A STUDY OF LIPID PROFILE AND SERUM OESTRADIOL LEVEL IN POSTMENOPAUSAL WOMEN

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BONAFIDE CERTIFICATE

This is to certify that the dissertation titled **"A STUDY OF LIPID PROFILE AND SERUM OESTRADIOL LEVEL IN POSTMENOPAUSAL WOMEN"** is a bonafide record work done by **Dr.A.Sivapriya**, under my direct supervision and guidance, submitted to The Tamilnadu Dr. M. G. R. Medical University in partial fulfilment of University regulation for **M.D., Branch-V (Physiology).**

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I, **Dr. A. SIVAPRIYA,** solemnly declare that the dissertation titled **"A STUDY OF LIPID PROFILE AND SERUM OESTRADIOL LEVEL IN POSTMENOPAUSAL WOMEN"** has been prepared by me. I also declare that this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad. This is submitted to The Tamilnadu Dr. M .G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of **M.D. degree Branch-V (Physiology)** to be held in **April-2017.**

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CONTENTS

INTRODUCTION

Data released by the **Health and Family Welfare Ministry of India** show that life expectancy for females is increased by five years, from 63.9 years in 2001-2005 to 69.6 years in 2011-2015. In India, with the rise in life expectation in females, number of postmenopausal women is increasing. Approximately woman today, will live for about one third of her life, beyond menopause.

Menopause is a normal physiological change wherein the permanent stoppage of menstruation takes place. Primarily menopause is due to loss of stocks of oocyte in ovary with a consequent fall in the level of hormones like oestrogen and progesterone. This results in the cessation of cyclical changes in the endometrium and hence menstruation. The loss of fertility and menstrual function that accompany menopause may have an impact on a woman's sense of wellbeing.

Women from fetal life till menopause experience different stages under the influence of female hormones. These hormones are secreted in very little quantity. According to different phases of her reproductive life, these hormones undergo a complex and ever changing trend.

During menopause, woman passes from fertile to infertile stage. The oestrogen production is grossly reduced in postmenopausal period. It is due to the peripheral conversion of adrenal androgens and this occurs mainly in adipose tissue, liver and brain.

Decrease in the level of oestrogen in postmenopausal period of females alter their general health by producing physiological, biochemical and structural changes. In a very significant way the body metabolism is affected.

Lipid metabolism is affected by the level of oestrogen. Changes in serum lipid and lipoprotein levels indirectly lead on to coronary heart disease which determine the life expectation among postmenopausal women.

According to **Framingham study**, morbidity rate due to coronary heart disease accelerate more quickly in females of age more than 45 years than in males. Before menopause, oestrogen protects females against coronary artery disease by its anti-atherogenic effect.

Altered serum lipid profile is associated with menopause and thus it is a major determining factor predisposing to cardiovascular diseases. It makes the screening of postmenopausal women for abnormal lipid profile mandatory.

Significance of duration of menopause on serum oestradiol level and its correlation with lipid profile is to be investigated so that postmenopausal women can undergo further evaluation and earlier management.

Hormonal alteration and the associated changes in serum cholesterol and lipoproteins level in relation to the duration of menopause is aimed to study at present so that specific health strategies can be promoted and thereby emerging cardiovascular diseases can be prevented among the postmenopausal women.

AIM AND OBJECTIVES

1. Estimation of serum oestradiol level in postmenopausal women and are divided into three groups based on the duration of menopause.
2. Comparison of serum oestradiol level between these three groups.
3. Estimation of lipid profile in the postmenopausal women included in these groups.
4. Comparison of lipid profile values between the postmenopausal women of these three groups.
5. Correlation of serum oestradiol level with the changes in lipid profile.

REVIEW OF LITERATURE

HISTORY

Since biblical times, menstruation and menopause were dealt in our society. Even before the year 1800, references to menopause were found. **Aristotle** stated that menopause began even at the age of 40 years in females. The term "menopause" (la ménépausie) was coined by **Charles Pierre Louis De Gardanne in 1821.**

Oestrogen is responsible for the development of the organs of reproductive system and secondary sexual characters in females. The name oestrogen is derived from the Greek word **"oistros",** which means **"verve or inspiration"** and the suffix -**gen**, means**" producer of"**. The structure of oestrogen was determined by **Adolf Butenandt** in 1929 and was isolated by **Edward Adelbert Doisy**. The speed in hormonal drug research was increased thereafter.

In 1930, Emmentin was discovered by **Collip and Ayerst Laboratories**. It was the oral oestrogen derived from urine of pregnant Canadian women. A drug company in Germany synthesised a product like that of Emmenin and German women with menopausal symptoms were treated with it.

For the treatment of menopausal symptoms, nonsteroidal oestrogen diethylstilbestrol (DES) was formulated by the British scientists. That was cheaper and more powerful. The **Food and Drug Administration** finally accepted it by the year 1938.

The researches in modern lipid chemistry began in 17th century. Earlier observations were made by **Robert Boyle, Poulletier de la Salle and Antoine François de Fourcroy**. **Chevreul** discovered many fatty acids during 19th century. He gave the name '**cholesterine**' to the fat substances. The word **'glycerine'** was also coined by him. He explained the components of fats.

Lipoprotein structure and function were understood in detail in 20th century. Relationship of lipoproteins with disease states was investigated. The discovery of methods for the separation of lipoproteins like ultracentrifuge and the substances used for estimation of lipoprotein levels improved our knowledge about lipoprotein metabolism in normal and diseased state.

In postmenopausal period, the hormonal changes like decreased level of oestrogen and markedly increased level of luteinizing and follicle stimulating hormone are seen which exert an important impact on lipid metabolism **(Sacks F.M, A.M. Murray et al).** According to genetic and epidemiologic studies, lipoprotein (a) can predispose to atherosclerosis. In 1963, **Kare Berg** discovered lipoprotein (a). In 1987, human gene encoding apolipoprotein A was cloned.

Cardiovascular disorders are the leading causes of death among females after menopause in developed world **(Ariyo et al., 2002).** Female hormones protect against the development of cardiovascular disease **(Jeanes et al., 2007).** Postmenopausal women are at particular risk for acquiring cardiovascular disorders **(Schulz et al., 2004).**

FEMALE REPRODUCTIVE PHYSIOLOGY

The female reproductive system is responsible for many important functions. The ova produced in ovaries are necessary for the reproductive function. In addition, they also produce sex hormones that maintain the reproductive cycle in females.

Functional anatomy

The important organs of reproduction in females are described as follows.

- Vagina is also called as birth canal which meets the cervix.
- Uterus is otherwise called womb which accommodates the growing baby. It has two parts: lower part is cervix which joins with vagina and upper part is called as body of the uterus or corpus. During pregnancy, size of the body of uterus increases which enable to accommodate the growth of the fetus. Through the cervical canal, sperms enter and menstrual blood comes out of the uterus.
- The ovaries are present in the pelvic cavity and are connected to uterus on both sides with the help of various ligaments. They can produce ova and synthesis hormones during the reproductive period.
- Fallopian tubes arise from the cranial part of uterus. Through these tubes ova are transported from the ovaries to uterus. Fertilization occur in the ampullary part of the tube.

Development

The mullerian ducts persist in females and they undergo further development. A portion of mullerian ducts fuse and form uterus and vagina. This fusion starts at the third month of intrauterine life. The fused walls form a septum which disappears later. The parts that do not fuse form the fallopian tubes on both sides. The ostia of fallopian tubes are present in the anterior portion of tubular invagination inside the peritoneal cavity.

A ring-like constriction develops at about fifth month which demarcates the cervical position. After sixth month of gestation, thickening of the walls of uterus begins.

The vagina is developed as a solid rod of epithelial cells and at the lower end of the uterus, a ring like outgrowth occurs which represents the developing vaginal fornix. By fifth month, due to the breakdown of central cells of the epithelium vaginal lumen is produced. The remains of the mullerian eminence represent the hymen.

From the mesothelial layer of peritoneum, ovary is developed. During third week of intra uterine life, from the endodermal lining of yolk sac, the primordial germ cells get differentiated. By the fifth week, the germ cells migrate to the genital ridge and undergo mitotic division. Only by the seventh week of gestation, the primitive ovary can be distinguished from testis until then the gonads exist in an undifferentiated state.

HORMONAL CHANGES AND MENOPAUSE

Hormones are produced by the endocrine glands and they are secreted directly into blood. They are takenup by the target organs and other systems. Thereby hormones regulate the activities of target organs.

As we grow older, natural changes occur in our body systems. Some target organs will have reduced sensitivity to their regulating hormone. The quantity of hormones synthesised may also change. The blood level of some hormones rise, some are reduced and some remain unchanged. Metabolism of hormones occur more slowly with increase in age.

Most of the endocrine organs which secrete hormones are regulated by some other hormones. This regulation is also changed with age. For example, an endocrine organ may secrete less amount of hormone at an older age or it may secrete at a slower rate but the same amount.

Female hormones

The female gonads produce female sex hormones and are important to maintain the menstrual cycle in the reproductive period. Only when we understand the effects of hormones on body, mind and emotions, we will be able to decrease their negative effects and increase their positive effects in a better way.

- **Fetal life**

From ovaries the oestrogen formation starts by 8 to 10 weeks of gestation. Oogonia develop from primary oocytes and about 6 to 7 million oogonia are present in ovary by fifth to sixth week of intra uterine life.

Then the germ cells undergo atresia and at birth only 2 million oogonia remain. The gonadotrophic hormone levels are increased at birth and are decreased in childhood.

- **Puberty**

The physical maturation from a child to an adult which enable a female for sexual reproduction is called puberty. This is because of the hormonal signals from brain to ovaries. In response to the signals from brain, the ovaries produce female sex hormones that are responsible for the libido and development of brain, bones, muscle, blood, skin and breasts. Height and weight are increased in the first half of puberty and are finished after the complete development to an adult body.

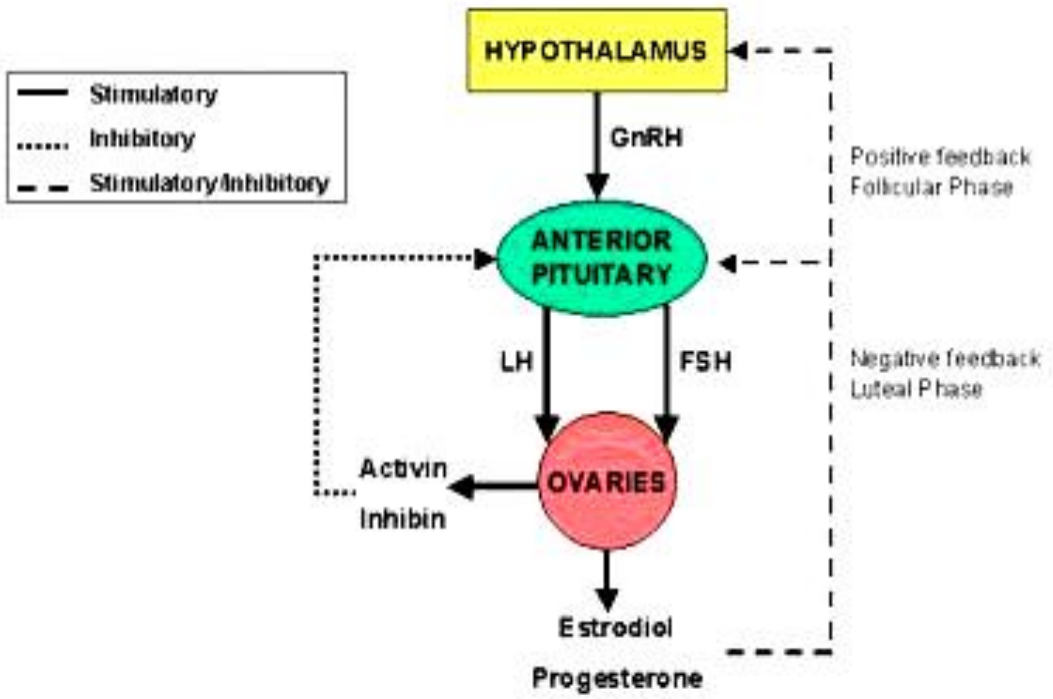
The onset of puberty vary from individual to individual and it is determined by genetic control of the signals from hypothalamus. This process is also influenced by some environmental factors which may play a permissive role. The age of menarche is influenced by health, genetic and socioeconomic factors (**V.V. Khadilkar et al., 2006)**.

In India as per **Agarwal's data,** the age of menarche have reduced from 17 years to 12.8 years. The average age of menarche is shown as 12.6 years in urban India**.**

Even at birth every structure necessary for attaining puberty is present but our body system keeps it switched off for particular years. Only at the time of maturity, hormones which previously have been held in check start to exert their action on the body.

At puberty, the hypothalamo–pituitary–ovarian axis (HPO axis) is activated leading to increased pulsatile secretion of gonadotrophin releasing hormone (GnRH) by hypothalamus that allows for increased secretion of follicle stimulating hormone (FSH), luteinizing hormone (LH) and oestradiol levels **(Jiska S. Peper et al., 2009)**.

An increase in oestrogen secretion from ovary exerts a positive feedback and there is a development of cyclical pattern of gonadotrophin secretion.



During reproductive period of females the menstrual cycle is controlled by five main hormones. Three hormones are secreted from brain and two other hormones are produced from ovaries.

- **Gonadotrophin releasing hormone** is synthesised by hypothalamus. It reaches anterior pituitary and regulates the release of follicle stimulating hormone and luteinizing hormone.

- **Follicle stimulating hormone** is released from anterior pituitary. It is transported to ovaries where it induces the growth of ova.

- **Luteinizing hormone** is also released from anterior pituitary gland and it again is transported by the blood stream to ovaries. It helps in ovulation and in the formation of corpus luteum.

- **Oestrogen** is synthesised by the developing ova. Oestrogen regulates the levels of gonadotrophin releasing hormone**,** follicle stimulating hormone and luteinizing hormone by feedback mechanism. It helps to prevent the formation of more than one ovum in each cycle. Oestrogen also helps in the development of female reproductive organs.

- **Progesterone** is synthesised from ovary. It works along with oestrogen to increase the uterine thickening so that fertilised ovum can get implanted. It helps to increase the growth of breasts and helps in milk production. Level of progesterone also helps in regulating the release of gonadotrophin releasing hormone and gonadotrophins.

During puberty, the hypothalamo–pituitary–ovarian axis in females gets activated which helps the individuals to develop secondary sexual characters. The activation and deactivation of this axis also regulates the female reproductive cycles.

Oestrogen at the time of puberty causes development of breasts and maturation of other reproductive organs. In females, it plays an essential part in growth spurt and fat distribution typically resulting in more deposition around the hips, buttocks and thighs.

The ovaries also synthesis little amount of testosterone, a male hormone **(Sang T et al., 1980).** Testosterone increases growth of muscles and bones.

After puberty, follicle stimulating hormone, luteinizing hormone, oestrogen and progesterone all play a significant role in regulating the menstrual cycle. The menstrual cycles are irregular and anovulatory during the initial years and it implies

that a maturation of the hypothalamo–pituitary–ovarian axis is needed. Regular cyclical changes result in ovulatory menstruation start only after adequate maturation of this axis **(Buttram VC et al., 1975).**

- **Reproductive period**

The hypothalamo–pituitary–ovarian axis meant that hypothalamus, pituitary gland and ovaries act together. This axis has an important role in the development of our body systems like reproductive and immune systems and also it regulates the action of these systems.

The hypothalamo-pituitary system is involved in the control of gonadal development and reproductive rhythmicity **(Guillemin et al., 1967; McCann and Porter et al., 1969; Frohman et al., 1973)**. This axis regulates the growth and reproduction in human beings.

Gonadotropin releasing hormone expressing neurons present in hypothalamus secrete gonadotropin releasing hormone. Follicle stimulating hormone and luteinizing hormone are secreted from anterior part of pituitary gland. Oestrogen, progesterone and testosterone are produced from ovaries. The hypothalamo–pituitary–ovarian axis is having an important role in regulating the uterine and ovarian cycles in females.

The positive feedback loop between oestrogen and luteinizing hormone aids to produce follicles in ovary and ovulation. It also helps the uterus to thicken during implantation.

When the ovum is released from follicle, the empty sac begins to synthesise progesterone which inhibit hypothalamus and pituitary gland. This stops the positive feedback loop between oestrogen and luteinizing hormone.

In case of conception, the progesterone will be secreted by placenta; and so the mother cannot ovulate during pregnancy. If there is no conception, decreasing level of progesterone stimulate hypothalamus to start the secretion of gonadotropin releasing hormone again. These hormones control all the phases of menstrual cycle.

Oestrogen accelerates the growth and development of female reproductive organs. It increases the vascularity, moisture and elasticity of vagina **(Evan R et al., 1996)**. During the reproductive period of females, oestrogen protects the heart and bones. It also maintains the healthy state of breasts, uterus, vagina and bladder.

Other important female sex hormone is progesterone. When it is decreased, menstrual cycle and sexual function are affected. Decrease in the level of testosterone may reduce the libido in females.

MENSTRUATION

In reproductive period, females experience cycles of hormonal activity that repeat regularly at every month. With every cycle, the woman's body gets ready for a potential pregnancy even without her intention. The term **menstruation** means the periodic shedding of uterine lining. **(Menstru** means **"monthly")**

The menstrual cycle on an average takes about 28 to 35 days. Each cycle is divided into three phases depending on the events occurring in ovary and uterus. The phases of ovarian cycle are follicular phase, ovulatory phase and luteal phase. The phases of uterine cycle are menstruation, proliferative phase and secretory phase.

Follicular phase of the menstrual cycle

The events that take place during follicular phase are:

- Follicle stimulating hormone and luteinizing hormone are secreted from pituitary gland and are transported to ovaries.
- They stimulate the growth and development of ova inside the ovarian follicles.
- They also stimulate the production of female sex hormone, oestrogen.
- Increase in oestrogen level turns off the release of follicle stimulating hormone from pituitary by feedback mechanism. Balance between these hormones maintain the number of follicles that attain maturity.
- During follicular phase, one of the follicles in one of the ovaries becomes dominant and attain full maturity. The development of other follicles are suppressed by this dominant follicle. Oestrogen is synthesised by the dominant follicle and other follicles die eventually.

Ovulatory phase of the menstrual cycle

The ovulatory phase occurs at about 14^{th} day of the normal 28 days menstrual cycle. It occurs in the middle of menstrual cycle between follicular phase and luteal phase. The next menstrual cycle begins about two weeks later.

The events occurring in ovulatory phase are

- Increase in the level of oestrogen during follicular phase stimulates anterior pituitary gland to secrete more of luteinizing hormone.
- This results in release of ovum from the dominant follicle of ovary.
- As the ovum is released, it is captured by fimbrial end of the fallopian tubes which is transported along the tube.
- The amount of mucus produced by the cervix is increased during this phase. In case of intercourse during this time, this mucus captures the sperm, nourishes it and helps it to move towards the ovum for fertilization.

Luteal Phase of the Menstrual Cycle

After ovulation, luteal phase begins and the events occur in this phase are:

- Once ovum is released from the follicle, the empty follicle is transformed into corpus luteum.
- The hormone progesterone is synthesised by corpus luteum which is essential for the implantation of fertilized ovum on the lining of uterus.

- If ovum is fertilized by the sperm, it is transported through fallopian tube and get implanted in uterus. The woman is now pregnant.
- If there is no fertilization of ovum, it passes down the uterus. There is no occurance of pregnancy. Breaking down and shedding of the lining of uterus occur which results in next menstruation.

Every hormone follows its own pattern of increasing and decreasing trend in different phases of the menstrual cycle but altogether they form a predictable chain of events. One mature ovum is released from the ovary in every cycle and it passes down the fallopian tube to reach uterus.

If that ovum is not fertilised, the secretion of oestrogen and progesterone by ovary is decreased. When the action of these hormones is less, uterine lining is filled with blood and shed resulting in menstruation.

PREGNANCY

If the ovum released during ovulatory phase is fertilised, pregnancy results. Level of female sex hormones change dramatically. At the end of cycle there will be a normal fall in the level of oestrogen and progesterone which does not occur in case of pregnancy so no menstruation is seen.

Human chorionic gonadotrophin, a new placental hormone is produced and it stimulates the ovaries of mother to secrete a large amount of oestrogen and progesterone which are needed to maintain pregnancy.

The placenta takes over the function of producing oestrogen and progesterone from ovaries by the end of fourth month of gestation.

The hormones oestrogen and progesterone increase the thickening of uterine lining and also the circulating blood volume. They relax the uterine muscles to make sufficient space for the fetus to grow.

Progesterone and another hormone called relaxin increase the relaxation of ligaments, joints and muscles. Increase in the joint mobility of the pelvic girdle will increase the pelvic capacity so that the baby can pass through it during parturition.

During delivery of the baby, many other hormones come into play and help in uterine contraction. They also stimulate breast milk production and ejection after the childbirth.

AFTER CHILDBIRTH

After the delivery of baby, level of female sex hormones falls sharply. This results in many physical changes in mother. The uterine size decreases to its previous non-pregnant size, improvement in the tone of pelvic floor muscle and the blood volume becomes normal.

- **The Menopause**

Again significant change in hormonal levels occurs in females around the time of last menstrual period. The normal functioning of ovaries starts to deteriorate at about five to ten years before the woman's last period. Menstrual cycle may become

quite erratic. Bleeding may become heavier or lighter and the cycle may either be shorter or longer **(Santoro N et al., 1996).**

Changes around the years of menopause are due to the changing levels of hormones mainly oestrogen synthesised by ovaries. There is an irregular decrease in the level of oestrogen during perimenopause.

In males, the hypothalamo-pituitary-gonodal axis once activated continues to function for the rest of their life. But in females, it becomes deregulated in later life leading to menopause. This deregulation is mainly due to lack of oocytes which synthesis oestrogen so that the positive feedback loop cannot be maintained.

As the age of women increases, hypothalamo-pituitary-ovarian axis activity decreases and women can no longer be fertile **(Reyes FI et al., 1997).**

In postmenopausal women, ovary secretes androgens but virtually no oestrogen **(Grodin J.M et al., 1973).** Eventhough the ovary contain some oocytes, the follicles are not capable of responding to gonadotropins and producing oestradiol. After menopause, the oestrogen is produced mainly due to the peripheral conversion of androgens from adrenal gland. It occurs in peripheral adipose tissue and also in liver, kidney, brain etc **(Longcope C et al., 1978).**

Very little oestrogen is produced by ovaries so that the uterine lining is failed to thicken up and this results in stoppage of menstruation. Physiological levels of oestradiol selectively potentiate endothelium dependent vasodilation in healthy postmenopausal women **(David M. Gilligan MD et al., 2015).**

The normal age of attaining natural menopause is earlier in India at about 44 years **(Ringa V. et al., 2000)**. Sometimes, the ovaries stop working at an earlier age even before the age of 40 years and this condition is called premature ovarian failure. This condition affects about 1% of females.

Menopause is defined to occur if a female had no menstrual bleeding for twelve months continuously. This can also be explained by a decreased synthesis of female sex hormones by ovaries. Marked deficiency of oestrogen is seen in the body of woman just before and after menopause. It can therefore produce some detrimental effects on her health.

During transitional period of menopause, the menstrual cycles become irregular. The interval between each cycles vary from one another. There is a gross fluctuation in the level of hormones. Ovulation does not occur in every menstrual cycle. Usually the date at which last menstrual period occurred is considered as menopause.

In a woman's life, menopause is a normal physiological alteration and need not be a diseased state. The transition of menopausal period has various effects on the health of a woman and can produce lot of symptoms. The phases of menopausal transition can be classified by the bleeding pattern said by the woman.

We can assess the impact of menopausal effects on the life of women by Greene Climacteric Scale questionnaire devised by **Greene JG (1998),** Cervantes

Scale **(Monterrosa-Castro A et al., 2012)** and the Menopause Rating Scale **(Chedraui P et al., 2010).**

- **Premenopause**

The years just before the last menstrual period is termed as premenopause. At this time the level of female sex hormones has become more variable and there is a presence of effects of hormone withdrawal on target organs **(Harlow SD., et al 2012).** Premenopause usually begins some years before the irregular menstrual cycles.

- **Perimenopause**

The meaning of "perimenopause" is "around the menopause". It means the years of menopausal transition which is a period of time that precede and follow the last menstrual period.

According to the **North American Menopause Society**, this menopausal transition presents for about four years. **The Centre for Menstrual Cycle and Ovulation Research** explains this transition as a period of six to ten years resulting in menopause at the end.

In perimenopausal period, the level of oestrogen is about 20–30% higher than in premenopausal period but with wide fluctuations in its level. During perimenopausal and postmenopausal period these hormonal fluctuations produce many of the physical changes in females **(Chichester et al., 2011)**.

The changes like hot flushes, difficulty in sleeping, night sweats, vaginal dryness, urinary incontinence, osteoporosis and cardiac disease are due to changes in the level of hormones.

In this period fertility decreases but we cannot consider this to reach zero until menopause has occurred officially. The date of official menopause can only be determined retrospectively. Only when one year have completed after the final date of menstruation, we can declare menopause.

Even around the age of 35 years signs and symptoms of menopausal transition start. Although many women experience the effects of transition in the age of forty, this is about many years after the real beginning of perimenopausal period.

The period of this menopausal transition and the effects experienced can be just a few years or it may extend even to ten years. The time period and severity of effects menopausal transition for any postmenopausal woman cannot be predicted earlier.

Even though the course and effects of menopausal transition is unpredictable, the age of perimenopause is predictable to some extent. Women usually experience these perimenopausal symptoms at about the same range of age as their mother did **(Kessenich et al., 2013).**

Some studies show that melatonin supplementation in women of menopausal transition can increase their gonadotropin levels and function of thyroid gland. In some women it can even restore the fertility and can prevent the menopause associated depression **(Bellipanni G et al., 2005).**

❖ **Postmenopause**

The term "postmenopausal" refers to women who have not experienced any menstrual period for atleast twelve months, even though they still have uterus and are not pregnant or lactating **(Harlow SD et al., 2012)**.

In women after the surgical removal of uterus, postmenopausal change can be diagnosed by a very high level of follicle stimulating hormone in their blood.

Thus in a woman's life, postmenopause is considered to occur after twelve months of her last menstrual period and by that time her ovaries become inactive.

MENOPAUSAL SYMPTOMS

- **Hot flushes:**

The most important and common symptom of menopause is hot flushes seen in about 75% of perimenopausal women. This symptom vary among the postmenopausal women. Hot flush is a feeling of warmth experienced by the women which spreads all over the body and lasts for about 30 seconds to a few minutes.

Often hot flushes are accompanied by palpitations, flushed skin and sweating. It increases the temperature of body and pulse rate. It can result even insomnia. Hot flushes can last for about 2 to 3 years but women may experience them for more than 5 years.

- **Urinary incontinence and burning micturition**

- **Changes in vagina:**

Due to decreased oestrogen level, perimenopausal women may experience pain during intercourse because of vaginal atrophy and decrease in vaginal discharge.

- **Changes in breasts:** The shape of breasts may be changed after menopause.

- **Skin thinning**

- **Weight gain:**

A three year study conducted in healthy postmenopausal women show an average increase in weight of about five pounds.

- **Osteoporosis:**

Bone loss is rapid and common after menopause. Peak bone density is reached by females at the age of about 25 to 30 years. After that age loss of bone averages as 0.13% per year. During perimenopause, loss of bone is accelerated for about 3% per year. This bone loss can result in osteoporosis, a condition which increases the risk of fracture in bones. These bone fractures are intensely painful and can affect the day to day activities.

- **Cardiovascular disease:**

Although it is not well defined how much of risk to develop heart disease is due to ageing and how much is due to the hormonal changes of menopause. Women

who underwent premature menopause or surgical menopause at a younger age have an accelerated risk of developing cardiac disorder.

Hormonal changes in women after menopause may contribute to the development of depression, mental irritability and poor concentration. But the menopause need not be a disastrous time with unpleasant symptoms for every woman. Treatments such as hormone replacement therapy can be effective **(Col NF et al., 1997).**

So in every woman's life, from the cradle to grave hormones play an important role.

LIPIDS AND LIPOPROTEINS

Lipids play an important role in every aspect of biological life. They are the basic structural components in all human cells. They are involved in many of the metabolic pathways. Lipids are the organic compounds which are water insoluble but miscible in organic solvents. The study of lipid metabolism is called as **Lipidology**.

Cholesterol

Cholesterol is a steroid substance found only in animals. It is present in every cell of the body. It is a precursor of various biological substances including steroid hormones and bile acids. Cholesterol esters are formed from the plasma cholesterol which is esterified with fatty acids.

According to **WHO Report 2002,** factors which increase the risk of developing diseases are high blood pressure, alcohol consumption, tobacco consumption, deficiency of iron, unsafe water, underweight, high cholesterol, smoke from fuels, obesity, sanitation and hygiene **(Chockalingam et al., 2006).**

Lipoproteins

As lipids are insoluble in water media, they have to be transported in body fluids with the help of spherical soluble protein complexes which are called lipoproteins.

Lipids can be derived from food called exogenous lipids or synthesized in our body called endogenous lipids. The inner core with water insoluble triglycerides and cholesterol esters is surrounded by the water soluble group of proteins, phospholipids and free cholesterol.

The function of lipoprotein particles is to transport triglycerides and cholesterol in the blood stream to all tissues. The most common tissues are the liver and adipose tissue. All our body cells rely on cholesterol to use as building-blocks in the synthesis of cell membranes. It helps to control the water content and water soluble substances inside the cell and also to construct their internal structure and cellular enzymes. All lipoprotein particles are synthesized in liver and small intestine but interestingly not in adipose tissue.

Most of the enzymes, structural proteins, transporters, antigens, toxins and adhesins are lipoproteins. Examples are the plasma lipoprotein particles which are classified into high and low density lipoproteins, bacterial lipoproteins and transmembrane proteins present in mitochondria.

Structure

The hydrophilic groups of the lipoprotein particles are phospholipids, apoproteins and cholesterol which are faced outward. This property make them soluble in the aqueous medium like blood. Internally they carry triglycerides and cholesteryl esters which are shielded from water by the apoproteins and single layer of phospholipid.

The addition or removal of triglycerides and cholesterol from lipoprotein transport particles is determined by proteins forming the surface of particles. Development of atheroma depends upon the pattern of cholesterol transport and not on the concentration of cholesterol itself.

- **Classification**

Depending upon the buoyant density, lipoproteins are classified. The density is inversely related to their size. When lipid to protein ratio is greater, larger the size and density is less. Lipoproteins are classified into five major classes.

1. **Chylomicrons**

They are the largest lipoproteins with least density. Their function is to transport lipid which are exogenous, from gut to all other cells.

2. **Very low density lipoproteins**

These lipoproteins transport endogenous lipid from liver to other cells.

3. **Intermediate density lipoproteins**

They are produced when very low density lipoproteins are converted to low density lipoproteins. They are transient and do not usually present in plasma.

4. **Low density lipoproteins**

They are produced from very low density lipoproteins. They transport cholesterol to cells.

5. **High density lipoproteins**

They are the lipoproteins with maximum density. Their function is to transport cholesterol back to liver from peripheral cells. This process is called reverse cholesterol transport.

Lipoprotein	Source	Diameter (nm)	Density (g/mL)	Composition		Main Lipid Components	Apolipoproteins
				Protein (%)	Lipid (%)		
Chylomicrons	Intestine	90–1000	< 0.95	1–2	98–99	Triacylglycerol	A-I, A-II, A-IV,[1] B-48, C-I, C-II, C-III, E
Chylomicron remnants	Chylomicrons	45–150	< 1.006	6–8	92–94	Triacylglycerol, phospholipids, cholesterol	B-48, E
VLDL	Liver (intestine)	30–90	0.95–1.006	7–10	90–93	Triacylglycerol	B-100, C-I, C-II, C-III
IDL	VLDL	25–35	1.006–1.019	11	89	Triacylglycerol, cholesterol	B-100, E
LDL	VLDL	20–25	1.019–1.063	21	79	Cholesterol	B-100
HDL	Liver, intestine, VLDL, chylo-microns					Phospholipids, cholesterol	A-I, A-II, A-IV, C-I, C-II, C-III, D,[2] E
HDL_1		20–25	1.019–1.063	32	68		
HDL_2		10–20	1.063–1.125	33	67		
HDL_3		5–10	1.125–1.210	57	43		
Preβ-HDL[3]		< 5	> 1.210				A-I
Albumin/free fatty acids	Adipose tissue		> 1.281	99	1	Free fatty acids	

- **Metabolism**

The changes that occur in the lipoprotein particles inside our body is called as lipoprotein metabolism. Metabolism of lipoproteins take place by two pathways. In exogenous pathway, the metabolism of lipoprotein particles occur which are derived from dietary or exogenous lipids and in endogenous pathway, the metabolism of lipoprotein particles occur which are originated in liver through de novo synthesis of triacylglycerols or so called endogenous lipids.

The cells of liver are the main platform for the metabolism of triacylglyerols and cholesterol. Some amounts of triacylglycerols and glycogen are stored in hepatocytes. But the main storage cells are adipocytes for triacylglycerols which do not synthesis any lipoproteins.

Exogenous pathway

During absorption of fat, emulsification of fats present in chyme is by bile. Then triacylglyceride molecules are cleaved into two molecules of fatty acids and one molecule of 2-monoacylglycerol by pancreatic lipase. These small molecules can easily be absorbed by the intestinal cells. Inside of the intestinal cells, triacylglycerides are again formed from fatty acids and monoacylglycerides.

The lipids like triacylglycerols, cholesterol, cholesteryl esters and phospholipids are attached with apolipoprotein B-48 and form nascent chylomicrons. These chylomicrons are secreted into villous lacteals. This process depends mainly on the presence of apolipoprotein B-48.

As the nascent chylomicrons particles passes in the lymphatic system they bypass the hepatic circulation. They reach the bloodstream through the thoracic duct. In the blood stream, they interact with high density lipoprotein particles. Apolipoprotein E and apolipoprotein C-II are donated from high density lipoproteins to the nascent chylomicrons and convert the chylomicrons to a mature stage.

The enzyme lipoprotein lipase present on endothelial cells of the blood vessels is activated by these mature chylomicrons through apolipoprotein C-II. Triacylglycerol present in chylomicrons is hydrolysed by lipoprotein lipase, glycerol and fatty acids are released. The peripheral tissues like adipose tissue and muscle absorb this glycerol and fattyacids and are utilised for energy or storage.

After hydrolysis, the chylomicrons are now termed as chylomicron remnants. These chylomicron remnants circulate in bloodstream until they are taken up by liver. It is due to the interaction of apolipoprotein E with the receptors for chylomicrons present in the surface of liver.

This interaction results in the endocytosis of chylomicron remnants and are hydrolyzed by hepatic lysosomal enzymes. Glycerol and fatty acids are released into the cell by this lysosomal hydrolysis and this can be utilised for energy. It can also be stored for later use.

Endogenous pathway

Liver is the main platform for lipid metabolism as it can store glycerols and fatty acids in its cells. Hepatocytes can also synthesis triacylglycerols de novo. By using cholesterol they synthesis bile.

In liver, nascent very low density lipoproteins particles are formed from cholesteryl esters and triacylglycerols and are attached with apolipoprotein B-100. The release of these particles into bloodstream depends upon the presence of apolipoprotein B-100.

Nascent very low density lipoproteins interact with high density lipoproteins in the blood stream. This results in the donation of apolipoprotein C-II and apolipoprotein E from high density lipoproteins particles to nascent very low density lipoproteins.

Once the apolipoproteins C-II and E are attached with nascent very low density lipoproteins they become mature. Very low density lipoprotein particles are then circulate in blood and encountered by the enzyme lipoprotein lipase present in the endothelial cells.

The very low density lipoprotein particles are hydrolyzed by lipoprotein lipase, glycerol and fatty acids are released. Apolipoprotein C-II activates this process. Glycerol and fatty acids can be absorbed from blood by the tissues like adipose tissue and muscle.

Once hydrolyzed very low density lipoproteins are named as very low density lipoprotein remnants or otherwise called intermediate density lipoproteins. These very low density lipoprotein remnants circulate in blood until apolipoprotein E interact with the remnant receptors present in liver where they can be hydrolyzed by the enzyme hepatic lipase.

Hydrolysis of very low density lipoprotein remnants by hepatic lipase releases fatty acids and glycerol leaving behind intermediate density lipoprotein remnants. They are called low density lipoproteins which have more cholesterol concentration **(Kumar, Vibhor et al., 2011).**

Circulating low density lipoproteins are absorbed by the hepatocytes and other cells. Low density lipoproteins bind to their target tissue by an interaction between the low density lipoprotein receptors in liver and other cells with apolipoprotein B-100 present on low density lipoprotein particles.

In liver through endocytosis absorption occurs and the internalized low density lipoproteins are hydrolyzed by the lysosomes of hepatocytes and lipids are released mainly cholesterol.

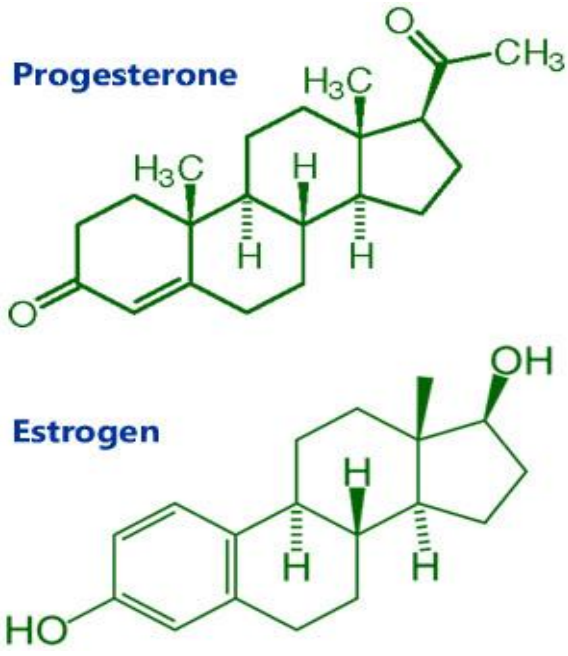
Lipoproteins are associated with the proteins called apolipoproteins (apo). ApoA is associated with high density lipoprotein particles and the subtypes are apoA1and apoA2. In apoB series, apoB100 is very important seen in low density lipoprotein particles which acts as a ligand for low density lipoprotein receptor.

In general lipid levels in normal range is needed to maintain a healthy cardiac function and to decrease the risk of developing cardiac disease or stroke. Individual components of a lipid profile with other known risk factors increase the overall risk of causing cardiovascular disease in a person.

In 2002, the **National Cholesterol Education Programme (NCEP) Adult Treatment Panel III** suggested the guidelines for evaluating the lipid levels and to decide the management accordingly.

PHYSIOLOGY OF OESTROGEN

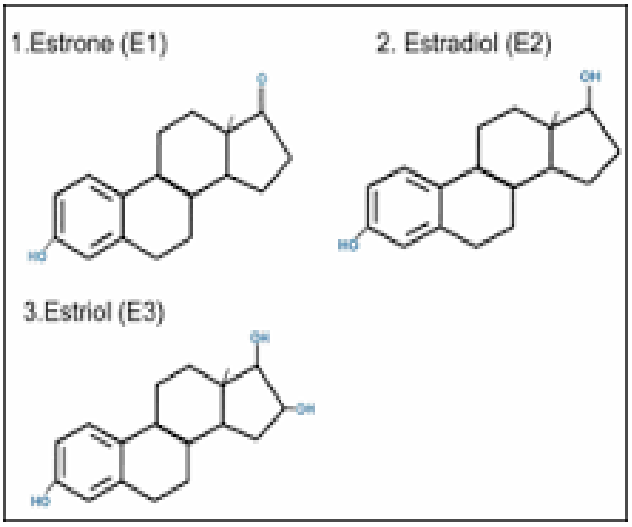
There is a close association between the female sex hormone, oestrogen and the emotional wellbeing of a female. Oestrogen is a vital hormone essential for the proper functioning of our body. Our body needs oestrogen in its natural form. Only then it can function normally without being interfered by other hormones like progesterone.



At the time of puberty, the ovaries of a female start releasing oestrogen in coordination with the menstrual cycle. Around the middle of cycle, level of oestrogen increases suddenly stimulating the release of an ovum and then it decreases quickly. During other days of the month there is a gradual rise and fall in the level of oestrogen. There is a wide variation of oestrogen levels present in a same woman on different days of the cycle and between two different women on the same day of their menstrual cycles.

Types

In women, oestrogens are present in three forms. They are oestrone, oestradiol and oestriol. During reproductive period oestradiol is considered as the predominant oestrogen having increased serum levels as well as increased oestrogenic activity. After menopause, oestrone is the predominant oestrogen and during the time of pregnancy, oestriol is the predominant oestrogen in our circulation.



The amount of oestriol is more out of the three oestrogens but it is the weakest. Strongest oestrogen is oestradiol whose potency is about 80 times more than that of oestriol **(Files JA et al., 2011).**

Thus the most important oestrogen is oestradiol in non-pregnant females during reproductive period. But during pregnancy, oestriol is more important and oestrone is the primary form of oestrogen in postmenopausal women.

- **Biosynthesis**

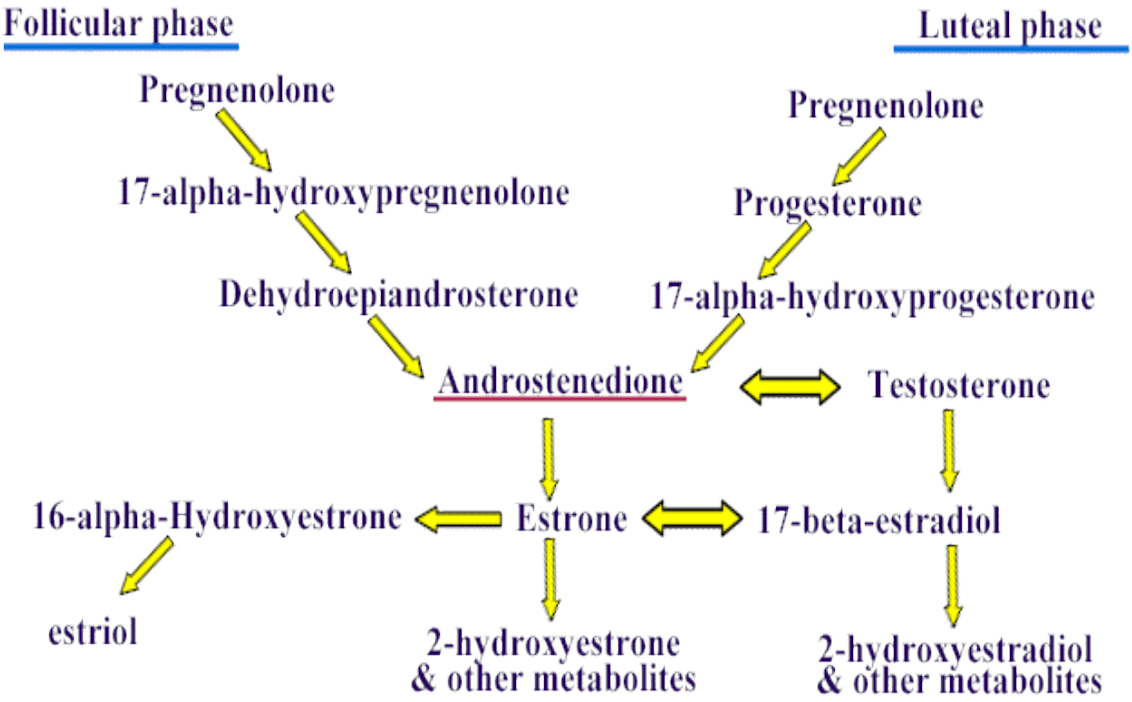
All the three different forms of oestrogen are produced from androgens especially testosterone and androstenedione by the action of aromatase. In females, oestrogens are synthesised mainly by ovaries and at the time of pregnancy, placenta is the main site of production of oestrogen. Oestrogen production is stimulated by follicle stimulating hormone which acts on the granulosa cells of ovary and corpus luteum.

Smaller amount of oestrogens are also produced by the tissues such as liver, breast, adipocytes and adrenal glands. This peripheral synthesis of oestrogen is particularly important in women of postmenopausal period **(Nelson LR et al., 2001).**

In females, oestrogen synthesis starts from the theca interna cells of ovary where the androstenedione is synthesised from cholesterol. A weak androgen, androstenedione is a precursor for other more potent forms of androgens like testosterone and also for oestrogen.

Androstenedione crosses the basal lamina of granulosa cells. Here it is converted immediately into either oestrone or testosterone and then oestradiol is formed in an additional step. The enzyme 17β-hydroxysteroid dehydrogenase converts the androstenedione to testosterone. Aromatase converts the androstenedione into oestrone and testosterone into oestradiol. These enzymes are expressed only in the granulosa cells of ovary.

In granulosa cells 17α-hydroxylase and 17, 20-lyase are not present. In theca cells these enzymes and 17β-hydroxysteroid dehydrogenase are expressed but they lack the enzyme aromatase. Therefore the presence of both granulosa cells and theca cells are mandatory for the synthesis of oestrogen in ovaries.



Mode of action

Oestrogens, like any other steroid hormones can easily diffuse through the cell membrane. After getting inside the cell, they combine with and activate the oestrogen receptors. They form a dimeric nuclear protein which binds to DNA and regulates gene expression. In addition oestrogens combine with rapid signalling membrane oestrogen receptors and activate them **(Soltysik K et al., 2013).**

In our cells, the expression of oestrogen receptors determines the actions of oestrogen. The oestrogen receptor is present specifically in organs like uterus, ovary and breast. In postmenopausal women, the genetic polymorphic characters of oestrogen receptor are associated with the metabolic effects of oestrogen **(Darabi M et al., 2011).**

- **Functions**

1. Structural

i. Development of female secondary sexual characters

ii. Elevated lipid store

iii. Potentiate the growth of the endometrium

iv. Stimulate the growth of the uterus

v. Maintain the integrity of the vessel wall

vi. Increase the formation of bone and reduce its resorption

2. Reproductive function

a. **Uterus**

Oestrogen along with progesterone prepares the uterine lining so that the fertilized ovum can be implanted. It increases oxytocin receptors present in the myometrium.

b. **Ovary**

Increase in oestrogen level stimulates the anterior pituitary to release luteinizing hormone which results in ovulation.

c. Libido

Libido is dependent on androgen levels **(Warnock JK et al., 2005)** only in the presence of oestrogen.

3. Metabolism

a. **Protein**

Increase in hepatic production of binding proteins

b. Lipid

By antioxidant effect it prevents LDL oxidation and atherosclerosis

Enhances LDL clearance by increasing hepatic LDL receptor expression.

Reduces hepatic lipase and increases HDL level

4. Coagulation

Increase in the level of plasminogen and clotting factors II, VII, IX, X

Decrease in the level of antithrombin

Increase in adhesiveness of platelets

5. Water balance

Retention of sodium and water

Increase in the level of sex hormone binding globulin and cortisol

6. Alimentary system

Decrease in motility of bowel

Increase in cholesterol concentration of bile

7. **Melanin**

Elevate pheomelanin and decrease eumelanin levels

8. **Malignancy**

Induce breast cancers which are hormone-sensitive

9. **Respiratory system**

Support alveoli and controls respiratory function

10. **Development of breast**

Oestrogen together with growth hormone and insulin like growth factor-1 is essential for the development of breast at the time of puberty and also the maturation of breast at the time of pregnancy and lactation.

Oestrogen causes development of ductal component of the breast and it also induces deposition of fat and growth of connective tissue. It indirectly influences the development of lobuloalveolar component by promoting the expression of progesterone receptors.

Prolactin secretion is also induced by oestrogen. During pregnancy, prolactin along with oestrogen and progesterone increases the lobuloalveolar development of breast **(Blackburn S et al., 2014).**

11. **Skin**

Oestrogen promotes the collagen content, increases the thickness of skin and improves the vascularity of skin. Oestrogen acts through the oestrogen receptors present on human skin.

The different numbers of oestrogen receptors are present in different body parts. More number of receptors are seen on the skin over face, thigh and breast.

12. Cardiovascular disorders

Oestrogen prevents atherosclerosis in younger women by its vasculo protective action and thereby protects against cardiovascular disorders **(Rosano GM et al., 1999).**

Due to its antioxidant property it fights against infections and protects arteries from oxidative damage. This again lowers the risk of developing cardiovascular diseases.

13. Cognitive function

Verbal memory score is a reliable measure to test the level of cognition. These scores in directly related to the oestrogen level in females.

Oestrogen if administered immediately after menopause, it prevents any reduction in the verbal memory **(Hara Y et al., 2015).**

14. Immunity

Oestrogen by its anti-inflammatory action helps to mobilise the neutrophils **(Sherwin BB et al., 2012).**

15. Psychology

Oestrogen has a significant role in the mental health of females. Sudden decrease in the level of oestrogen in postpartum, withdrawal of oestrogen in perimenopause and sustained low levels of oestrogen in postmenopause correlate with significant lowering of mood (**Lasiuk GC et al., 2007).**

Therapeutic uses

- **Hormonal contraception**

  Most of the oral contraceptives used to prevent pregnancy contain a synthetic oestrogen and progestin. Because increased level of circulating oestrogen can reduce the levels of follicle stimulating hormone and luteinising hormone by negative feedback.

- **Hormone replacement therapy**

  Lack of oestrogen in women after menopause can accelerate the risk of heart disease **(Sarrel PM et al., 1989).** To treat the menopausal symptoms such as hot flushes, urinary incontinence, vaginal dryness, chilly sensations, fatigue, dizziness, sweating and mental irritability oestrogen can be suggested to postmenopausal women.

  It can also be used to prevent osteoporosis. Oestrogen therapy decreases the fractures of spine, hips and wrist by about 60% and increases the bone density of spine by 5% in postmenopausal women who are treated within three years of the duration of menopause.

  Oestrogen replacement therapy also decreases serum cholesterol level. If it is started immediately after menopause it may lower the development of coronary heart disease. Oestrogen also protect from atherosclerosis by lowering the level of low density lipoproteins and triglycerides, increasing high density lipoproteins, properties of vasodilatation and anti-inflammatory effect.

- **Miscellaneous**

In humans, oestrogen promotes wound healing **(Oh DM Phillips et al., 2006).** Oestrogen is also used to treat dryness of vagina, amenorrhoea, dysmenorrhoea and oligomenorrhoea. Oestrogen can be used as a lactation suppressant.

Side effects

Increased level of oestrogen is seen after exogenous administration in oestrogen therapy or due to physiological conditions like pregnancy. There is an increased risk of thrombosis expected in any of the above situation **(Mitchell RS et al., 2007).** Report from **Woman's Health Initiative** suggested an elevated risk of developing deep vein thrombosis and cerebrovascular disease in postmenopausal women after the age 50 years who are on hormone replacement therapy.

In cirrhosis of liver, metabolic function is decreased leading to palmar erythema and spider angioma due to excess of oestrogen.

EFFECT OF OESTROGEN ON LIPID PROFILE

Gy, AD Blann et al., 1997 studied the alteration in lipoprotein levels during perimenopause and correlated with the level of oestrogen**.** Oestrogen increases the level of high density lipoproteins by decreasing the hepatic lipase activity which catabolizes the high density lipoproteins. Oestrogen decreases the oxidation of low density lipoproteins and increases the hepatic expression of low density lipoprotein receptors thereby decreasing the level of low density lipoproteins by accelerating the clearance. The alteration in lipid and lipoprotein values in postmenopausal women towards atherogenicity is due to the deficiency of oestrogen.

Cardiovascular disease are uncommon in women until their menopause. The delay in the development of cardiovascular disease expression in women compared with men is possibly as a result of the protective effects of oestrogen during the reproductive years of a woman.

Nurses' Health Study states that in women who underwent surgical menopause by bilateral oophorectomy and not provided with oestrogen replacement, the chance of developing coronary heart disease is twice as that of the women who received oestrogen therapy after surgery **(Colditz GA et al., 1987).**

According to the population based observational study report, favourable results of oestrogen therapy are seen on cardiovascular disease and this led to its extensive use by the women after menopause.

In premenopausal women, low density lipoprotein levels are less and high density lipoprotein levels are more when compared with same age group men. In postmenopausal women, low density lipoprotein levels rise and even exceed those of age matched men and there is a fall in the high density lipoprotein levels **(Campos H et al., 1988)**.

According to **Tikkanen MJ et al., in 1978,** oral oestrogen decreases low density lipoproteins level and elevates the level of low density lipoproteins in postmenopausal women whose baseline lipid values are normal.

The decrease in low density lipoproteins level may be due to the increased conversion of cholesterol to bile acids in liver and accelerated expression of low density lipoprotein receptors over the surface of hepatocytes which results in increased clearance of low density lipoproteins from blood.

The rise in high density lipoproteins level may be due to increased synthesis of apolipoprotein A-I and reduced hepatic lipase activity and thereby increase in the level of HDL2. This high density lipoprotein subparticle is more active in reverse cholesterol transport.

Very low density lipoproteins level may increase due to the enhanced synthesis of apolipoprotein B and triglycerides. But these particles may not have much of atherogenic potential **(Walsh BW et al., 1991).**

Oestrogen replacement therapy also reduces the levels of lipoprotein (a) which is a lipoprotein having structural similarity with low density lipoprotein and plasminogen. This is supposed to have antithrombolytic and proatherogenic properties. The concentration of lipoprotein (a) increases after menopause. Lipoprotein (a) which is considered as an independent predisposer for cardiovascular diseases is controversial **(Ridker PM et al., 1993).**

Secondary prevention cholesterol reduction trials suggest that the favourable effect of oral oestrogen on lipoproteins is it could decrease the development of atherosclerosis and its acute sequelae **(Levine GN et al., 1995)**.

According to **Lipid Research Clinic Follow-up Study** in postmenopausal women the effects of oestrogen on lipoproteins were not fully responsible for the decrease in cardiovascular deaths.

The guidelines released by the **American College of Physicians** for oestrogen therapy stated that "Women who have coronary heart disease and who are at increased risk for coronary heart disease are likely to be benefitted from hormone therapy."

Any advantage of oestrogen in cardiovascular disease and prevention of bone loss must be weighed against the risk of developing uterine cancer and breast cancer with long time use.

Cardiovascular benefit of oestrogen is due to its effect on lipoprotein levels, oxidation of low density lipoproteins, coagulation and vasomotor function.

There was a significant decrease in cardiovascular risk in women on oestrogen therapy who had no increased cholesterol level as per the **Nurses' health study.**

The alteration in the level of lipoprotein in hypercholesterolemic women can be achieved with oestrogen administration. For mildly hypercholesterolemic postmenopausal women, lipid lowering therapy is proved to be useful. According to the guidelines of **National Cholesterol Education Programme II,** it is desirable to reduce the level of low density lipoproteins to less than 100 mg/dl.

MATERIALS AND METHODS

PLACE OF STUDY

Study was conducted in the Department of Medicine, Government Rajaji Hospital, Madurai in co-ordination with the Institute of Physiology, Madurai Medical College for a period of one year.

COLLABORATION DEPARTMENT

Department of Biochemistry, Madurai Medical College, Madurai.

ETHICAL COMMITTEE

Approval obtained from the ethical committee of Government Rajaji Hospital, Madurai.

STUDY DESIGN

Prospective cross sectional study

SAMPLE SIZE

Total subjects - 90

STUDY POPULATION

Postmenopausal women attending the outpatient department of medicine, Government Rajaji Hospital / Madurai Medical College for master health check up.

Inclusion Criteria:

1. Age between 45 - 60 years
2. Attained natural menopause
3. Not on Hormone Replacement Therapy

Exclusion criteria:

1. Known congenital and acquired heart diseases
2. Systemic diseases - Hypertension, Diabetes mellitus, Hepatic and Metabolic diseases
3. Chronic drug intake like Rifampicin, Phenytoin, Anticoagulants, Statins etc
4. Thyroid dysfunction
5. Smoking

MATERIALS USED FOR STUDY

1. Proforma – to record the anthropometric measurements and the clinical findings of the subjects.
2. Portable weighing machine – to record the body weight in kilograms.
3. Stadiometer – to measure the standing height in centimeters.
4. Standardized mercury sphygmomanometer – to record the blood pressure in mm of Hg.

METHODOLOGY:

The study was initiated with the approval of Institutional ethical committee, Madurai Medical College, Madurai and was carried out after explaining the procedures in detail and getting written informed consent from the subjects.

The experimental protocol includes

1) **Recording of a detailed history** including type (natural/surgical) and duration of menopause, history of cardiovascular disease, diabetes mellitus, hypertension, surgery or any drug intake and history of endocrine disorders.
2) **General and systemic examination** done and the subjects who are eligible for the study are selected.
3) **Dividing into three groups**

   90 postmenopausal women are selected and are divided into three groups with 30 in each group based on the duration of menopause.

- **First group -** Thirty postmenopausal women whose duration of menopause is below 5 years.
- **Second group**-Thirty postmenopausal women whose duration of menopause is in between 5 years and 10 years.
- **Third group -**Thirty postmenopausal women whose duration of menopause is above 10 years.

4) **Measurement of Anthropometric Indices**:

The subjects are asked to stand erect with their arms relaxed at their side and feet together.

The following are measured:

- **Weight** (in kilograms) is recorded using a portable standard weighing machine.
- **Height** (in centimeters) is recorded using a stadiometer.
- **Body Mass Index** is found out using Quetelet's Index.

Body Mass Index = Weight (Kg)/ Height (sq.m).

1. **Recording of vital signs** viz. pulse rate, respiratory rate and measurement of blood pressure are done and documented.
2. **Blood investigations:** The investigations include

1. Serum oestradiol
2. Lipid profile includes parameters like Total cholesterol, Triglycerides, High density lipoproteins, Low density lipoproteins and Very low density lipoproteins.

After 10-12 hours of fasting, skin is sterilized with a spirit cotton swab and blood sample is collected from antecubital vein of front of forearm. About 3ml of blood is collected in a disposable syringe of 5ml capacity. For separation of serum, blood taken in a glass tube is first allowed to clot at room temperature and then centrifuged. This separated serum is used to estimate serum oestradiol and lipid profile.

ESTIMATION OF OESTRADIOL:

Method:

Quantitative determination of serum oestradiol is done by Chemiluminescence immunoassay method (CLIA).

Principle:

Luminescent immunoassays differ from the ELISA technique in which conversion to the product emitting photons of light takes place as an alternative to develop a noticeable colour.

This emission of photons is detected by a luminescent signal instrument. The radiant effect is evaluated in relative light units (RLU) which is in proportion to the quantity of the substance to be analysed in the test sample.

The essential ingredients needed for this assay include native antigen, biotinylated antibody, enzyme conjugate and signal reagent, the luminol.

Procedure:

- **13µl of samples and controls** are added into the appropriate wells of microplate coated with streptavidin.
- **25µl of Biotin reagent** is added into each well of microplate luminometer.
- Using orbital shaker the plate is swirled for 1minute and then incubated for 30 minutes at room temperature.

- **25µl of Tracer reagent- Horse Radish Peroxidase enzyme conjugate** is added directly on top of the reagent dispensed in the wells and mixing is done by swirling the plate for 1 minute followed by incubation for 60 minutes at room temperature.
- Plate is washed 5 times with **350µl of wash buffer** and then **50µl of** signal reagent, **the Luminol chemiluminescent substrate** is added into the microwells and incubated at room temperature for 5 minutes.
- Relative luminosity values (RLU) are scanned by photon counter reader.

Reference range:

Phase of menstrual cycle	**Range**
Follicular Phase	9 – 175 pg/ml
Luteal Phase	44 – 196 pg/ml
Postmenopausal phase	10 – 40 pg/ml

The comparison of the serum oestradiol level between the three groups of postmenopausal women is done.

ESTIMATION OF LIPID PROFILE

In this study, we measure serum levels of lipid profile comprising of total cholesterol, triglycerides, high density lipoproteins, low density lipoproteins and very low density lipoproteins.

A lipid profile typically includes:

- **Total cholesterol (TC) -** In this we measure all of the cholesterol content present in all the lipoprotein particles by Cholesterol oxidase - Peroxidase enzymatic method.
- **Triglycerides (TGL) -** We measure the triglycerides present in all the lipoprotein particles by Glycerol kinase - Peroxidase enzymatic method.
- **High density lipoprotein (HDL) -** We measure the cholesterol present in high density lipoprotein particles by precipitation method.
- **Low density lipoprotein (LDL) -** We calculate the cholesterol present in low density lipoprotein particles; The amount of low density lipoprotein is calculated by **Friedewald formula**.

  LDL = total cholesterol - (high density lipoprotein+ triglycerides/5)

- **Very low density lipoprotein (VLDL) -** We calculate from level of triglycerides.

  Very low density lipoprotein = triglycerides/5.

Reference range:

TYPES	FAVOURABLE	BORDERLINE	RISK
Total cholesterol (mg/dl)	Below 200	200-239	240
Triglycerides (mg/dl)	Below 150	150-199	200-499
High density lipoprotein (mg/dl)	60	50-59	<50
Low density lipoprotein (mg/dl)	60-130	130-159	160-189
Very low density lipoprotein (mg/dl)	2-30	30-40	40-100

Lipid profile values are compared between the three groups and correlation of serum oestradiol level with lipid profile is done.

RESULTS AND OBSERVATION

The comparison of oestradiol levels and lipid profile values between the three groups is done and the results are analysed using **ANOVA** calculations.

The correlation of serum oestradiol level with body mass index and lipid profile which includes total cholesterol, high density lipoprotein, low density lipoprotein, very low density lipoprotein and triglycerides is done by **Pearson's correlation**.

By means of **SPSS software version 16,** analysis of statistics is performed**.** The **'p' value < 0.05** is considered as significant statistically.

Table: 1

Mean values of various parameters

PARAMETERS	GROUP I (mean)	GROUP I (SD)	GROUP II (mean)	GROUP II (SD)	GROUP III (mean)	GROUP III (SD)	'p' value
AGE (years)	46.73	2.227	52.67	2.202	57.53	2.030	.000
DURATION OF MENOPAUSE (years)	3.200	0.714	7.800	1.095	12.60	1.354	.000
HEIGHT (centimetres)	152.43	7.718	155.70	7.489	151.10	5.448	.036
WEIGHT (kilograms)	55.83	11.354	63.90	10.233	64.90	8.314	.001
BODY MASS INDEX (kg/sq.m)	23.96	4.101	26.36	3.852	28.46	3.521	.000

Table : 2

Comparison of serum oestradiol levels between three groups

Duration of menopause	**Groups**	**Oestradiol (pg/ml)**		**'p' value**
		Mean	**Standard deviation**	
Less than 5 years	Group I	46.660	12.63	<0.001 Significant
5- 10 years	Group II	25.400	5.46	
More than 10 years	Group III	16.840	6.95	

The serum oestradiol level decreases significantly as the duration of menopause increases.

Table : 3

Comparison of lipid profile values between three groups

PARAMETERS	GROUP I (mean)	GROUP I (SD)	GROUP II (mean)	GROUP II (SD)	GROUP III (mean)	GROUP III (SD)	'p' value
Total cholesterol (mg/dl)	164.88	24.289	180.95	26.619	184.04	22.010	.006
High density lipoprotein (mg/dl)	44.53	7.860	35.00	4.331	32.77	4.606	.000
Low density lipoprotein (mg/dl)	94.72	22.437	122.54	28.739	127.71	23.430	.000
Very low density lipoprotein (mg/dl)	24.85	5.421	25.95	6.635	23.51	7.590	.365
Triglycerides (mg/dl)	123.47	28.084	128.08	33.874	129.95	32.083	.714

While comparing the mean values of lipid profile between the three groups, total cholesterol and low density lipoprotein levels are increased significantly. Level of triglycerides is increased but it is insignificant. There is a significant decrease in high density lipoprotein level.

Table : 4

Correlation of oestradiol level with body mass index

GROUPS	OESTRADIOL (pg/ml)	BODY MASS INDEX (kg/sq.m)	CORRELATION COEFFICIENT
Group I	46.660	23.96	-0.180
Group II	25.400	26.09	-0.174
Group III	16.840	28.46	-0.368

As the duration of menopause increases, the serum oestradiol level decreases with the increase in body mass index. So theserum oestradiol level is negatively correlated with body mass index.

Table : 5

Correlation of oestradiol level with total cholesterol

GROUPS	OESTRADIOL (pg/ml)	TOTAL CHOLESTEROL (mg/dl)	CORRELATION COEFFICIENT
Group I	46.660	164.87	-0.098
Group II	25.400	180.95	-0.220
Group III	16.840	184.04	-0.070

As the duration of menopause increases, the serum oestradiol level decreases with the increase intotal cholesterol. So the serum oestradiol level is negatively correlated with the level of total cholesterol.

Table : 6

Correlation of oestradiol level with high density lipoprotein

GROUPS	OESTRADIOL (pg/ml)	HIGH DENSITY LIPOPROTEIN (mg/dl)	CORRELATION COEFFICIENT
Group I	46.660	44.53	0.240
Group II	25.400	35	0.330
Group III	16.840	32.77	0.270

As the duration of menopause increases, the serum oestradiol level decreases with the decrease in high density lipoprotein. So the serum oestradiol level is positively correlated with the level of high density lipoprotein.

Table : 7

Correlation of oestradiol level with low density lipoprotein

GROUPS	OESTRADIOL (pg/ml)	LOW DENSITY LIPOPROTEIN (mg/dl)	CORRELATION COEFFICIENT
GROUP I	46.660	94.72	-0.097
GROUP II	25.400	122.54	-0.200
GROUP III	16.840	127.71	-0.070

As the duration of menopause increases, the serum oestradiol level decreases with the increase in low density lipoprotein. So the serum oestradiol level is negatively correlated with the level of low density lipoprotein.

Table : 8

Correlation of oestradiol level with very low density lipoprotein

GROUPS	OESTRADIOL (pg/ml)	VERY LOW DENSITY LIPOPROTEIN (mg/dl)	CORRELATION COEFFICIENT
GROUP I	46.660	24.85	-0.060
GROUP II	25.400	25.95	-0.060
GROUP III	16.840	23.51	-0.200

As the duration of menopause increases, the serum oestradiol level decreases without any significant change in the level of very low density lipoprotein.

Table : 9

Correlation of oestradiol level with triglycerides

GROUPS	OESTRADIOL (pg/ml)	TRIGLYCERIDES (mg/dl)	CORRELATION COEFFICIENT
GROUP I	46.660	123.47	-0.070
GROUP II	25.400	128.08	-0.110
GROUP III	16.840	129.95	-0.140

As the duration of menopause increases, the serum oestradiol level decreases with the increase in triglycerides. So the serum oestradiol level is negatively correlated with the level of triglycerides.

Table : 10

Correlation of serum oestradiol with body mass index and lipid profile in Group I

Group I (less than 5 years)	**Correlation coefficient**	
Oestradiol with BMI	-0.180	Negative correlation
Oestradiol with TC	-0.098	Negative correlation
Oestradiol with HDL	0.240	Positive correlation
Oestradiol with LDL	-0.097	Negative correlation
OestradiolwithVLDL	-0.060	Negative correlation
Oestradiol with TGL	-0.070	Negative correlation

Table : 11

Correlation of serum oestradiol with body mass index and lipid profile in Group II

Group II (5-10 years)	**Correlation coefficient**	
Oestradiol with BMI	-0.174	Negative correlation
Oestradiol with TC	-0.220	Negative correlation
Oestradiol with HDL	0.330	Positive correlation
Oestradiol with LDL	-0.200	Negative correlation
Oestradiol with VLDL	-0.060	Negative correlation
Oestradiol with TGL	-0.110	Negative correlation

Table : 12

Correlation of serum oestradiol with body mass index and lipid profile in Group III

Group III (more than 10 years)	**Correlation coefficient**	
Oestradiol with BMI	-0.368	Negative correlation
Oestradiol with TC	-0.070	Negative correlation
Oestradiol with HDL	0.270	Positive correlation
Oestradiol with LDL	-0.070	Negative correlation
Oestradiol with VLDL	-0.200	Negative correlation
Oestradiol with TGL	-0.140	Negative correlation

From Pearson's correlation it is found that there exists negative correlation between serum oestradiol level and the values of

- Body mass index
- Total cholesterol
- Low density lipoprotein
- Very low density lipoprotein
- Triglycerides

There is a positive correlation of serum oestradiol level with high density lipoprotein.

DISCUSSION

The term “menopause” literally means the last menstrual period and postmenopause is the time that follows menopause. Menopause usually occurs in between the age of 45 and 55 years.

In our present study, we have divided the postmenopausal women into three groups based on the duration of menopause. The mean age of postmenopausal women in group I is 46.73 ± 2.23 years, group II is 52.67 ± 2.20 years and group III is 57.53 ± 2.03 years. The mean duration of menopause in group I is 3.2 ± 0.71 years, group II is7.8 ± 1.09 years and group III is 12.6 ± 1.35 years.

Every woman has to undergo a normal physiological event in her life called menopause and it is due to changes in level of hormones which results from the loss of ovarian function. But a large amount of androgen is secreted from ovarian stroma and adrenal cortex in postmenopausal women which is converted to oestrogen in peripheral tissues. This quantity of oestrogen is very minimal as compared with the premenopausal state.

The postmenopausal period is a state of oestrogen deficiency. Lack of oestrogen causes unfavourable changes in the metabolism of glucose and insulin, blood coagulation, fat distribution in the body, fibrinolytic system, endothelial function of the blood vessels and alteration in the lipid profile **(Bales AC et al., 2000, S A Samaan et al., 1995).** It is essential to draw more of our attention to alleviate and understand the long term results of deficiency of the hormone oestrogen.

The mean value of serum oestradiol in group I is 46.660 ± 12.63 pg/ml, group II is 25.400 ± 5.464 pg/ml and group III is 16.840 ± 6.95 pg/ml. The level of oestradiol decreases significantly ($p < 0.001$) with increase in the duration of menopause.

Serum lipid levels vary in every individuals and they depend on body mass index, level of exercise, history of smoking, dietary habits, systemic diseases like hypertension, diabetes mellitus, liver and metabolic diseases **(Gordon T et al., 1981).** So in our study, we excluded these confounding variables.

In our study, mean value of body mass index in group I is 23.96 ± 4.10 kg/sq.m, group II is 26.36 ± 3.85 kg/sq.m and group III is 28.46 ± 3.52 kg/sq.m. The level of body mass index increases significantly ($p < 0.001$) with increase in the duration of menopause.

Blumel J E et al., 2001 studied on premenopausal women. He reevaluated after five years and found a similar weight gain present in women who attained menopause and those who did not attain menopause. According to **Akahoshi et al., 1996** body mass index is related to menopausal age and later the menopausal age, greater will be the body mass index. In studies of **Razay et al., 1992** and **Akahoshi et al., 1996,** it is shown that body mass index increases in postmenopausal period.

As suggested by **Jousilahti et al., 1996** factors determining body weight are physical activity, genetic and cultural factors, socioeconomic status, psychological factors etc.

Some other researchers suggest that any decrease in the level of basal metabolism and reduction of physical activity may increase the body weight in postmenopausal women.

Poehlman et al., 1995 stated that oestrogen deficiency after menopause is linked with an increased body mass in women. Oestrogen potentiate the secretion of growth hormone and if this potentiation is lost after menopause. Body weight increases due to the loss of this trophic effect on skeletal muscle growth

Oestrogen can modulate the cytokines activity which leads on to the catabolic milieu. For example the interleukin-6 production is prevented by oestradiol and oestrogen deficiency could cause an increased interleukin-6 activity. This results in catabolic effects

Dr. Maulik S. Varu et al., in 2011 compared the serum lipid profile between premenopausal and postmenopausal women. He concluded that the mean level of total cholesterol and low density lipoprotein were significantly elevated in postmenopausal women as compared with premenopausal women. Significant increase is seen when the duration of menopause is increased. The high density lipoprotein level was significantly decreased in postmenopausal women and it is decreased significantly when the duration of menopause is increased. The limitation of that study was failure of measuring the oestradiol level which could be the cause for lipid profile derangement in postmenopausal women and it is rectified in our present study. Here serum oestradiol level is measured and it is correlated with changes in the lipid profile in postmenopausal women of various duration of menopause.

Similar comparative studies of serum lipid profile between premenopausal and postmenopausal women were done by **HA Eltayeb et al., 2015, Dr.M.Swarnalatha et al., 2015, Gulab Kanwaret al., 2014 and Rajesh K Jambhulkar et al., 2014**.

Over all conclusion discussed in above studies is in postmenopausal women, mean values of total cholesterol and low density lipoprotein were significantly increased as compared with premenopausal women. While the high density lipoprotein level was significantly lower in postmenopausal women.

A correlative study with oestrogen and lipid profile in premenopausal and postmenopausal women was done by **Swarnalatha P K et al., 2012** in which she studied the influence of oestrogen on the levels of total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides, very low density lipoprotein and ratio between total cholesterol and high density lipoprotein. The correlation of oestrogen level with high density lipoprotein was decreased significantly in postmenopausal women whose duration of menopause is more than ten years but no significant correlation was noted in postmenopausal women whose duration of menopause is less than ten years.

In our present study, in postmenopausal women as the duration of menopause increases, the changes in lipid profile values are noted and are correlated with serum oestradiol level.

While comparing the mean values of lipid profile between the three groups, total cholesterol ($p=0.006$) and low density lipoprotein ($p<0.001$) levels are increased significantly. Level of very low density lipoprotein ($p=0.365$) and triglycerides

(p=0.714) are increased but insignificant. There is a significant decrease in high density lipoprotein (p<0.001) level.

OESTRADIOL WITH TOTAL CHOLESTEROL

In our study the mean value of total cholesterol in group I is 164.88 ± 24.29 mg/dl, group II is 180.95 ± 26.62 mg/dl and group III is 184.04 ± 22.01 mg/dl. This shows significant increase as the duration of menopause increases. In our present study level of oestrogen is negatively correlated with total cholesterol values (correlation coefficient in group I is -0.098, in group II it is -0.220 and in group III it is -0.070).

Niklila et al stated that ethinyloestradiol increases the turnover of cholesterol. **Edward et al** suggested that even though it appears that the cholesterol synthesis is increased by oestrogen actually the excretion rate is increased which results in the decline of serum cholesterol level.

Total levels of high density lipoprotein, low density lipoprotein and very low density lipoprotein constitute the total cholesterol. During postmenopausal period the level of low density lipoprotein and very low density lipoprotein are increased but the level of high density lipoprotein is decreased. The elevation of low density lipoprotein and very low density lipoprotein level is more than the reduction in high density lipoprotein level. This results in net elevation of total cholesterol level after menopause.

OESTRADIOL WITH HIGH-DENSITY LIPOPROTEIN

According to the report of **Do KA et al., 2000**, in postmenopausal women the rate of reduction in the level of high density lipoprotein was maximum at about nine months after menopause and the rate was calculated to be around 21.26 mg/dl per year**.**

In our study the mean value of high density lipoprotein cholesterol in group I is 44.53 ± 7.86 mg/dl, group II is 35 ± 4.33 mg/dl and group III is 32.77 ± 4.61 mg/dl. This shows significant decrease as the duration of menopause increases. Oestrogen levels are positively correlated with the level of high density lipoprotein (the correlation coefficient in group I is 0.240, in group II it is 0.330 and in group III it is 0.270).

Kalavathi et al., in1991 stated that oestrogen act on the enzyme hepatic lipase which is otherwise called Heparin Releasable Hepatic lipase (HRHL). This enzyme is present in the endothelial cells of liver and it catalyzes the high density lipoproteins.

The enzyme hepatic lipase is preferably attached with HDL2 than with HDL3 and low density lipoprotein. Hepatic lipase is therefore called HDL2 phospholipase and it increases the cholesterol uptake by liver. It also helps to convert the HDL2 to HDL3. Only in the form of HDL3, cholesterol is accepted from peripheral tissues. After the conversion of HDL3 to HDL2 it is taken up by liver. Oestrogen reduces the activity of hepatic lipase and thereby HDL2 level in plasma is increased.

The main action of high density lipoprotein is the esterification and exchange of cholesterol. The mobilisation of cholesterol from the body tissues and

transportation to liver is done by high density lipoprotein so that they subsequently undergo catabolism and are excreted **(Siteri P.K. et al., 1988).**

In studies of **Miller CJ et al., 1975,** the plasma cholesterol level has negative correlation with high density lipoprotein concentration**.** The transport of cholesterol from arterial wall to liver by high density lipoproteins reduces the development of atherosclerosis.

The enzyme lecithin cholesterol acyl transferase causes the esterification of cholesterol using high density lipoproteins as a substrate. The cholesterol esters are taken back to liver in the form of low density lipoproteins and very low density lipoproteins. In liver, the lipoproteins are degraded and hydrolysis of cholesterol esters takes place **(Sharma V.N. et al., 1998).**

In 2000, **Edmunds and Lip** suggested that the hepatic lipase which normally catalyzes thehigh density lipoprotein is inhibited by oestrogen. So in postmenopausal period the inhibition by oestrogen disappears and more of high density lipoproteins are destroyed by hepatic lipase. This results in decrease in the level of high density lipoproteins in women after menopause.

This high density lipoprotein also inhibits the process of uptake of low density lipoprotein which is rich in cholesterol by the smooth muscle cells of arteries. When the high density lipoprotein is decreased, accumulation of more amount of cholesterol in arteries results. This promotes the occurance of atherosclerosis due to lack of proper clearance of cholesterol.

Oestrogen replacement therapy increases the level of high density lipoproteins **(Vasudevan DM et al., 2001; Tapiero H et al., 2002).** Oestrogen also increases the receptors for high density lipoproteins in liver.

As per the study of **Allaupovic et al,** oestrogen specifically increases the production of high density lipoproteins in liver.

OESTRADIOL WITH LOW - DENSITY LIPOPROTEIN

In our study the mean value of low density lipoprotein cholesterol in group I is 94.72 ± 22.44 mg/dl, group II is 122.54 ± 28.74 mg/dl and group III is 127.71 ± 23.43 mg/dl. This shows significant increase as the duration of menopause increases. Oestrogen level shows a negative correlation with low density lipoprotein cholesterol (the correlation coefficient in group I is -0.097, in group II it is -0.220 and in group III it is -0.070).

Wakatsuki et al., in 1998 stated that a reduction in the concentration of oestrogen in postmenopausal period increases the activity of lipoprotein lipase and that leads to an elevation in the concentration of low density lipoproteins.

According to **Arca et al., 1994**, the hypercholesterolemia in women after menopause is mainly due to defect in low density lipoprotein receptors. In premenopausal period, oestrogen induces the production of low density lipoprotein receptors on hepatic surface that increases the clearance of low density lipoproteins resulting in decreased plasma level.

In the studies of **Abraham and Villablanca et al., 2002,** it is suggested that decrease in the level of low density lipoproteins after oestrogen therapy is due to

increased uptake of lipoproteins by liver, conversion of more of cholesterol into bile acids in liver and accelerated low density lipoprotein receptor expression on hepatocytes. This increases the clearance of low density lipoprotein particles from plasma.

They also suggest that the foam cell formation is an essential step in process of atherosclerosis which is due to the LDL oxidation and phagocytosis by macrophages.

OESTRADIOL WITH VERY LOW DENSITY LIPOPROTEIN

According to our study, mean value of very low density lipoprotein cholesterol in group I is 24.85 ± 5.42 mg/dl, group II is 25.95 ± 6.64 mg/dl and group III is 23.51 ± 7.59 mg/dl. This shows an increase in very low density lipoprotein level as the duration of menopause increases but it is insignificant. Oestrogen shows a negative correlation with very low density lipoprotein cholesterol (the correlation coefficient in group I is -0.060, in group II it is -0.060 and in group III it is -0.200).

The level of very low density lipoproteins may increase after menopause. As per the study of **Wakatsuki et al., 1998**, low density lipoprotein is formed from very low density lipoprotein in liver. An elevation in very low density lipoprotein secretion is mainly due to an increased activity of post heparin plasma lipoprotein lipase.

OESTRADIOL WITH TRIGLYCERIDES

As per our study, mean value of triglycerides in group I is 123.47 ± 28.08 mg/dl, group II is 128.08 ± 33.87 mg/dl and in group III is 129.95 ± 32.08 mg/dl. This shows an increase in triglycerides level as the duration of menopause increases but it is insignificant. Oestrogen level shows a negative correlation with triglycerides (the correlation coefficient in group I is -0.070, in group II it is -0.110 and in group III it is -0.140).

In women after menopause, the plasma levels of both oestrogen and progesterone decreases. Because of oestrogen deficiency, adipocyte size increases and there is an increased activity of lipoprotein lipase. This results in the release of triglycerides from adipocytes. The reduced level of progesterone also causes hepatic release of triglycerides. Ultimately the level of triglycerides increases in postmenopausal women.

According to **Pradhan P et al., 2013** in postmenopausal women, the major modifiable risk factors for coronary heart disease are

- Hypertension 53.8%
- Smoking 35.0%
- Diabetes mellitus 23.03%
- Hyperlipidemia 8.1%

In modern society, the coronary heart disease is one of the major etiology for morbidity in women after menopause. In females after menopause, the values of lipids and lipoproteins are changed towards increased atherogenicity (e.g. rise in low density

lipoprotein and fall in high density lipoprotein levels). These changes result in increased incidence of cardiovascular disease in postmenopausal women.

American Heart Association report in 2002, stated that 70% of women after menopause develop cardiovascular disease. Increased risk seen in postmenopausal women may be due to decrease in the favourable effects of oestrogen on blood vessels and lipid profile **(Marynard C et al., 1992).** According to **Bush et al., 1988**, in females the levels of lipids and lipoproteins are determined by female sex hormones**.**

Stevenson et al., in 1993 suggested that after menopause, adverse changes are seen in lipid and lipoprotein levels and are not due to the effect of ageing. This is due to the loss of endogenous oestrogen and its protective effects.

As per the study of **Kannel WB et al., 1995,** elevated plasma levels of low density lipoprotein and total cholesterol are the major risk factors for the development of cardiovascular disease**.**

A 10% reduction in cholesterol level may decrease the risk of cardiovascular disease by 10% in less than 4 years **(Pharoah PD et al., 1996).** Level of high density lipoprotein in contrast to those of low density lipoprotein and total cholesterol are inversely related to the risk of coronary heart disease **(Miller NE et al., 1977).**

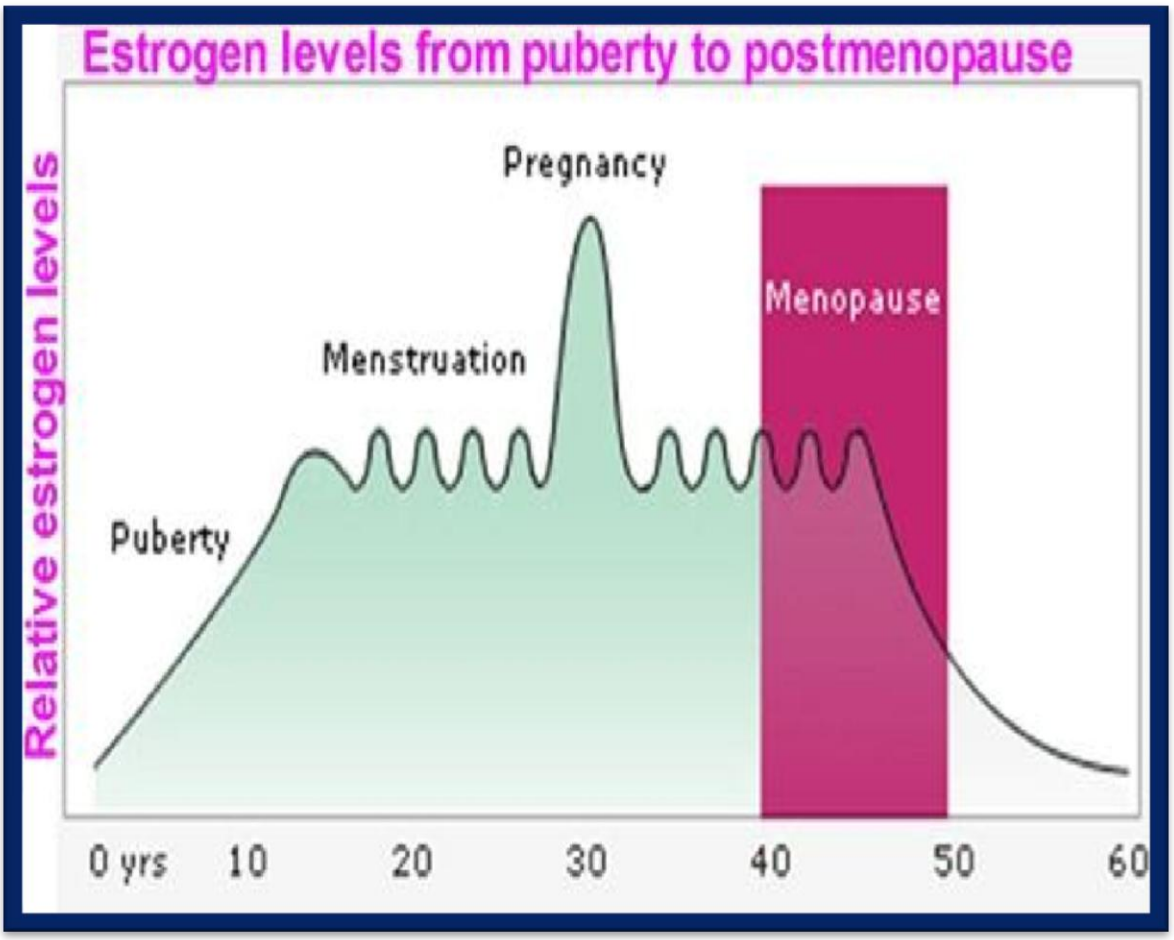
CONCLUSION

Menopause is the physiological process of ageing in which the general health of women is altered. The long term deficiency of oestrogen with increase in the duration of menopause decreases the protection from coronary heart disease by altering the lipid levels.

The lipid profile values are unfavourable in postmenopausal women with longer duration of menopause and it is considered as a strong predictor for cardiovascular disease. Therefore, screening of every postmenopausal woman for abnormal lipid profile is mandatory.

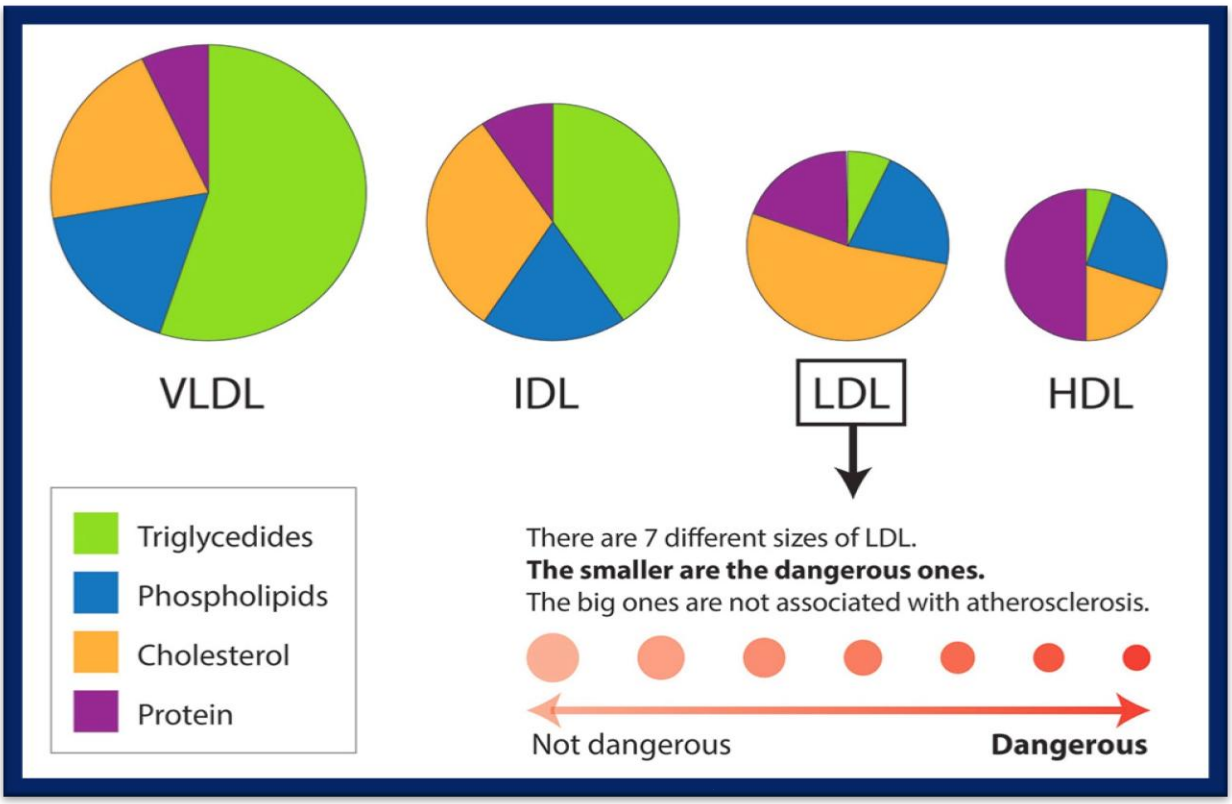
In postmenopausal women health strategies in the form of dietary interventions and increased physical activity are need to be encouraged. Lipid lowering drugs are proved to be useful. Hormone replacement therapy in postmenopausal women is likely to protect against cardiovascular disease through its action on lipid levels.

To conclude it is important to monitor the lipid profile of postmenopausal women regularly and to give proper guidance regarding diet and physical activities so that the population of older women can be expected to increase in the coming decades without any risk to their general health.

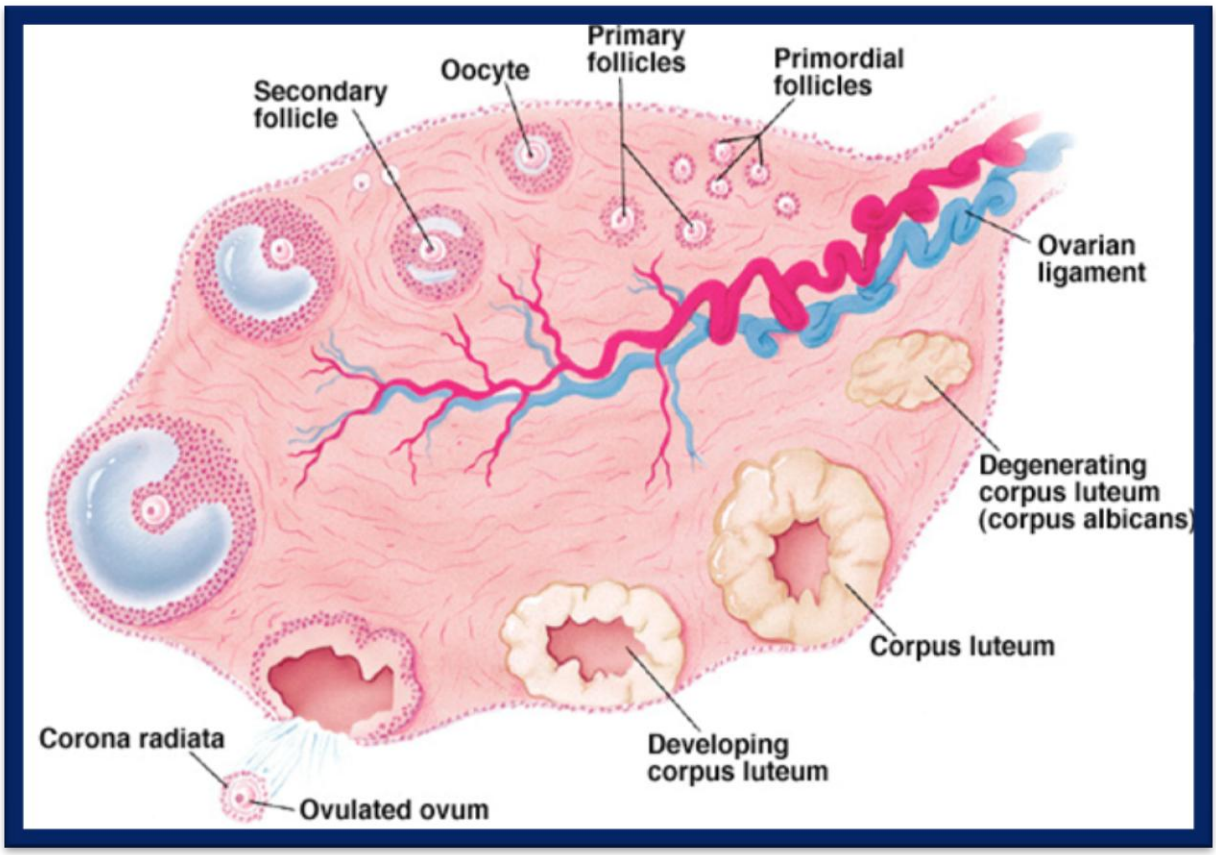

Estrogen levels from puberty to postmenopause
Relative estrogen levels
Pregnancy
Menopause
Menstruation
Puberty
0 yrs
10
20
30
40
50
60

AGE IN YEARS

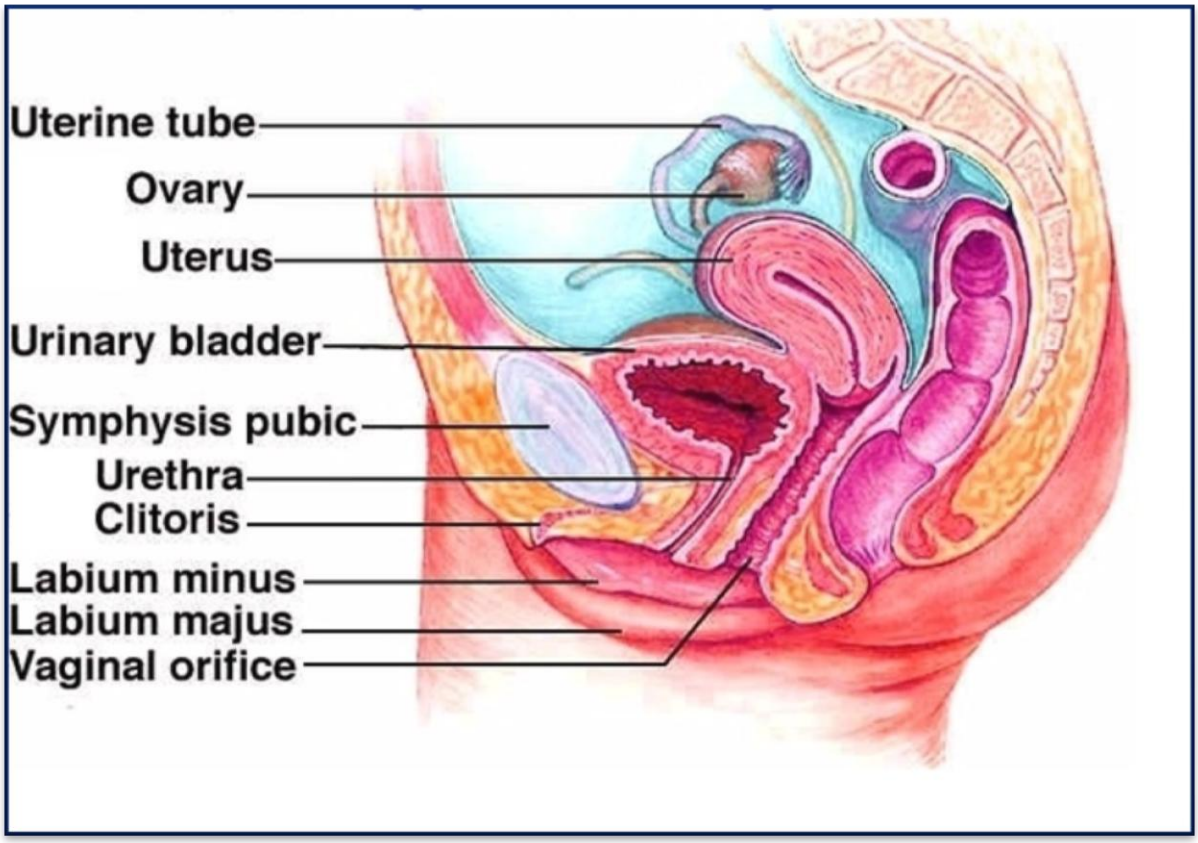
COMPOSITION OF LIPOPROTEINS



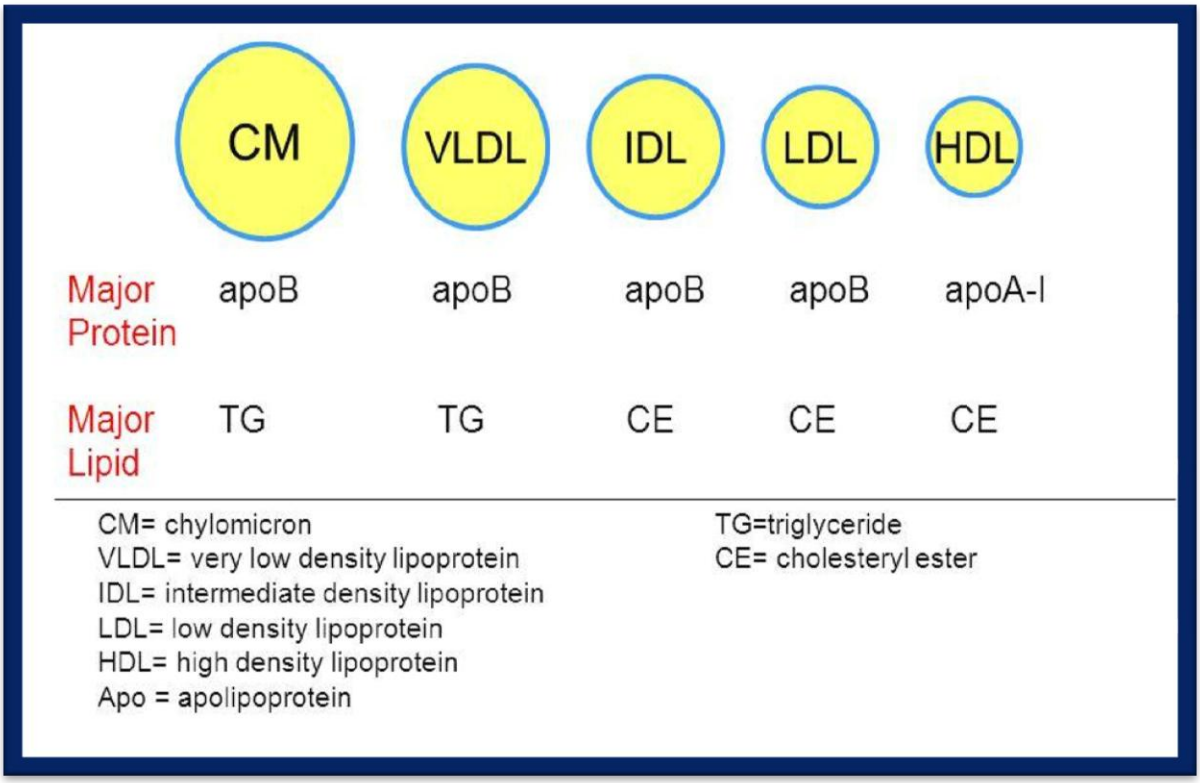
STRUCTURE OF AN OVARY



FEMALE REPRODUCTIVE SYSTEM

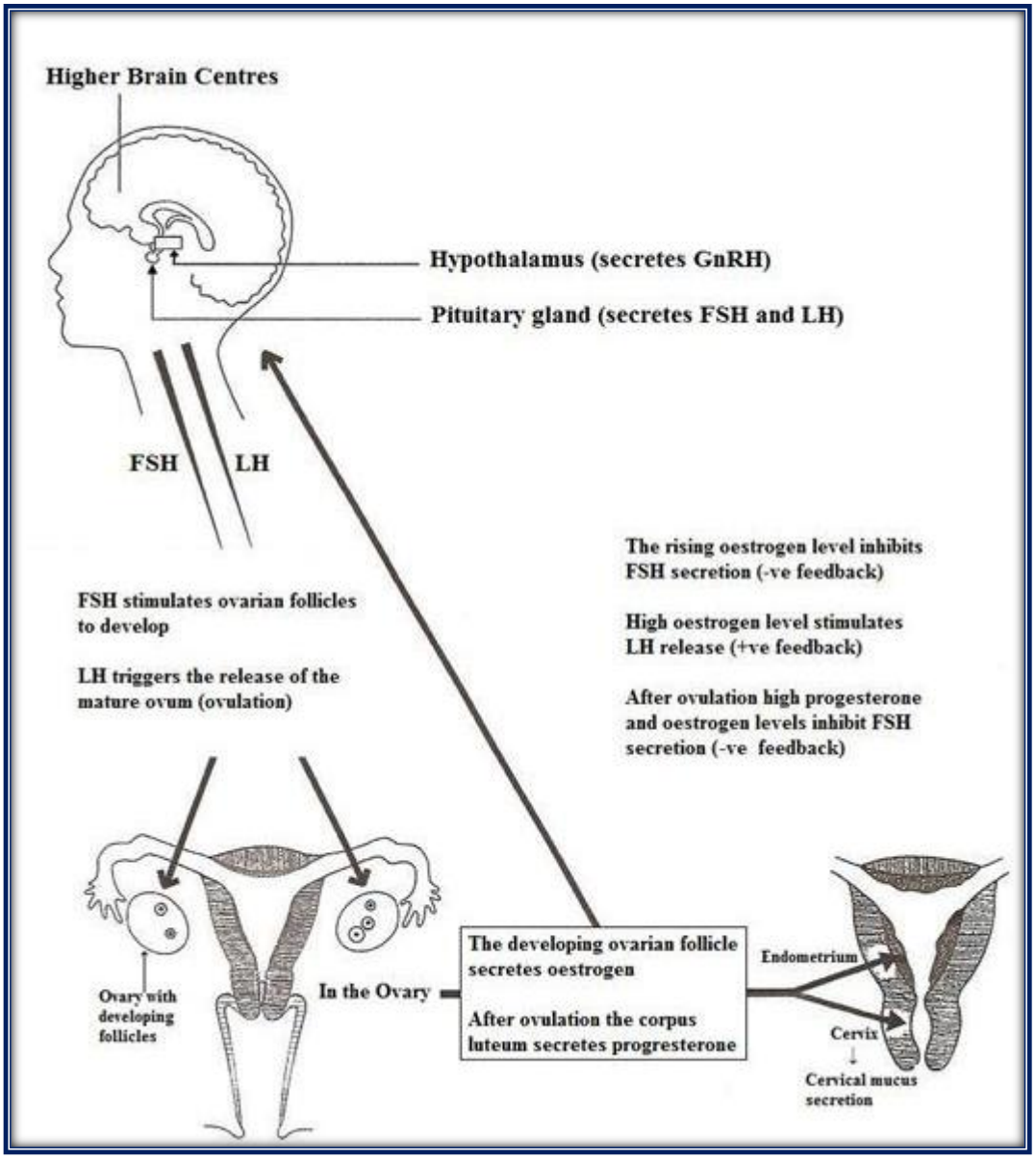


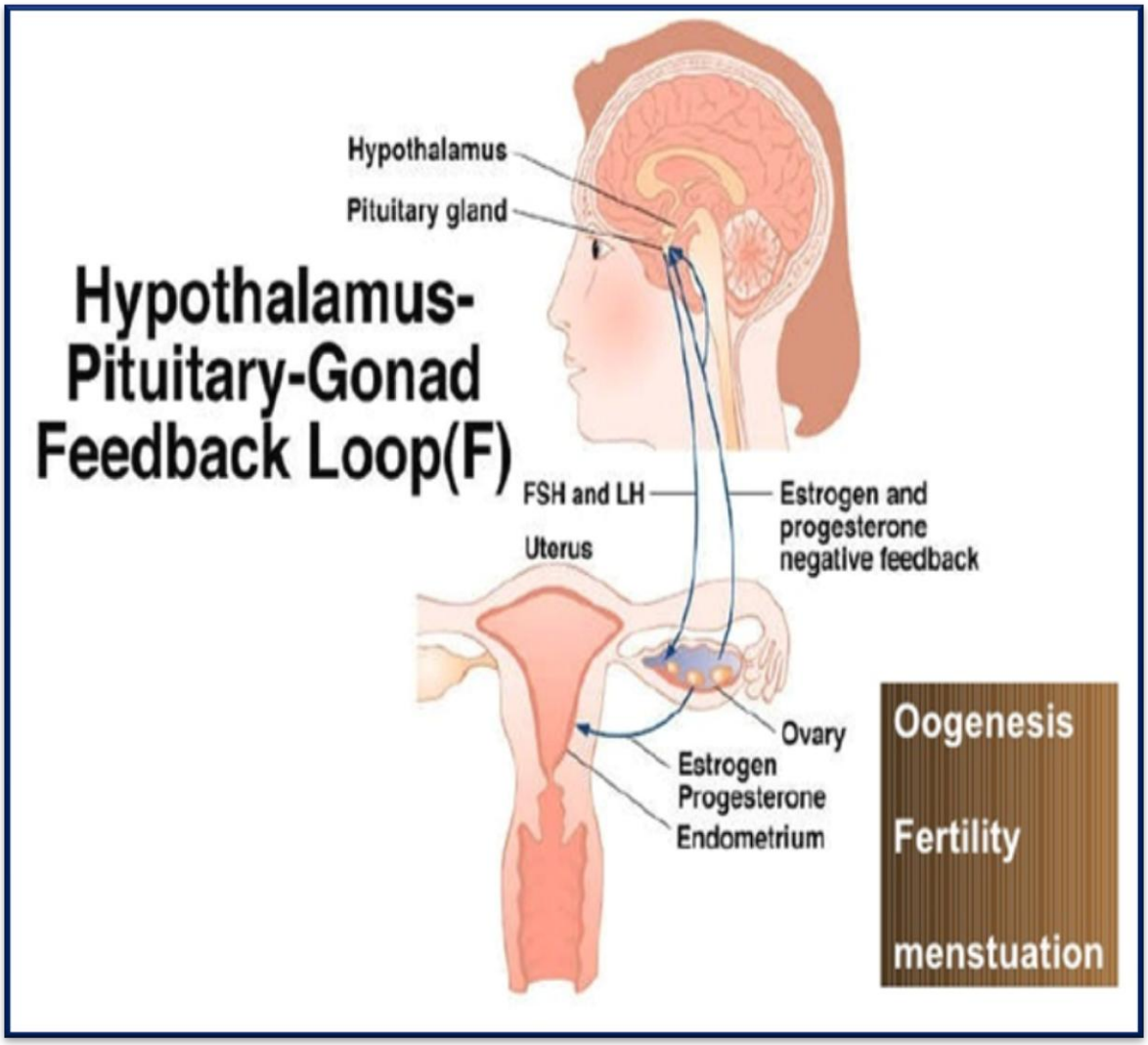
LIPOPROTEIN NOMENCLATURE AND COMPOSITION



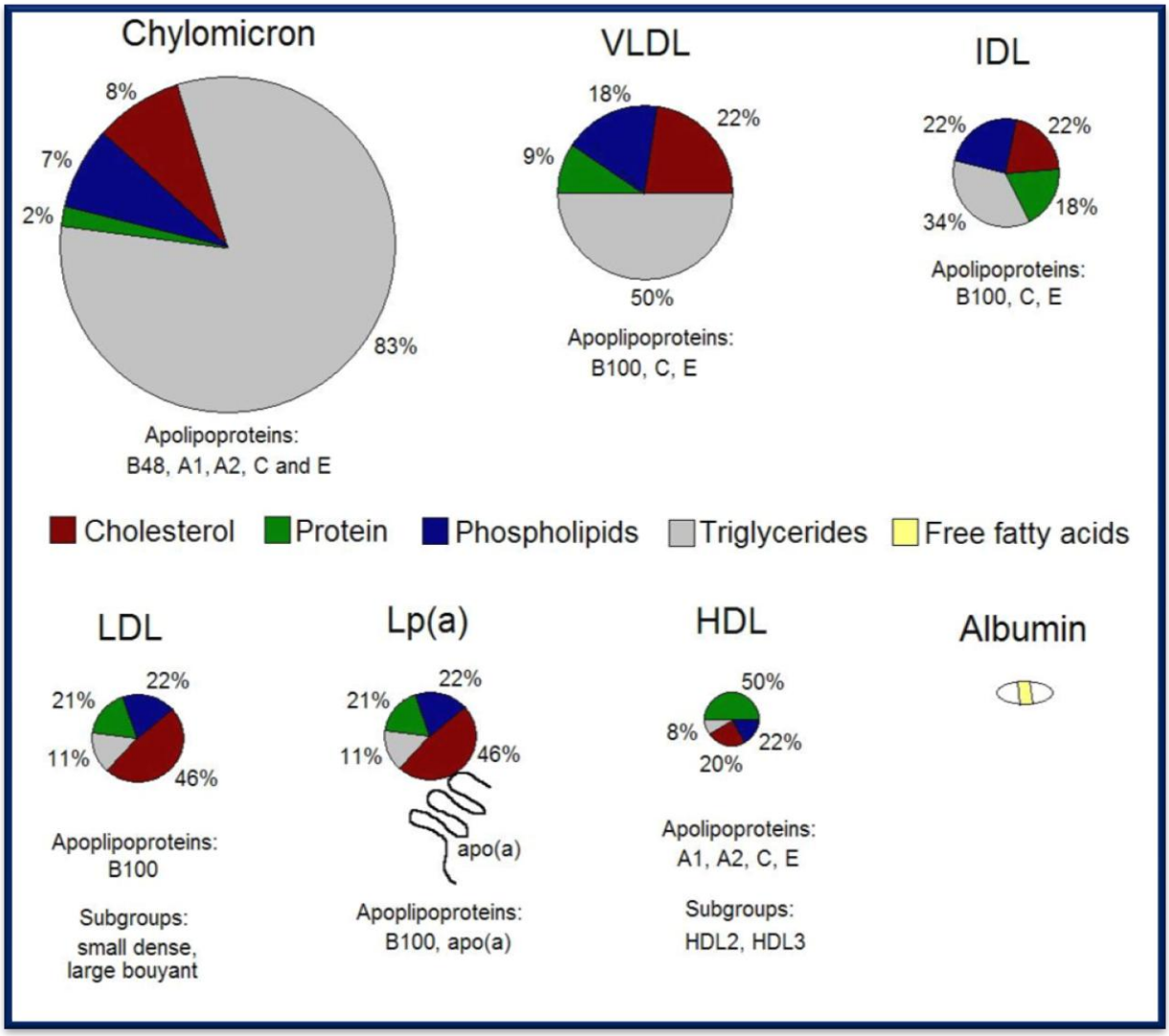
THREE TYPES OF ESTROGEN

FEEDBACK REGULATION

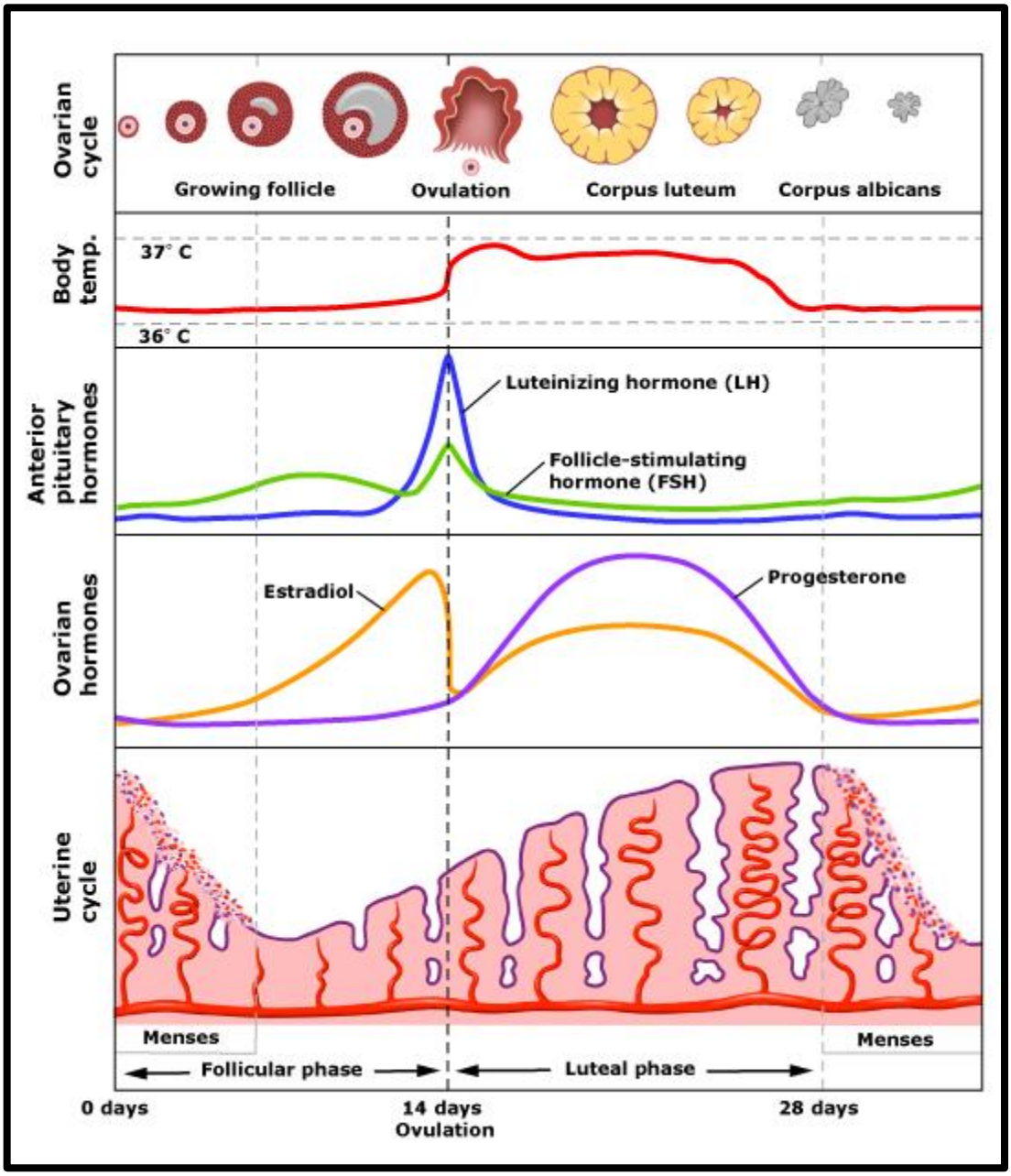



Hypothalamus-
Pituitary-Gonad
Feedback Loop(F)
Hypothalamus
Pituitary gland
FSH and LH
Estrogen and
progesterone
negative feedback
Uterus
Ovary
Estrogen
Progesterone
Endometrium
Oogenesis
Fertility
menstuation

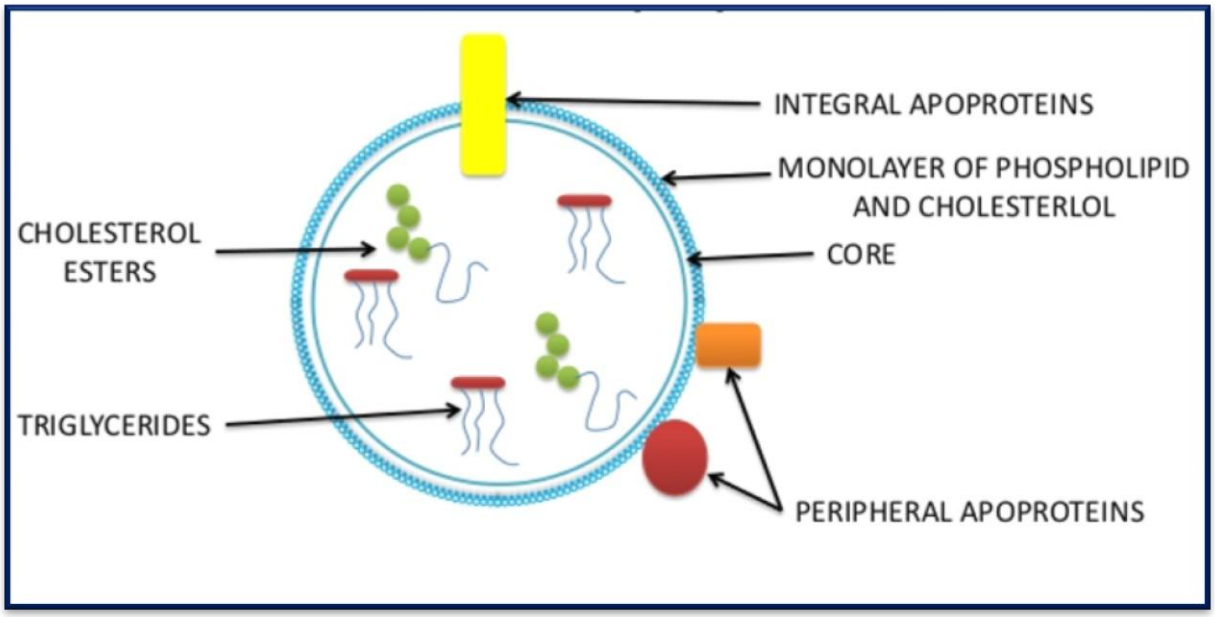
APOLIPOPROTEINS



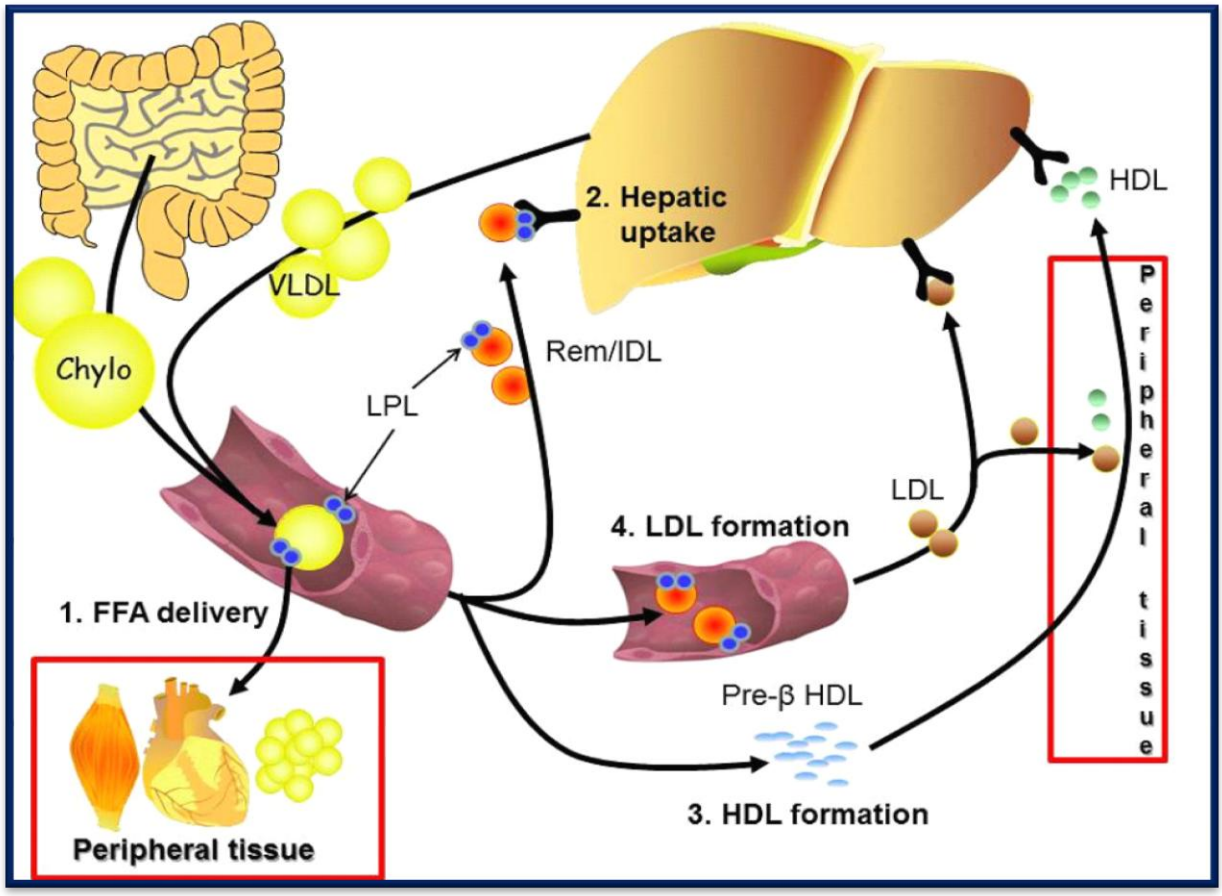
PHASES OF MENSTRUAL CYCLE

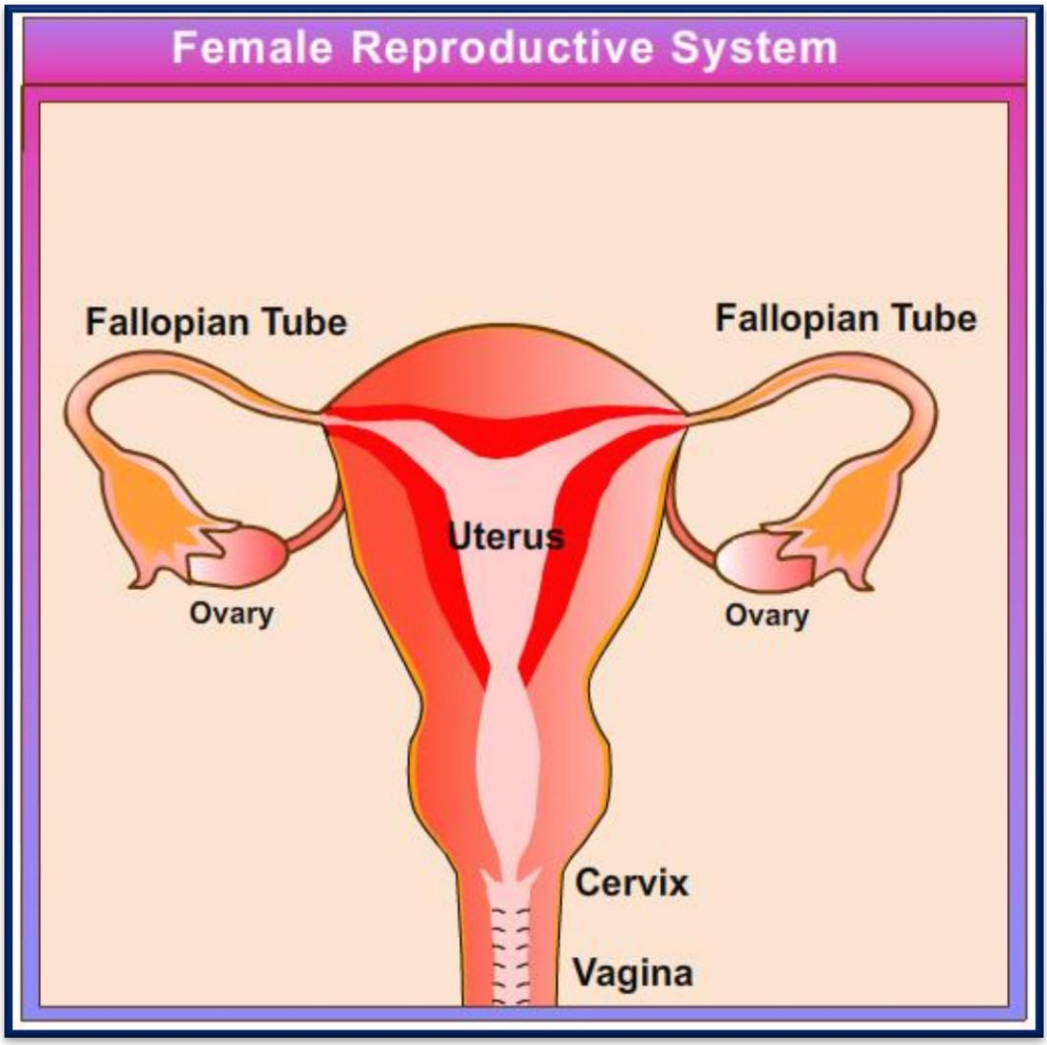


STRUCTURE OF LIPOPROTEIN

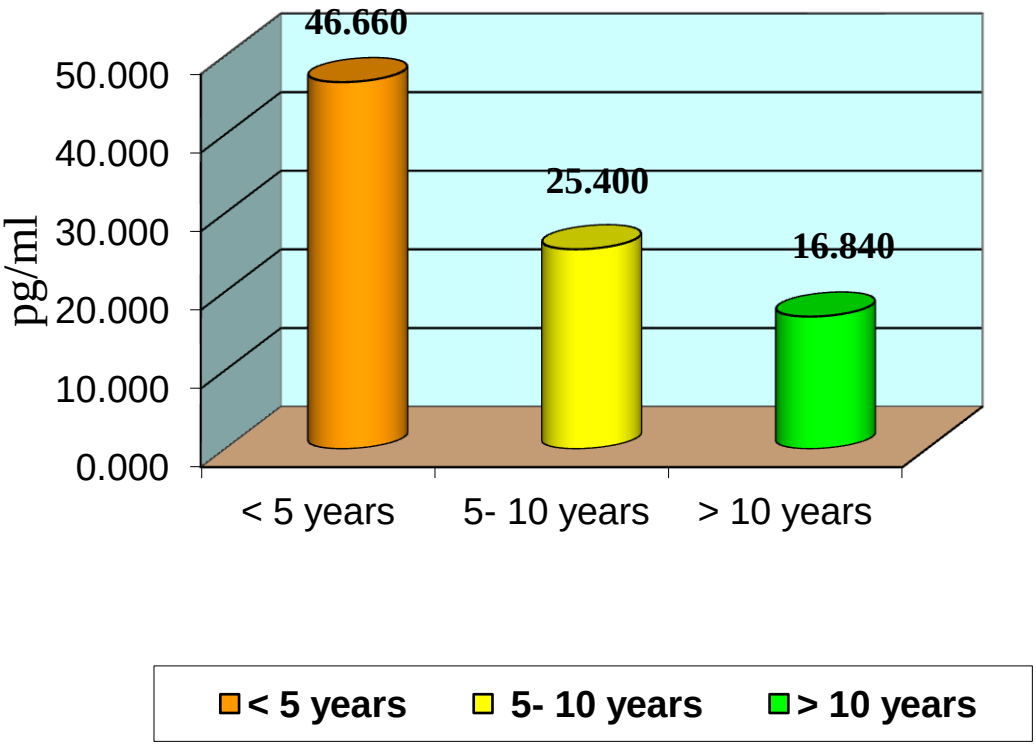


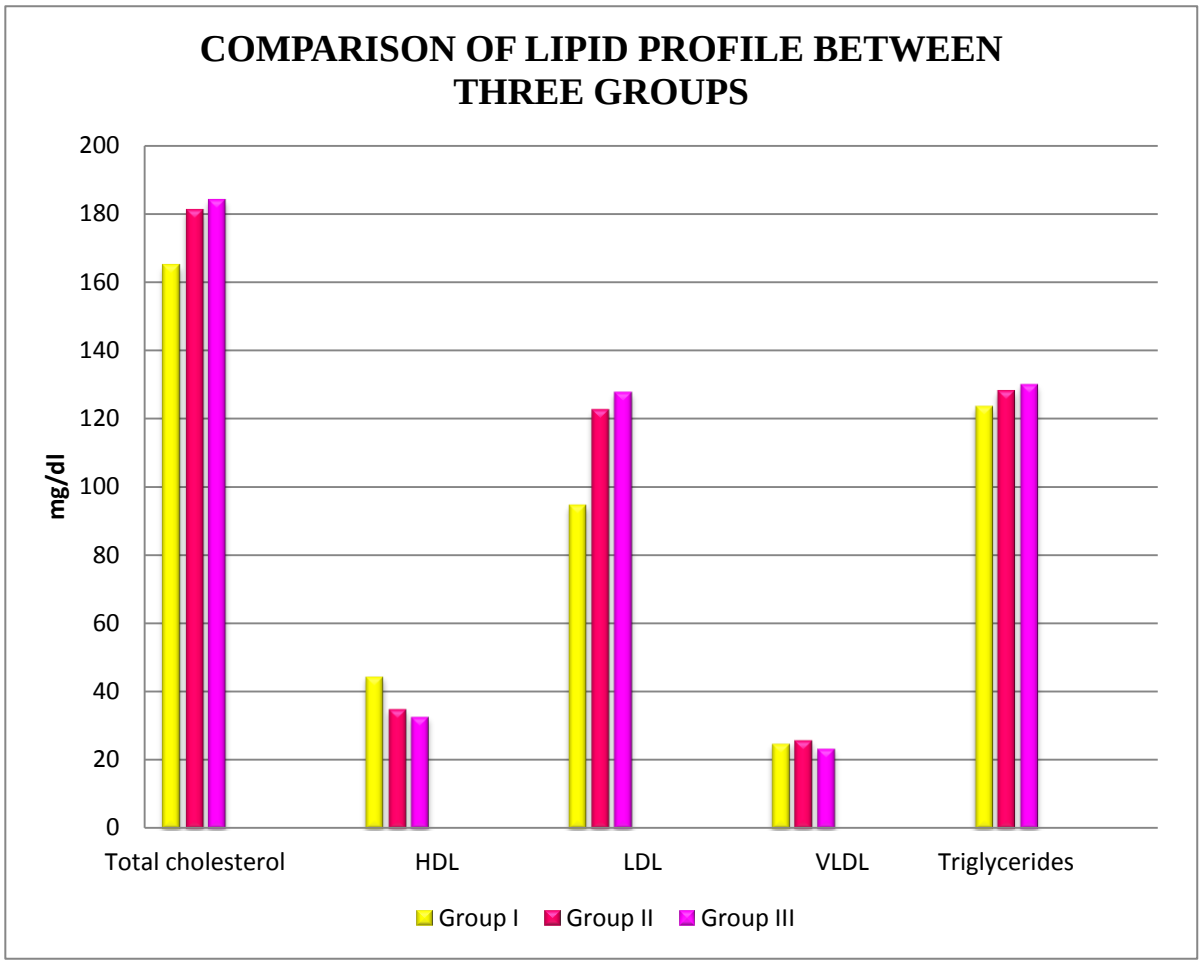
LIPOPROTEIN METABOLISM



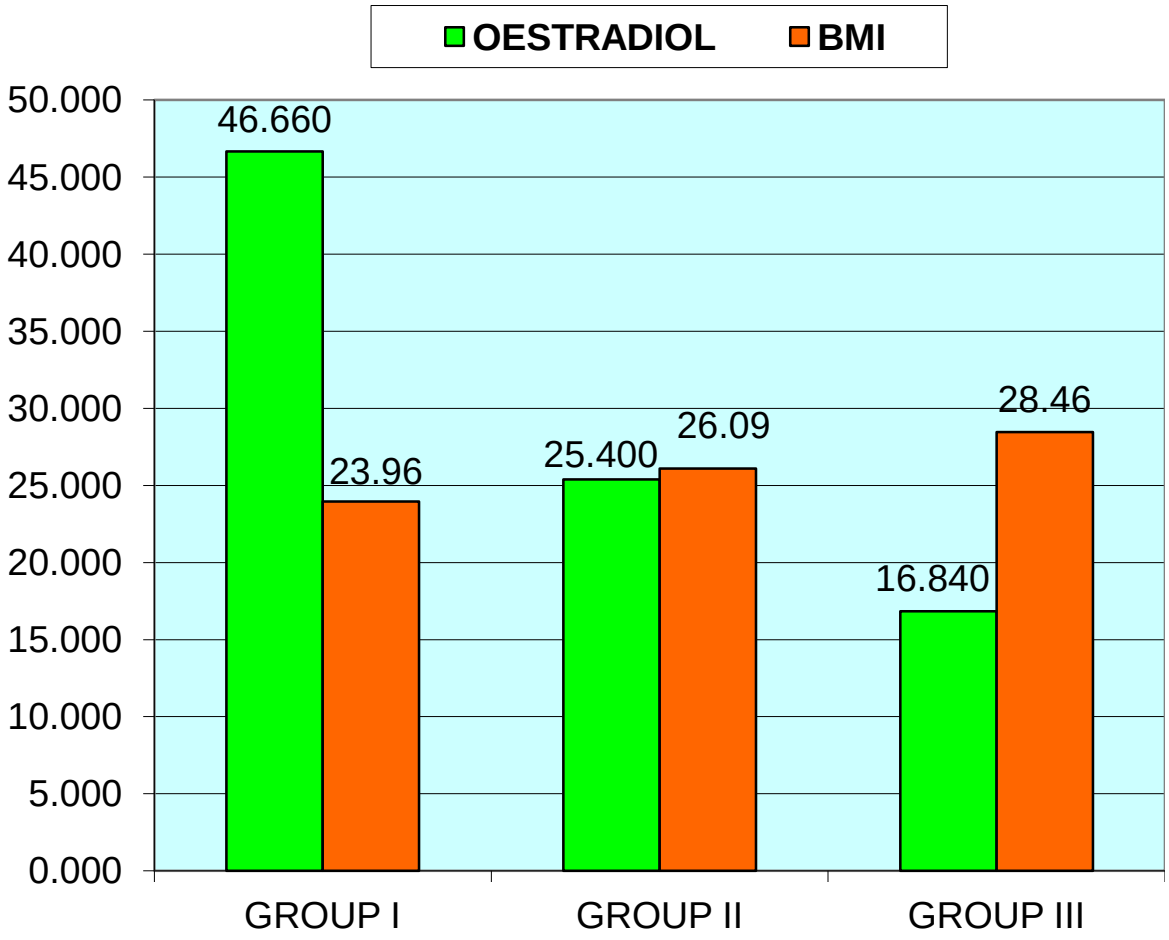

Female Reproductive System
Fallopian Tube
Fallopian Tube
Uterus
Ovary
Ovary
Cervix
Vagina

COMPARISON OF OESTRADIOL BETWEEN THREE GROUPS

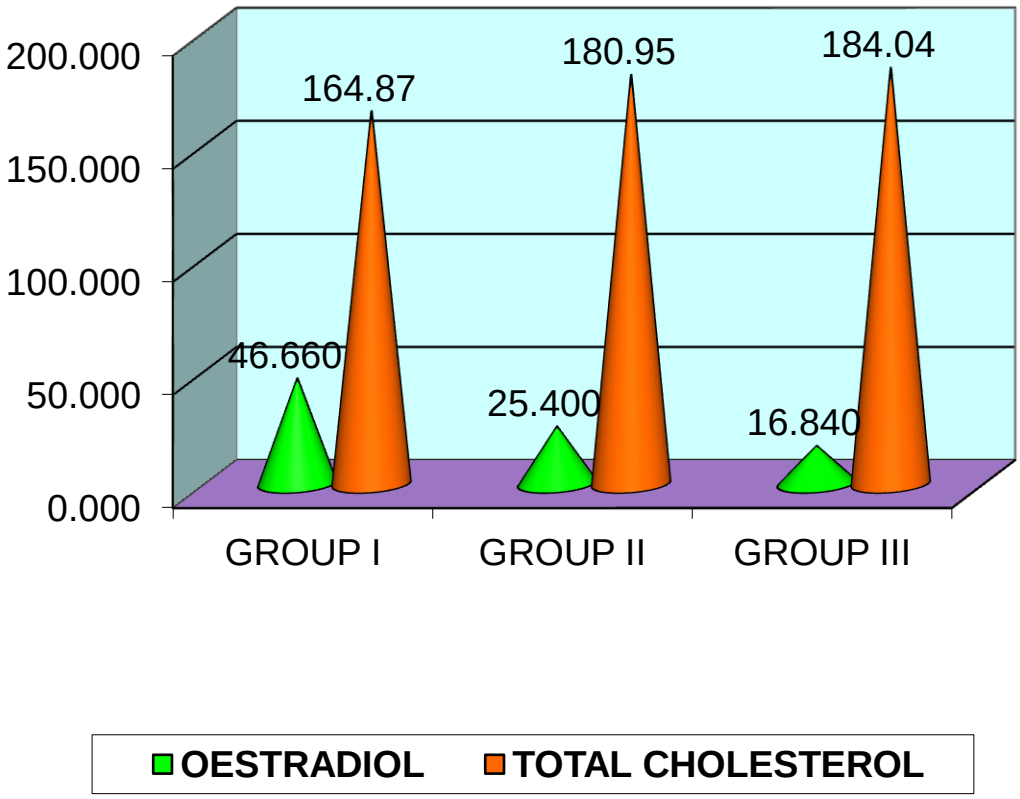



COMPARISON OF LIPID PROFILE BETWEEN THREE GROUPS
mg/dl
200
180
160
140
120
100
80
60
40
20
0
Total cholesterol
HDL
LDL
VLDL
Triglycerides
Group I
Group II
Group III

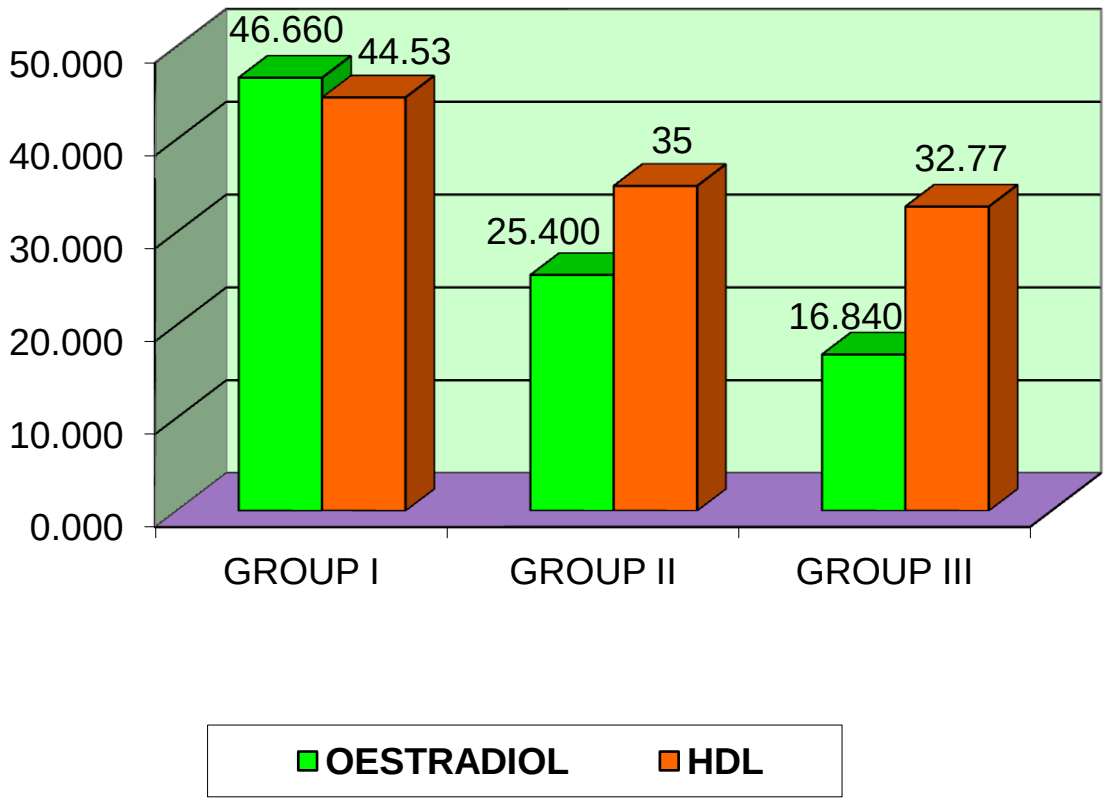
CORRELATION OF OESTRADIOL WITH BMI



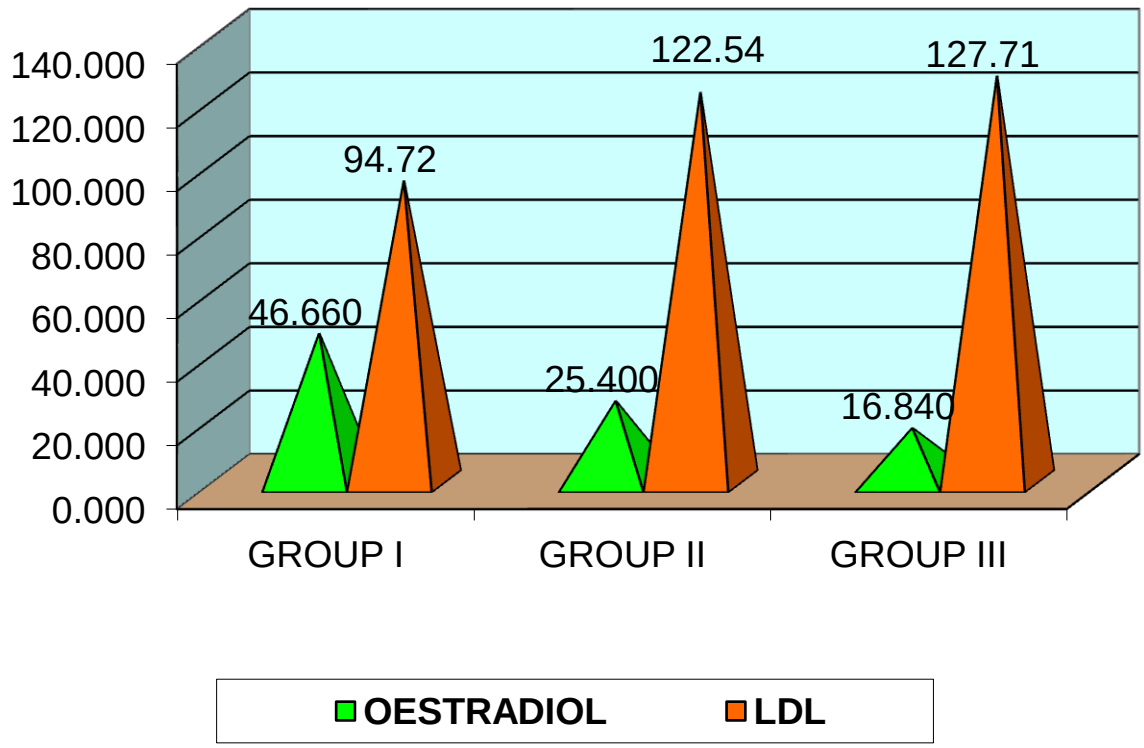
CORRELATION OF OESTRADIOL WITH TOTAL CHOLESTEROL



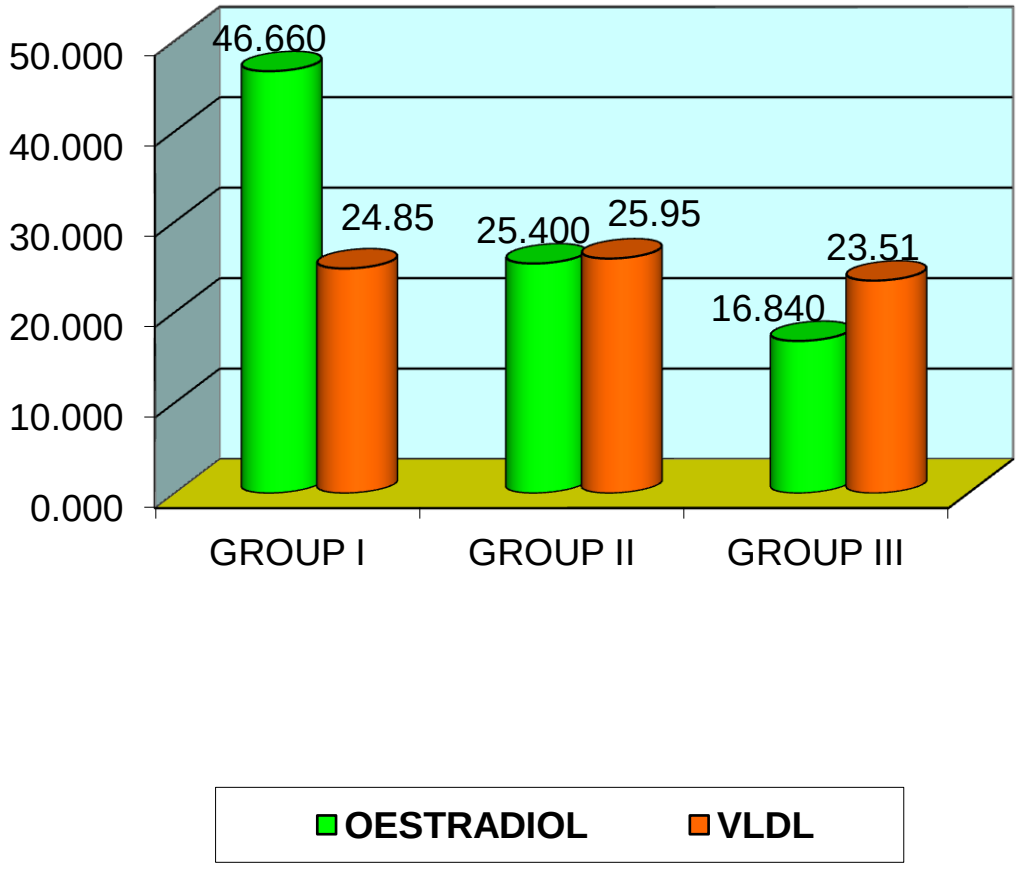
CORRELATION OF OESTRADIOL WITH HDL



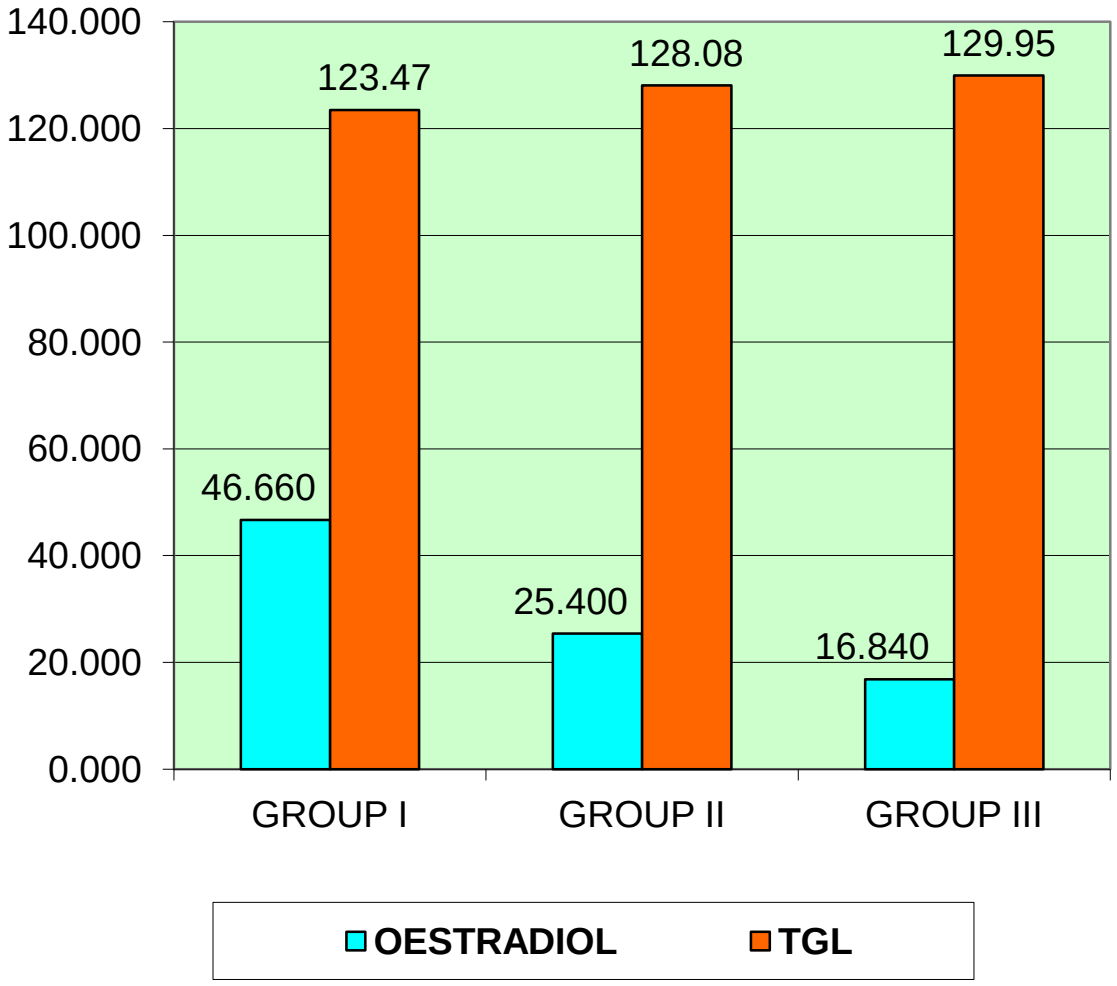
CORRELATION OF OESTRADIOL WITH LDL



CORRELATION OF OESTRADIOL WITH VLDL



CORRELATION OF OESTRADIOL WITH TRIGLYCERIDES



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ABBREVIATIONS

GnRH	Gonadotrophin releasing hormone
FSH	Follicle stimulating hormone
LH	Luteinizing hormone
BMI	Body mass index
TC	Total cholesterol
HDL	High density lipoprotein
LDL	Low density lipoprotein
VLDL	Very low density lipoprotein
TGL	Triglycerides
HPO axis	Hypothalamo-Pituitary-Ovarian axis

PROFORMA

Name: Age: Address:

HISTORY:

PRESENT HISTORY

H/o palpitation
H/o difficulty in breathing
H/o syncope
H/o weight gain

PAST HISTORY

H/o Hypertension
H/o Diabetes
H/o Heart diseases
H/o Thyroid disorders

PERSONAL HISTORY

H/o Drug intake
H/o Smoking

DIET HISTORY Vegetarian/Non vegetarian

MENSTRUAL HISTORY

Type of Menopause - Natural/Surgical
Duration of Menopause - Less than 5 years/5-10 years/More than 10 years

GENERAL EXAMINATION:

Comfortable at rest
Pallor
Cyanosis
Clubbing
Jaundice
Pedal edema

Height (cm): Weight (kg): BMI (Kg/sq.m):

Pulse rate (per min): JVP: BP (mm of Hg):

SYSTEMIC EXAMINATION:

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

ABDOMEN

CENTRAL NERVOUS SYSTEM

INVESTIGATIONS:

Total Cholesterol (mg/dl)	
High Density Lipoprotein (mg/dl)	
Low Density Lipoprotein (mg/dl)	
Very Low Density Lipoprotein (mg/dl)	
Triglycerides (mg/dl)	
Serum Oestradiol (pg/ml)	

நோயாளி தகவல் மற்றும் ஒப்புதல் படிவம்

இணைப்பு – 3

ஆய்விடத் தகவல் மற்றும் தொடர்பு விவரங்கள்

மாதவிடாயொழிவு நடந்த பெண்களுக்கு கொழுமிய விலக்கணச்சோதனை முடிவு மற்றும் ஊநீரின் ஈஸ்ட்ரடையால் அளவு பற்றி ஆய்தல்

இந்தப் பக்கத்தை கையொப்பமிடுவதன் மூலமாக, பின்வருவனவற்றை நான் உறுதி செய்கிறேன்.

- மேற்படி ஆய்விற்கான ஜனவரி 2015 தேதியிடப்பட்ட இந்த நோயாளித் தகவல் மற்றும் ஒப்புதல் படிவத்திலுள்ள அனைத்துத் தகவல்களையும் நான் படித்துப் பரிந்து கொண்டிருக்கிறேன் எனவும், அதைப் பற்றி சிந்திக்க எனக்கு கால அவகாசம் இருந்தது எனவும் நான் உறுதியளிக்கிறேன்.
- கேள்விகள் கேட்பதற்கான வாய்ப்பு எனக்கு இருந்தது. மேலும் எனது கேள்விகள் அனைத்தும் எனது திருப்திக்குத் தக்கவாறு பதிலளிக்கப்பட்டிருக்கின்றன.
- இந்த ஆய்வில் என் குழந்தையின் பங்கேற்பு என் தன்னார்வம் சார்ந்தது எனவும், பங்கேற்பை எப்போது வேண்டுமானாலும் எவ்விதக் காரணமும் அளிக்காமல், என் குழந்தையின் மருத்து கவனிப்பு அல்லது சட்ட உரிமைகள் பாதிக்கப்படாமல் விலக்கிக் கொள்ள நான் சுதந்திரமானவர் என்பதை நான் புரிந்து கொள்கிறேன்.
- வேண்டிக் கொள்ளப்பட்டப்படி, ஆய்வு நடைமுறைகளை பின்பற்றவும், மற்றும் மருத்துவர், செவிலிகள், அல்லது மற்ற ஊழிய உறுப்பினர்களுக்கு தேவையான தகவல்களை வழங்கவும் நான் தன்னார்வத்துடன் ஒப்புக் கொள்கிறேன்.
- மருத்துவ சோதனையின் நிதியுதவியளிக்கும் நிறுவனம், நிதியுதவியளிக்கும் நிறுவனத்தின் சார்பில் பணியாற்றும் மற்றவர்கள், நன்னெறிகள் குழு மற்றும் ஒழுங்கு முறை அதிகாரிகள் ஆகியோருக்கு, தற்போதைய ஆய்வு சம்பந்தமாகவும் தரவு பாதுகாப்பு அறிக்கையில் குறிப்பிட்டப்படியும், எனது

குழந்தையின் ஆரோக்கியப் பதிவேடுகளைப் பார்வையிடுவதற்கு எனது அனுமதி தேவைப்படாது என்பதை நான் புரிந்து கொள்கிறேன். இந்த அணுகலுக்கு நான் ஒப்புக் கொள்கிறேன். இருந்தாலும், மூன்றாம் நபர்களுக்கு வெளியிடப்படும் அல்லது பிரசுரிக்கப்படம் எந்தவொரு தகவல்களிலும் எனது குழந்தையின் அடையாளமானது வெளிப்படுத்தப்படாது என்பதை நான் புரிந்து கொள்கிறேன்.

- இந்த ஆய்விலிருந்து எழும் எந்தவொரு தரவு அல்லது முடிவுகளின் உபயோகத்தினையும், இது போன்ற உபயோகமானது தரவு பாதுகாப்பு அறிக்கையில் குறிப்பிட்டப்படி மட்டுமாக உபயோகிக்கப்படும் பட்சத்தில் அவைகளைத் தடுக்காமலிருக்க நான் ஒப்புக் கொள்கிறேன்.

  மேற்கண்ட ஆய்வில் என் குழந்தை பங்கெடுக்க நான் ஒப்புக் கொள்கிறேன்.

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(அல்லது பெருவிரல் ரேகை)

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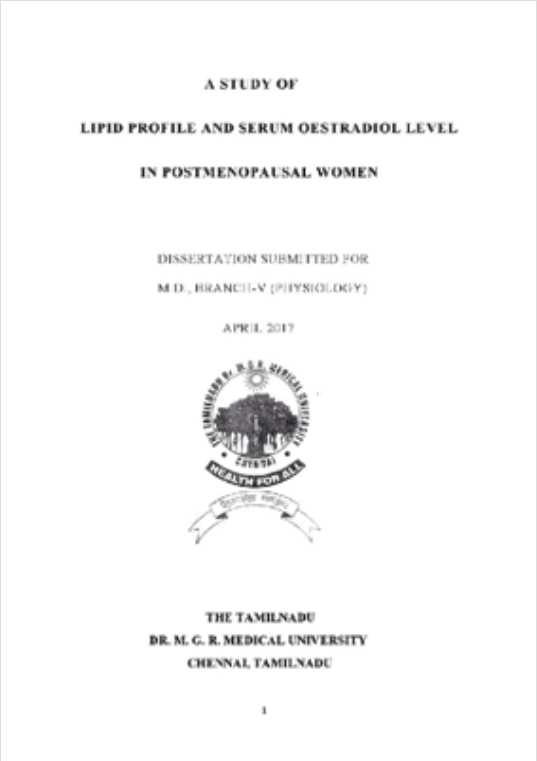

A STUDY OF

LIPID PROFILE AND SERUM OESTRADIOL LEVEL

IN POSTMENOPAUSAL WOMEN

DISSERTATION SUBMITTED FOR

M.D., BRANCH-V (PHYSIOLOGY)

APRIL 2017

THE TAMILNADU

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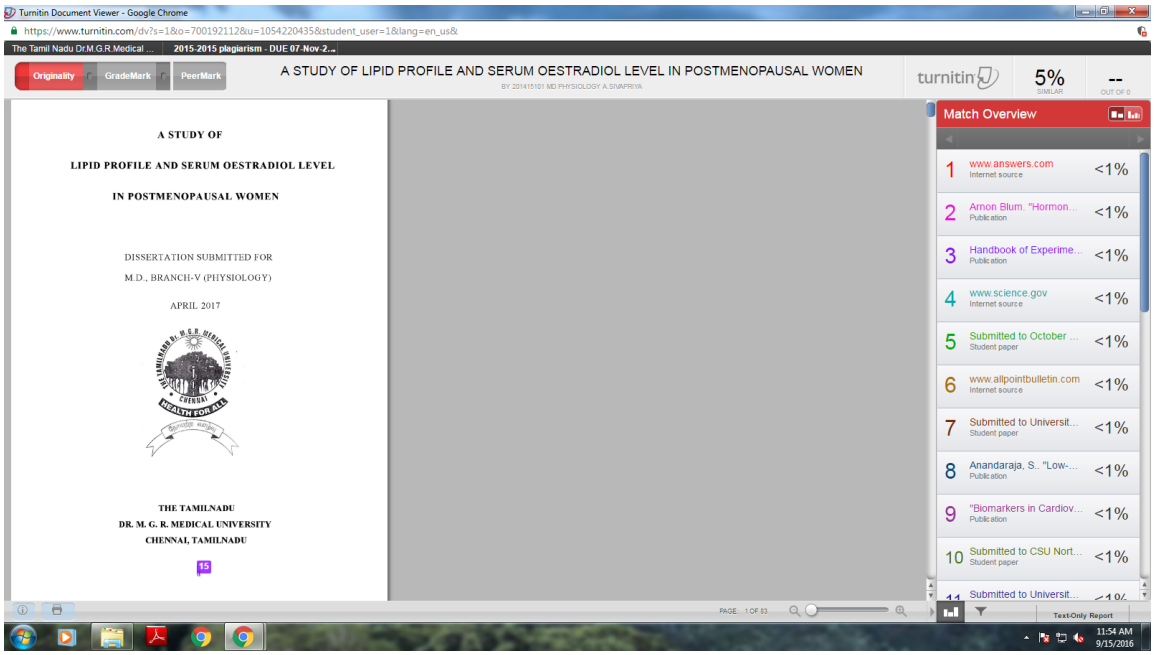
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Sl.no	NAME	AGE (years)	DURATION OF MENOPAUSE (years)	Ht (cm)	Wt (kg)	BMI (kg/sq.m)	OESTRADIOL (pg/ml)	TC (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	TGL (mg/dl)
1	Selvaboopathi	47	2	142	56	27.8	30.22	182	57	107	17.3	86.5
2	Anbumani	48	3	155	41	17.1	61.3	155	41	94	20	100
3	Shanthi	48	4	161	58	22.4	39.15	133.3	45	83	25	125
4	Mariyammal	45	3	149	54	24.3	43.75	237	50	158	29	145
5	Parameshwari	45	4	138	48	25.2	44	175	37	107	31	155
6	Palselvi	50	3	152	57	24.7	38.3	162	48	87	27	135
7	Mariammal	48	2	156	68	27.9	35.26	160	31	66	33	165
8	Tamilselvi	47	3	150	54	24	42.59	179	46	106	27	135
9	Rathinammal	46	4	162	75	28.6	57.3	151	56	77.2	17.82	89.1
10	Sundari	45	4	155	52	21.6	80	138	57	55.1	25.9	129.5
11	Ranikrishnawathi	45	3	158	60	24	40.46	147	55	71.4	20.6	103
12	Nagarathinam	45	3	155	65	27.1	48.2	174	52	91	21	105
13	Rakku	48	4	140	35	17.9	51.6	152	38	92	22	110
14	Ramalakshmi	45	2	156	56	23	38.3	162	38	99	25	125

15	Kamatchi	45	4	140	37	18.9	31.4	180	49	109	32	160
16	Shakthi	44	3	157	57	23.1	39	142	35	84	23	115
17	Rajeshwari	44	3	140	58	29.6	60.8	167	39	105	23	115
18	Nagoorammal	47	4	155	52	21.6	78.2	204	45	134	25	125
19	Valli	49	3	158	60	24	41.4	128	37	69	22	110
20	Nagarathinam	48	4	147	52	24.1	52.3	161	38	89	34	170
21	Maruthayee	44	3	156	68	27.9	31.3	184	58	109	37	185
22	Kavitha	47	2	165	60	22	48	126	40	61	15	58
23	Angayarkanni	44	4	163	47	17.7	62.1	182	43	108	31	148
24	Nagalakshmi	51	3	160	94	36.7	54.2	133	40	69	24	120
25	Petchiammal	45	3	151	46	20.2	46.7	141	46	75	26	130
26	Anar	51	2	146	57	26.7	30.8	189	42	102	17	85
27	Bagavathi	44	4	142	51	25.3	44.6	167	32	116	19	95
28	Muthulakshmi	50	4	147	48	22.2	35.3	175	41	112	22	110
29	Selvi	50	3	160	61	23.8	42.8	188	43	119	26	130
30	Shanthi	47	3	157	48	19.5	50.4	172	57	87	28	140

Sl.no	NAME	AGE (years)	DURATION OF MENOPAUSE (years)	Ht (cm)	Wt (kg)	BMI (kg/sq.m)	OESTRADIOL (pg/ml)	TC (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	TGL (mg/dl)
1	Dhanalakshmi	52	6	153	61	26.1	18.99	201	30	143.7	15.3	76.5
2	Velthai	50	7	157	72	29.2	27	162	35	198.8	28.2	141
3	Pitchaiammal	53	10	161	76	29.3	24.73	215.5	31	155.5	19	95
4	Mariammal	51	8	154	64	27	26.3	209	47	140	22	110
5	Subbulakshmi	50	9	147	60	27.8	16.15	163	31	147.8	26.2	131
6	Shanthi	50	9	158	64	25.6	17.35	269	32	192.3	18.7	93.9
7	Dhanalakshmi	54	8	155	67	27.9	20.98	185	37	124	24	120
8	Rani	52	7	145	59	28.1	17.2	165	38	96	31	155
9	Latha	52	7	164	65	24.2	30.6	202	34	133	35	175
10	Alagu	55	6	153	88	37.6	28.2	172	36	124	12	60
11	Arulrani	53	7	158	68	27.2	31.3	189	38	134	17	85
12	Mallika	57	8	150	65	28.9	34.2	171	36	108	27	135
13	Muthulakshmi	56	9	159	59	23.3	26.8	181	34	125	22	110
14	Kanagavalli	53	7	153	64	27.3	29.4	144	36	85	23	115

15	Lakshmi	52	7	151	62	27.2	25.6	148	32	91	25	125
16	Pitchaiammal	50	8	162	75	28.6	31.7	144	30	86	28	140
17	Chandra	53	9	156	68	27.9	26.9	169	41	99	29	145
18	Sathyavanimuthu	54	10	147	58	26.8	24.3	177	34	111	32	160
19	Indhumathi	55	8	153	50	21.4	20.6	169	31	98	34	170
20	Seribabeevi	54	7	153	66	28.2	27.4	178	29	112	37	185
21	Noorjahan	54	9	144	57	27.5	28.1	186	41	130	15	75
22	Savithri	55	6	158	70	28	31.4	159	33	98	28	90
23	Palaniammal	51	7	146	59	27.7	38.6	172	42	108	22	110
24	Asimbegam	50	8	159	39	15.4	17.4	166	28	101	28	140
25	Kaliammal	57	7	149	47	21.2	19.1	156	34	91	31	155
26	Jothi	55	7	149	47	21.2	24.6	215	36	145	34	170
27	Vasuki	51	8	166	69	25	27.7	178	32	108	38	190
28	Meenatchi	51	9	169	84	29.4	24.8	225	38	158	26	130
29	Jeyakumari	50	8	174	64	21.1	21.4	186	34	124	28	140
30	Muneesmeena	50	8	168	70	24.8	23.2	172	40	109	23	115

Sl.no	NAME	AGE (years)	DURATION OF MENOPAUSE (years)	Ht (cm)	Wt (kg)	BMI (kg/sq.m)	OESTRADIOL (pg/ml)	TC (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	TGL (mg/dl)
1	Renganayagi	55	12	162	74	28.2	22.4	189	38	130.8	19.2	101
2	Perumalammal	60	14	152	68	29.4	24.88	161	40	94.7	18.5	96
3	Sulochana	55	11	155	56	23.3	23.04	167	37	141.6	16	92
4	Mariyammal	59	12	143	59	28.9	10.87	214	24	175	15	75
5	Devaki	54	11	146	62	29.1	5	199.2	31	146.2	22	125
6	Fatima	58	12	151	72	31.6	5	145	37	82	26	130
7	Saroja	58	13	153	67	28.6	5	184	27	134	23	115
8	Madathi	58	14	155	72	30	16.9	229	34	168	27	135
9	Renganayaki	57	12	150	81	36	15.06	152	28	81.8	42.2	181
10	Kalavathi	59	15	147	67	31	8.22	190	38	139.7	12.3	120
11	Vijayalakshmi	57	12	149	75	33.8	5.74	160	38	99.7	22.3	111.5
12	Rahmathbeevi	60	14	150	55	24.4	11.3	170	31	122	17	125
13	Pushpavalli	59	12	152	65	28.1	13.4	196	33	131.8	31.2	156
14	Savithri	60	12	140	58	29.6	15	216	32	154	21	150

15	Otahammal	59	11	164	65	24.2	26	146	25	129	19.2	120
16	Ponrakku	55	13	145	58	27.6	18.2	223	27	175	21	105
17	Kamatchi	58	12	151	59	25.9	24	198	30	113	20.5	165
18	Stella	60	15	148	80	36.5	20.8	169	26	109	22	170
19	Karuppayammal	60	11	152	65	28.1	16.4	188	34	132	22	110
20	Anitha	59	12	150	62	27.6	11.2	181	27	148	34	170
21	Saraswathi	55	13	157	87	35.3	17.3	193	35	135	23	115
22	Selvi	58	16	160	58	22.7	21.3	170	35	110	18.6	120
23	Shanthi	54	14	150	54	24	25.6	163	30	129	18.2	95
24	Rani	60	11	148	60	27.4	14.2	199	35	120	44	220
25	Muthupetchi	58	12	143	55	26.9	16.8	186	30	127	29	145
26	Chithrakani	54	13	146	59	27.7	15.2	201	40	132	29	145
27	Karpagam	57	11	151	62	27.2	23.4	180	33	113	14	90
28	Rukmani	58	12	154	68	28.7	28.9	208	34	130	24	126
29	Meenambikai	55	14	156	64	26.3	18.2	173	36	103	34	170
30	Kalamani	57	12	153	60	25.6	26	171	38	125	20.2	120