ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

The Menopause's Clinical Biochemistry and Hormone Replacement Treatment

Dr. Jyoti Batra[1], Dr. Juhi Aggarwal[2], Dr. Eram Hussian Pasha[3], Nikita Chaudhary[4]

[1] Professor, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[2] Professor & Head, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[3] Assistant Professor, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[4] MBBS Student, Batch 2021-22, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

Email- [1] dean.research@santosh.ac.in, [2] jaggarwal38@gmail.com, [3] pasha.eram7@gmail.com, [4] nikitachoudharyg@gmail.com

ABSTRACT:

The need for hormonal assessments of menopausal status in laboratories is rising as a result of rising interest in women's health, the menopause, and the use of hormone replacement therapy (HRT). Most requests come from general practitioners, many of whom run menopausal or well-women clinics.Clinicians increasingly need scientific proof of the menopausal transition before making judgments about how to treat a patient.In light of these changes, it is appropriate to review the literature on the measurement of reproductive hormones around the menopause and look at how these measurements are used to classify menopausal status and manage patients who are on HRT.

Keywords: menstrual cycle; LH;FSH; oestradiol; progesterone; inhibin.

INTRODUCTION:

Menopause, according to the World Health Organization (WHO), is the period of time when menstruation stops permanently as a result of a decrease in ovarian follicular activity. The following are some more phrases used to refer to the period before and after the menopause:

1. The period between the first interruption of the menstrual cycle and the menopause is known as the menopausal transition.
2. The period between the start of the menopausal transition and at least one year following the menopause is referred to as the perimenopause (or climacteric).

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

3. Postmenopause: the period of time following the menopause; it cannot be identified until 12 months have passed without the occurrence of spontaneous amenorrhea.

Physiology

The ovary: Only one year or longer after the onset of the menopause can the condition be accurately diagnosed. This is because many women do not transition consistently from pre- to postmenopause, and erratic menstrual patterns precede the menopause. The average age at menopause, according to research of Western populations, is 49 to 51 years old. However, according to reports, the menopausal transition begins at a median age of 44 years (range: 34–55 years) and lasts for a median of 4–5 years.[1]

It is believed that the menopause starts when the ovarian oocyte pool is depleted. During foetal development, the full complement of oocytes is established in utero and maintained in an arrested meiotic stage. A tiny number of follicles are then daily recruited, going through limited development before atresia (cell death), such that by the time a baby is born, the number of follicles has already decreased by half, to 500 000. This process lasts till menopause and is not dependent on gonadotrophins.[2] After puberty, approximately 20 follicles begin to grow each month in response to the increase in follicle-stimulating hormone that occurs between periods (FSH). Most of the time, only one (the dominant) follicle matures and ovulates, the others becoming atretic. Because it has not been demonstrated that pregnancy or oral contraceptive usage can postpone menopause, it is likely that these factors have no impact on the gonadotrophin-independent recruitment of follicles. According to some data, early menopause is primarily caused by an increase in the rate of oocyte atresia and may also be a result of smoking and maybe poor nutrition. Infections or physical harm like chemotherapy or irradiation can also destroy follicles, which leads to early ovarian failure.[3]

Prior to the menopause, fertility declines and the menstrual cycle changes.Eventually, the fewer ovarian follicles produce insufficient oestradiol to cause endometrial growth and subsequent monthly bleeding. Women who are perimenopausal have ten times fewer follicles than women of the same age who are menstruating regularly, indicating that the amount of the follicular reserve is a crucial factor in both the change from regular to irregular menses and the menopause itself.[4] Only if exposure to the hormone is followed by withdrawal do hot flushes appear to happen.Despite being hypergonadotrophic and deficient in oestrogen, patients with Turner's disease who have gonadal dysgenesis don't get hot flushes. Since 24% of women with low oestradiol concentrations do not suffer hot flushes, the mechanism underlying them is poorly known. [5]

It has been shown that the commencement of the hot flush and luteinizing hormone (LH) pulses have a startling link. Given that the preoptic anterior nuclei, which control body temperature, are located adjacent to the hypothalamic neurones that contain gonadotrophin

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

releasing hormone (GNRH), neurotransmitter impulses linked to GNRH production may also change thermoregulating neurones. [6]

The elevated risks of osteoporosis and ischemic heart disease (IHD) in postmenopausal women have a bigger effect on long-term morbidity and death. Epidemiological studies show that after menopause, women experience an accelerated loss of bone, which can be avoided by taking oestrogen.[7,8,9] Due in part to their lower bone density, women are more likely than males to experience osteoporotic fractures as they age. The data is less clear for women who experience normal menopause. Women who experience an early menopause, whether natural or iatrogenic, are at greater risk of IHD. The detrimental shift in lipid profile with age, which includes increased total cholesterol and lower HDL cholesterol, is one of the variables that may contribute to this. [10] Treatment with oestrogen is linked to a lower risk of IHD and a positive impact on the lipid profile. [12]

HORMONE CONCENTRATIONS DURINGTHE MENOPAUSAL TRANSITION:

There are not many longitudinal investigations of endocrine alterations related to menopause. [13–17], and some writers have employed a different cross-sectional methodology to analyse a sizable number of women of various ages. [18,19] Few cross-sectional studies have tried to standardise when blood samples were taken during the follicular phase in relation to the mid-cycle peak or taken into account the pulsatile nature of gonadotrophin secretion (especially LH). The longitudinal study gives greater specifics about the various hormone levels that are present at this period.

Regular menstruation

According to the Metcalf study, women over 40 years old continue to ovulate in 98.17 percent of cycles as long as menstruation is normal. Similar to younger, fertile women, these women excrete pregnanediol and oestrogen through their urine, and there is little difference in the serum steroid profiles that are tested. P However, other studies have revealed that a portion of women who are said to have regular menstruation had high serum levels of follicular phase FSH, oestradiol that is between pre- and postmenopausal, and LH concentrations that are comparable to controls. [14,18,21.22] The ladies in these trials were probably closer to or had already entered the menopausal transition period than Metcalf's group. Take Sherman's little group as an example! Chakravarti et al. included those women in their study who had not menstruated in the previous three months and who "were aged 46-56 years and indicated an increased frequency of anovulatory cycles."

The declining secretion of the ovarian glycoprotein hormone, inhibin, may be responsible for the selective increase in FSH seen in the follicular phase of women over 40 "which circulates at its highest levels in the luteal phase of the cycle and preferentially inhibits FSH production and or secretion. [22] The endocrine alterations mentioned above might help to explain why

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

cycle length was observed to shorten around the age of 40 to 45. [14,16,18] The follicular period is shorter by 5 to 9 days. [14,18,24] The commencement of follicular maturation at more frequent intervals, which results in a shorter cycle duration but maintains steroidogenesis, may be caused by the higher FSH concentrations "Reduced fertility is also linked to high FSH levels, Day 3 FSH levels are a good indicator of outcome, according to data from pregnancy rates in IVF programmes: performance reduces with increases > 15 U/L and drops sharply with elevations > 25 U/L,26,27.In conclusion, an increased follicular phase serum FSH concentration in women with regular cycles is the most accurate indicator of deteriorating ovarian function.

Irregular menstruation (menopausal transition)

Prior to menopause, the majority of women go through a phase of menstrual irregularity during which the frequency of ovulatory cycles significantly decreases. Only 540/0 of cycles in 31 women going through the menopausal transition who had urine pregnanediol values studied by Metcalf were ovulatory. Long cycles were also more common; 40% of them lasted longer than 40 days, and 80% of them were anovulatory. This suggests a significant decline in fertility, but since four of the study's participants ovulated in their final cycles before menopause, conception may still be feasible.

FSH

Even though menstruation patterns can vary during the menopausal transition, the presence of high FSH concentrations is a distinguishing trait. [14,15,19,21,25] Metcalf discovered that one-third of women had elevated urine FSH levels at the beginning of the menopausal transition. There are no comparable statistics for serum FSH measurements taken right after the first irregularity in regular cyclicity, yet 800/0 of women with irregular cycles between the ages of 45 and 55 have follicular phase FSH levels above 15 U/L! 9 with increased concentrations among individuals with regular cycles as opposed to merely 40-500/0.FSH levels can be measured more accurately in serum than in early-morning urine, it seems.

LH

Regarding the variations in LH secretion during the menopausal transition, there is significant debate in the literature. Studies on serum indicate that the rise is less constant than for FSH [14,25] and that it may take place a few years after the rise in FSH and closer to the menopause. [18,25] Using once-weekly urine samples, Metcalf et al., IS discovered that a persistent elevation in urinary LH excretion lasting two to eight weeks occurred more frequently than an increase in FSH without a corresponding increase in LH. About 50% occurrences of high LH excretion on their own were linked to low oestradiol and could not be explained by a prolonging of the typical mid-cycle surge of LH. Although FSH has a longer plasma half-life than LH29, it is unclear if the high urine LH results may be explained by LH having a higher renal clearance than FSH.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

Poslmenopause

In the first 6–12 months following the end of menstruation permanently, 20–40% of women may have oestrogen concentrations indicative of follicular function, according to cross-sectional studies of hormone levels in plasma taken from women in whom the diagnosis of menopause was established retrospectively. [13,30] By 12 to 24 months, practically all subjects' oestrogen levels were in the postmenopausal range.Some postmenopausal ovaries still contain primordial follicles, however this is uncommon three years after menopause.[31]

Plasma hormone levels were examined in a cross-section of 60 women who had been postmenopausal for 1 to 30 years by Chakravarti et al. 2-3 years after menopause, FSH and LH reached their peak levels, with FSH showing a higher increase in follicular concentrations than LH. After then, gonadotrophin levels gradually dropped until 15% of women who were 20 to 30 years following menopause had concentrations similar to those seen during reproductive life.[32]

Oestradiol levels were low throughout, despite the fact that six individuals who were more than 20 years post menopause had levels at the lower end of the normal reproductive range. It is important to note that postmenopausal women with serious illnesses, such as stroke, cerebral haemorrhage, and head trauma, may experience temporary suppression of FSH and LH concentrations. LH and FSH concentrations from premenopausal women have been linked to hypothyroxinemia in more than 50% of postmenopausal women admitted to intensive care units (medical, cardiac, surgical, and neurological).[33]

Oestrone

At menopause, serum oestrone concentrations decrease by 50–800%, but because oestradiol production is declining, oestrone becomes the quantitatively most abundant oestrogen in postmenopausal serum. Circulating oestrone is produced when androstenedione from the adrenal gland is peripherally aromatized in adipose tissue. "[34]

Androgens

Around 25% of the circulating testosterone in premenopausal women is secreted by the ovary and 25% by the adrenal gland. Androstenedione is converted to testosterone in peripheral tissues, which provides the remaining 50%. Prior to menopause, the ovary and adrenal both provide roughly the same amounts of androstenedione to the bloodstream. Although androstenedione concentrations in postmenopausal women fall by more than 50% [31,35], the ovary still contributes a tiny but significant 20% to this decreased pool. [38] At menopause, interconversion to testosterone will also decline.

Lnhibin

Inhibin, a gonadal glycoprotein hormone, completes a closed-loop feedback system between the pituitary and ovary by preferentially inhibiting the synthesis of FSH. After age 40,

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

follicular phase inhibitor serum levels significantly decrease, and there is an inverse relationship between them and FSH levels. [22] The decrease in inhibin may be due to a change in the way granulosa cells produce this hormone or an aging-related decline in follicular quantity. Although it's not obvious if these tests have a significant advantage over blood FSH, serum inhibin may offer a sensitive and early indicator of deteriorating ovarian function.

THE CLINICAL VALUE OF HORMONETESTS OF MENOPAUSAL STATUS:

Clinical indications for biochemical confirmationof menopause

Due to the strong temporal correlation of symptoms with menstruation disturbance, the perimenopause can frequently be diagnosed in women over 45 on the basis of clinical findings alone. However, there are several circumstances in which it would be beneficial to have biochemical proof that a woman is peri- or postmenopausal.

Conventionally, premature menopause is described as ovarian failure occurring before the age of 40? Menopause before age 45 could be seen as premature because the usual age range (95% of confidence interval) for natural menopause is 45-55 years. After early surgical menopause, the long-term risks of osteoporosis and atherosclerosis rise "and following menopause, the risk of osteoporosis has increased over time." [40]

Assessment of the need for contraception inwomen of menopausal age

It is well known that 9DJo of women over 45 who have experienced amenorrhea for six months will start menstruating again and that despite having "postmenopausal" hormone profiles, ovulation can continue up to menopause. Hormone measures cannot, therefore, serve as a reliable foundation for the recommendation of contraception. According to current recommendations, non-hormonal methods of contraception should be used until amenorrhea has subsided for 1 year in women over 50 and 2 years in younger women.

Selection of women for HRT

This section relates to women under the age of 45 who seek hormone replacement therapy (HRT) and to those who appear with menopausal symptoms but whose clinical diagnosis is uncertain. According to a survey of the age distribution of menopause-related requests made in our lab, the distribution is biassed toward women who are just starting this transition at a median age of 45, which is to the left of Treloar's description of the distribution for perimenopausal women. This reflects the fact that, in women between the ages of 40 and 50, clinicians may find it challenging to differentiate between symptoms of oestrogen shortage, premenstrual syndrome, and mental or sociodomestic issues.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

Guidelines for biochemical investigation of womenseeking help for menopausal symptoms

The women who are looking for information on menopausal symptoms or guidance on using HRT to use hormone tests in an effective manner. The situations when they might be useful have been described above. Advice about contraception cannot be given based solely on hormone results. The general strategy recommended is:

1. Consider how age, menstrual history, and symptoms affect the likelihood of menopause.
2. Take into account additional causes of symptoms, particularly in women with regular cycles, such as thyroid disease, depression, excessive alcohol usage, etc.
3. If the history suggests it, rule out other secondary amenorrhoea causes, such as pregnancy, hyperprolactinemia, hypopituitarism, etc.
4. When necessary, measure serum FSH and LH levels. For accurate interpretation with regular cycles, measure in the jollicular phase, days 1–7 (FSH is elevated in the mid-cycle surge; progesterone and inhibin in the luteal phase lower FSH).

HORMONE REPLACEMENT THERAPY:

Indications for HRT: possible long-term risks andbenefits

Menopausal symptoms were initially treated with oestrogens alone (unopposed therapy). The formulations of HRT that are currently available have changed, including the addition of progestogens (combined therapy), and the indications for prescribing treatment have been expanded as a result of long-term monitoring of the advantages, side effects, and adverse effects of unopposed therapy.[55]

The most recent licenced justifications for prescribing HRT. The effectiveness of prescribing HRT as a public health measure to prevent osteoporosis and ensuing fractures is now being investigated**,** and it may not be as beneficial as originally thought (see Law et al. for discussion').[57]

Formulations and pharmacologicaleffects of HRT

The structural formulae of various oestrogens, both natural and manufactured.Oestrogens can be administered orally, transdermally (in the form of "patches"), or by subcutaneous implants. There are many oestrogen doses available for each formulation of unopposed oestrogen.

All delivery methods are successful in reducing menopausal symptoms. A list of the oestrogenic substances utilised in HRT and primary circulating products. Transdermal preparations lack complete data on bone protection.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

Natural progestogens are quickly rendered inactive when taken orally due to liver and intestinal metabolism. Therefore, synthetic derivatives that differ in their affinity for various steroid receptors and side effect profile have been employed. Norethisterone and norgestrel, which are produced from testosterone, have modest androgenic adverse effects that include lowering HDL cholesterol and triglycerides. They don't have androgenic effects because they are progesterone-derived (medroxyprogesterone acetate, cyproterone acetate).

The withdrawal bleeding that follow from taking combined HRT in its present formulations are the biggest complaint from women who are administered it. Therefore, efforts have been made to prevent this. To stop endometrial growth, oestrogen and a progestogen are continuously administered in place of cyclical progesterone therapy. Amenorrhoea with endometrial atrophy affect about 60070 people. Some people experience unacceptably erratic bleeding. Therefore, some patients may experience greater patient compliance as a result of this kind of preparation.

Limitations of hormone measurements in patientsreceiving HRT

For a number of reasons, biochemical monitoring of hormone replacement is not widely used. Drug dosages that relieve patients' symptoms and stop menopausal bone loss have been developed. In contrast to thyroxine, the dose is not intended to provide physiological replacement, and neither oral nor topical oestrogens lower serum gonadotrophin levels in the premenopausal range. [76,79]

There are no reference values for advice, although extremely high gonadotrophin concentrations may indicate non-compliance, malabsorption, or accelerated metabolism for oral HRT administered at the highest dose. In general, when receiving treatment for symptom relief, patients should be observed for changes in their clinical response. A dosage of a formulation that has been proven to protect bone should be administered for osteoporosis prevention.

Monitoring HRT and indications for endocrineassessment

Pre-treatment: Where eligible for the national breast screening programme or where there are risk factors, a "well woman" checkup with weight, blood pressure, urinalysis, breast and pelvic exams, and mammography is advised.

Regarding the process of treatment: To evaluate clinical efficacy and adverse effects, a 3-month follow-up is advised. A 6-month evaluation is then advised. At every consultation, the lipid profile can be examined and the proper advise given if there are any concerns.

Future trends: optimization of HRT to preventosteoporosis

There is proof that the perimenopause is when bone resorption begins to rise. In one study, perimenopausal women who had a follicular phase FSH > 12 U/L had significantly poorer

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

bone density in the lumbar spine and femoral neck compared to women in the 35–50 age range who had an FSH 12 U/L,92.

CONCLUSION:

There are significant, regular changes in the levels of circulating reproductive hormones during a typical menstrual cycle. Ovulatory cycle frequency decreases and this dynamic system is subjected to additional noticeable change throughout the menopausal transition. Serum hormone measurements offer a "picture" of the pituitaryovarian axis, but this image must be treated with caution because the perimenopause is a highly unpredictable period. The perimenopause may typically be identified clinically in women, and routine biochemical testing of women over 45 with oligo/amenorrhoea should be discouraged because the results will not significantly increase the certainty of the diagnosis of the perimenopause in this age range. Since other disorders are more likely in younger women with menstruation irregularity, biochemical analysis is useful in verifying the clinical diagnosis.

If a woman is amenorrheic or the blood sample was drawn during menstruation (days 1–7 of the cycle), when FSH secretion is most sensitive to deteriorating ovarian function, the results of FSH and LH tests are easier to interpret. Although the frequency of this is unknown for samples acquired during the follicular phase of the cycle, normal menstrual FSH concentrations can occur during the menopausal transition. Therefore, the FSH result should be carefully interpreted in light of the patient's age, menstrual history, and symptoms. In younger women with premature ovarian failure, serum oestradiol levels may be helpful in identifying remaining follicular activity and, consequently, a chance of regaining fertility. With the exception of serum oestradiol tests to evaluate the effectiveness of oestrogen implants in patients with recurring menopausal symptoms, measuring reproductive hormones in women using HRT currently has a limited purpose.

REFERENCES:

1. Report of a WHO Scientific Group. Research on the menopause. In: WHO Technical Report, Series 670. Geneva: WHO, 1981
2. Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. Int J Fertill967; 12: 77-126
3. Khaw KT. Epidemiology of the menopause. Br Med Bull 1992; 48: 249-61
4. Richardson Sl, Nelson IF. Follicular depletion during the menopausal transition. Ann NYA cad Sci 1990; 592: 13-20
5. Sturdee D, Brincat M. The hot flush. In: StuddlW, Whitehead MI, eds. The Menopause. Oxford: Blackwell Scientific Publications, 1988: 24-42

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

6. Caspar RF, Yen SSC. Menopausal flushes: effect of pituitary gonadotrophin desensitization by a potent lutenizing hormone-releasing factor agonist. J ClinEndocrinolMetab 1981; 53: 1056-8

7. Compston IE. HRT and osteoporosis. Br Med Bull 1992; 48: 309-44

8. Lindsay R, Aitken 1M, Anderson IB, Hart DM, MacDonald EB, Clark AC. Longterm prevention of postmenopausal osteoporosis by oestrogen. Lancet 1976; i: 1038-41

9. Rosenberg L, Hennekens CH, Rosner B. Early menopause and the risk of myocardial infarction. Am J ObstetGynecol 1981; 139: 47-51

10. Matthews RA, Meilahn E, Kuller LH, Kelsey SF, Caggiu1aAW, Wing RR. Menopause and risk factors for coronary heart disease. N Engl J Med 1989; 321: 641-6

11. Colditz GA, Willett WC, Stampfer Ml, Rosner B, Speizer FE, Hennekens CH. Menopause and the risk of coronary heart disease in women. N Engl J Med 1987; 316: 1105-10

12. L'Hermite M. Risks of estrogens and progestogens. Maturitas 1990; 12: 215-46

13. Rannevik GK, CarlstromSl, leppsson S, Bjerre B, Svanberg L. A prospective long-term study in women from pre-menopause to post-menopause: Changing profiles of gonadotropins, oestrogens and androgens. Maturitas 1986; 8: 297-307

14. Sherman BM, West IH, Korenman SG. The menopausal transition: analysis of LH, FSH, oestradiol and progesterone concentrations during menstrual cycles of older women. J ClinEndocrinolMetab 1976; 42: 629-36

15. Metcalf MG, Donald RA, Livesey IH. Pituitary ovarian function in normal women during the menopausal transition. Clin Endocrinol1981; 14: 245-55

16. Metcalf MG, Donald RA, LiveseylH. Pituitaryovarian function before, during and after the menopause: a longitudinal study. ClinEndocrinoi 1982;

17. Metcalf MG. The approach of menopause: a New Zealand study. N Z Med J 1988; 101: 103-6

18. Lenton EA, Sexton L, Lee S, Cooke 1D. Progressive changes in LH and FSH and LH: FSH ratio in women throughout reproductive life. Maturitas 1988; 10: 35-43

19. Ushiroyama T, Yoshikawa M, Saeki M, Okuda K, Sugimoto O. Hypergonadotropinemia with oestradiol secretion in peri- and postmenopausal period. ActaObstetGynecolScand 1989; 68:139-43

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

20. Lee Sl, Lenton EA, Sexton L, Cooke ID. The effect of age on the cyclical patterns of plasma LH, FSH, oestradiol and progesterone in women with regular menstrual cycles. Hum Reprod 1988; 3: 851-5

21. Chakravarti S, Collins WP, Thom MH, StuddlWW. Relation between plasma hormone profiles, symptoms, and response to oestrogen treatment in women approaching the menopause. BMJ 1979; i: 983-5

22. MacNaughton 1, Banah M, McCloud P, Hee 1, Burger H. Age related changes in follicle stimulating hormone, luteinizing hormone, oestradiol and immunoreactiveinhibin in women of reproductive age. ClinEndocrinol 1992; 36: 339-45

23. Burger HG, Igarashi M. Inhibin: Definition and nomenclature, including related substances. J ClinEndocrinolMetab 1988; 66: 885-6

24. Sherman BM, Korenman SG. Hormonal characteristics of the human menstrual cycle throughout reproductive life. J Clin Invest 1975; 55: 669-706

25. Van look PFA, Lothian H, Hunter WM, Michie EA, Baird DT. Hypothaiamic-pituitary-ovarian function in perimenopausal women. ClinEndocrinol 1977; 7: 13-31

26. Scott RT, Toner lP, MuasherSl, Oehninger S, Robinson S, Rosenwaks Z. Follicle stimulating hormone levels on cycle day 3 are predictive of in vitro fertilisation outcome. FertilSteril 1989; 51: 651-4

27. Khalifa E, Toner lP, MuasherSl, Acosta AA. Significance of basal follicle stimulating hormone levels in women with one ovary in a program of in vitro fertilisation. FertilSteril 1992; 57: 835-9

28. Kaufert PA, Gilbert P, Tate R. Defining menopausal status: the impact of longitudinal data. Maturitas 1987; 9: 217-26

29. Yen SSC, Llerena 0, Pearson OH, Littel AS. Disappearance rates of endogenous folliclestimulating hormone in serum following surgical hypophysectomy in man. J ClinEndocrinolMetab 1970; 30: 325

30. Trevoux R, DeBrux 1, Castavier M, Nahoul K, Soule lP, Scholler R. Endometrium and plasma hormone profile in the peri-menopause and post-menopause. Maturitas 1986; 8: 309-26

31. Chakravarti S, Collins WP, Forecast lD, Newton lR, Dram DH, StuddlWW. Hormone profiles after the menopause. BMJ 1976; 2: 784-6

32. Woolf PD, Hamil RW, McDonald rv, Lee LA, Kelly M. Transient hypogonadotropic hypogonadism caused by critical illness. J ClinEndocrinolMetab 1985; 60: 444-50

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved,** **UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

33. Quint AR, Kaiser FE. Gonadotrophin determinations and thyrotropin-releasing hormone and luteinizing hormone-releasing hormone testing in critically ill post-menopausal women with hypothyroxinemia. J ClinEndocrinolMetab 1985; 60: 464-71

34. Gosden RG. In: Biology of Menopause. London: Academic Press, 1985: 27-33

35. Longcope C. Hormone dynamics of the menopause. Ann NY AcadSci 1990; 592: 21-30

36. Judd HL, Shamonki 1M, Frumar AM, Lagasse LD. Origin of serum oestradiol in postmenopausal women. ObstetGynecol 1982; 59: 680-6

37. Longcope C, Hui SL, lohnston CC. Free oestradiol, free testosterone, and sex hormone binding globulin in perimenopausal women. J ClinEndocrinolMetab 1987; 64: 513-18

38. Chang RJ, ludd HL. The ovary after the menopause. ClinObstetGynecol 1981; 24: 181

39. Moraes MDE, lones GS. Premature ovarian failure. FertilSteril 1967; 18: 440-61

40. Ribot C, Pouilles 1M, Bonneu M, Tremollieres F. Assessment of the risk of postmenopausal osteoporosis using clinical factors. ClinEndocrinol 1992; 36: 225-8

41. Rebar RW. Hypergonadotropic amenorrhoea and premature ovarian failure. A review, J Reprod Med 1982; 27: 179-86

42. Siddle NC, Sarrell P, Whitehead Ml. The effect of hysterectomy on the age of ovarian failure: identification of a subgroup of women with premature loss of ovarian function and literature review. FertilSteril 1987; 47: 94-100

43. Metcalf MG, Braiden V, LiveseylH. Retention of normal ovarian function after hysterectomy. J Endocrinol 1992; 135: 597-602

44. Beastall GH, Ferguson KM, O'Reilly DStJ, Seth 1, Sheridan B. Assays for follicle stimulating hormone and luteinising hormone: guidelines for the provision of a clinical biochemistry service. Ann ClinBiochem 1987; 24: 246-62

45. Marsh MS, Whitehead Ml. Management of the menopause. Br Med Bull 1992; 48: 426-57

46. O'Herlihy C, Pepperell Rl, Evans lH. The significance of FSH elevation in young women with disorders of ovulation. BMJ 1980; 281: 1447-50

47. Cohen BL, Katz M. Further studies on pituitary and ovarian function in women receiving hormonal contraception. Contraception 1981; 24: 159-73

48. lung Hoffman C, Heidt F, Khul H. Effect of two oral contraceptives containing 30 microgram ethinyloestradiol and 75 microgram oestrogene or 150 microgram desogestrel upon various hormonal parameters. Contraception 1988; 38: 593-603

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

49. Von Schoultz B. Potency of different oestrogen preparations. In: StuddlW, Whitehead MI, eds. The Menopause. Oxford: Blackwell Scientific Publications, 1988: 130-7

50. Whitehead MI, Godfree V. In: Hormone Replacement Therapy: Your Questions Answered. Edinburgh: Churchill Livingstone, 1992: 217-18

51. Burgay GT, Vessey MP, McPherson CK. Study of symptoms in middle life with special reference to the menopause. BMJ 1980; ii: 181-3

52. McKinlay SM, Jeffreys M. The menopausal syndrome. Br J Prey Soc Med 1974; 28: 108-15

53. Robinson S, Rodin DA, Deacon A, Wheeler MJ, Clayton RN. Which hormone tests for the diagnosis of polycystic ovary syndrome? Br J ObstetGynaecol 1992; 99: 232-8

54. Zakut H, Zer J, Bernstein D. A new biological carrier for follicle stimulating hormone: an aid for the diagnosis of menopause. GynecolEndocrinol 1987; i: 263-8

55. BMA. Sex Hormones (Section 6.4). In: British National Formulary. London: British Medical Association and The Pharmaceutical Press, 1992: 267-73

56. Naessen T, Persson I, Adami HO, Bergstrom R, Bergkvist L. Hormone replacement therapy and the risk for first hip fracture. A prospective, populationbased cohort study. Ann Intern Med 1990; 113: 95-103

57. Law MR, Wald NJ, Meade TW. Strategies for prevention of osteoporosis and hip fracture. BMJ 1991; 303: 453-9

58. Stampfer MJ, Willett WC, Colditz GA, Rosner B, Speizer FE, Hannekens CH. A prospective study of postmenopausal estrogen therapy and coronary heart disease. N Engl J Med 1985; 313: 1044-9

59. Bush TL, Barrett-Conner E, Cowan LD, Criqui MH, Wallace RB, Suchindran CM, et al. Cardiovascular mortality and non-contraceptive use of estrogen in women: results from the Lipid Research Clinics programme follow-up study. Circulation 1987; 75: 1102-9

60. Hunt K, Vessey M. The risks and benefits of hormone replacement therapy: an updated review. CurrObstetGyneco/1991; 1: 21-7

61. Beaglehole R. Oestrogens and cardiovascular disease. BMJ 1988; 297: 571-2

62. Paterson M. A randomised double-blind cross-over trial into the effect of norethisterone on climacteric symptoms and biochemical profiles. Br J ObstetGynaecol 1982; 89: 464-72

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

63. Hunt K, Vessey M, McPherson K, Coleman, M. Long-term surveillance of mortality and cancer incidence in women receiving hormone replacement therapy. Br J ObstetGynaecol 1987; 94: 620-35

64. Smith DC, Prentice R, Thompson DJ, Herrmann W. Association of exogenous estrogen and endometrial cancer. N Engl J Med 1975; 293: 1164-7

65. Padwick ML, Pryse-Davies J, Whitehead MI. A simple method for determining the optimal dosage of progestin in post-menopausal women receiving estrogens. N Engl J Med 1986; 315: 930-4

66. Whitehead MI, Lobo RA. Progestogen use in postmenopausal women. Lancet 1988; ii: 1243-4

67. Whitehead MI, Hillard TC, Crook D. The role and use of progestogens, ObstetGynecol 1990; 75: 59S-76S

68. Grady D, Ernster V. Invited commentary: does postmenopausal hormone therapy cause breast cancer? Am J Epidemiol 1991; 134: 1396-400

69. Whitehead MI, Fraser D. Controversies concerningthe safety of estrogen replacement therapy. Am JObstetGynecol 1987; 156: 1313-22.