[54].

Insulin receptor substrate proteins: The Gly972Arg IRS-1 and Gly1057Asp IRS-2 mutations are linked to insulin resistance in women with PCOS. There was no correlation between IRS-1 and PCOS. Non-diabetic White and African-American women with PCOS were shown to have higher blood glucose levels if they had the IRS-2 Gly/Gly polymorphism, whereas girls with a history of precocious puberty were more likely to have the G972R variation of the IRS-1 gene^[55].

Follistatin: Siblings with follistatin mutations showed a statistically significant association to the disorder. In

spite of this, later studies of the follistatin gene have shown no evidence of substantial connection^[56].

Calpain-10: Cystine protease Calpain-10 has been linked to an increased risk of developing type 2 diabetes. African-American women with the 112/121-haplotype had higher insulin levels and are more likely to develop PCOS. However, there was no connection observed between the CAPN10 UCSNP-44 allele and PCOS when looking at the whole genome^[57].

CONCLUSION

A large number of functioning components make up the female reproductive system. Because of this, the hypothalamus, pituitary and ovary work together to maintain proper reproductive function. Furthermore, the absence of systemic dysfunctions induced by illness or toxicity is necessary for the preservation of good reproductive efficiency. As a result, in order to provide a clearer picture of how it works.

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