Psychiatric Disorders in the Perimenopause

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Abstract

Menopause is a daunting time in a women's life. In the medical literature, Menopause has been regularly referred to as a deficiency state and a condition to be actively medically managed. Perimenopause is defined by the WHO as the 2–8 years preceding menopause and the 1-year period after final menses, resulting from the loss of follicular activity. Perimenopause includes the period immediately prior to menopause and the first year after the final menstrual period (FMP). At this stage, the ovaries become resistant to the stimulatory effects of the pituitary gonadotropins luteinizing hormone (LH) and follicle stimulating hormone (FSH). Women, during the perimenopause often have irregular menses, heavier and longer menstrual periods and prolonged episodes of amenorrhea. In addition, the perimenopause is marked by vasomotor symptoms. There is undoubtedly a large group of women who experience psychological distress that coincides with the hormonal function of the climacteric, as demonstrated by the large population of women reporting psychological complaints at menopause clinics. Results from a multiethnic community based cohort study of premenopausal and perimenopausal women showed that mood symptoms and irritability are more likely to occur in perimenopausal than the premenopausal women. Recent epidemiologic studies have also documented an increased risk of first onset and recurrent major and minor depressions during the perimenopause as compared with the premenopause. This review paper is an attempt to highlight the problems of women in perimenopause and factors contributing to psychiatric morbidity during this time.

Keywords: Menopause; Perimenopause; Depression; Psychiatric morbidity.

Introduction

Being a woman is special. Menarche, pregnancy, labour, motherhood and menopause are the series of transitions that every women undergoes from her birth until death. The above mentioned stages stand for different stages in her life which involves both physical and psychological changes. Menopause is considered a natural part of aging by most women although many are bothered by menopausal symptoms and very few women seek treatment.[1]

For many decades' women's health has been a global concern. As compared to men women have a more complex and stressful aging process, a consequence of hormonal changes which occur during

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the menopausal transition. The menopausal transition marks the end of women's reproductive function. It also makes them susceptible to various health problems such as cardiovascular diseases, osteoporosis and so on. [1] Though the vulnerability of middle aged women to major depression may be a myth, accumulating data suggests that the perimenopause is a period of increased risk for minor, but potentially impairing, depressive symptoms. [3] In both community- and clinic-based studies "psychological distress" or depressive symptoms are reported by perimenopausal women significantly more than either premenopausal or postmenopausal women. [3]

Majority of studies on perimenopausal women, despite wide variations in methodology, report some degrees of depression among subjects, indicating an increased susceptibility to depression during the perimenopause. This susceptibility has been ascribed to the effects of declining estrogen levels, subjective experience of somatic symptoms due to reduced hormonal levels, and/or the more frequent "exit" or "loss" events occurring during this stage of life.[4] In India the number of menopausal women is increasing as a consequence of increased life expectancy. Therefore, there is an urgent need to clear misconceptions and to increase awareness about menopause. This will also encourage affected women to seek medical treatment if warranted.[5]

Definitions

Menopause which means cessation of menses is derived from Greek "meno" which means "month or menses", and "pausis" which means "pause". In 1821 the French physician Gardanne invented the term menopause. The term gradually came into wide circulation in medical circles in Europe by the middle of the 19th century. [6] Before the 1980's problems related to menopause were given scant attention. 'Research on the Menopause' a 1981 publication of the World Health Organization (WHO) highlighted the paucity of data on the age distribution of the menopause and its socio-cultural significance in the developing countries.[7] Perimenopause is defined as the 2–8 years preceding and the 1-year period after menopause, resulting from the loss of follicular activity.[8] The initiation of perimenopause is characterized by intense biological variability secondary to endocrinological and clinical changes.[9] The timing of menopause may be influenced by different factors such as living at high altitudes, cigarette smoking and history of depression. [9]

The Biopsychosocial Contexts of Midlife Women

A woman's understanding of menopause is defined by the psychological, cultural and social setting in which she lives; her expectancies; and the reactions of significant otehrs in her life.[10]The experience of menopause by a women is largely shaped by social, psychological and cultural context in which she lives.

The Medical Context: In the medical literature, menopause has been regularly referred to as a state of deficiency and a condition to be actively medically managed.[10]

The Sexual Context: Outlook to midlife female sexuality have gathered at two opposing poles. One view is that due to loss of fertility women to lose their sexuality as well; they are neither sexually interested nor sexually attractive. The other view claims that females are sexual through midlife and until death.[10] The refusal to recognize or accept sexuality throughout the life span has deprived us of accurate information about women's feelings and behaviours.[11] It prevents middle aged women consulting doctors about their sexual problems.

The Psychosocial Context: The roles of perimenopausal women in society have changed drastically over recent decades. Many middle ages women are caregivers for their growing children and elderly relatives. More often than not women are the primary caregivers for family members, including their spouses, than are men. These women have a high incidence of depression. [10]

The Cultural Context: The meaning of menopause varies from subculture to subculture and family to family. The timing, nature, severity, and presumed importance of menopausal symptoms vary as well.[12] The experience of menopausal symptoms is closely related to a woman's expectations of symptoms.[10] Some cultures honour traditions in which women gain respect and support as they age, while in others females are side-lined as they age. In cultures where traditional ideas are denigrated in favour of newer lifestyles, older women are perceived as irrelevant, if not burdensome.[10]

The Context of Body Image: Dissatisfaction with their bodies is present in many women. There are opposing forces affecting the midlife women's body image. One is a preoccupation with decline and a dread of the loss of the youthful appearance that is synonymous with femininity.[10] The other is a newfound sense of acceptance of one's body and freedom from the need to follow accepted benchmarks of appearance.[10]

Age and Onset of Perimenopause

Best available data on the age at onset of perimenopause comes from the Study of Women's Health Across the Nation (SWAN), based on 16,063 and 3,306 multi-ethnic women in a cross-sectional study and longitudinal study respectively, and the Massachusetts Women's Health Study (MWHS), a 5-year prospective, longitudinal, population-based study of 2,570 women.[12,13, 14]

In the perimenopausal period women often have heavier and longer menstrual periods, irregular menses, and prolonged periods of amenorrhea, VMS, decreased fertility, changes in sexual function, insomnia, and psychological changes. [13] The perimenopausal transition begins about 4 years before the FMP. The median age at onset of perimenopause and menopause is 47.5 years and 51.3 years (range: 47–55 years) respectively.[13]

Earlier natural menopause is associated with a history of heart disease; lower educational attainment; non-employment; and being separated, widowed, or divorced.[13] Dysfunction of the hypothalamic-pituitary-ovarian axis and an earlier decline of ovarian function is seen in women with longstanding depression as compared with women who are not depressed.[15]Women who are malnourished, thinner or vegetarians experience an earlier menopause. Women who are regular consumers of alcohol have a delayed menopause as a result of higher levels of estrogen. Prior use of oral contraceptives, parity and Japanese ethnicity are also associated with later age of natural menopause.[16]

Culture & Menopause

Many women during perimenopause suffer from palpitations, hot flushes, vertigo, decrease in concentration, arthralgia which may be related not only the effect of decreasing levels of ovarian steroids but also changes in the social environment and cultural influences. Reviewing research among women in other societies Banger noted that the Rajput caste of women in India and Bantu women in South Africa attain a higher social position with more freedom on entering menopause. Such women complain of very few symptoms. [17.] Chinese and Japanese women report far fewer symptoms during the climacteric.[18,19] In societies which view menopause as a positive and not a negative event probably menopausal symptoms are less.[17]

Culture and Menopause: Definitions, Attitudes and Expectations.

The meaning of menopause varies greatly across cultures. In non-Western cultures menopause is often viewed more positively, in which menopause removes constraints and prohibitions imposed upon menstruating women.[20] Perceptions, expectations and attitudes are part of the psychosocial phenomena surrounding menopause.[20] Studies which have looked at how women's attitudes toward menopause change as they experience menopause, consistently show that attitudes towards menopause are much more positive among postmenopausal women as compared to premenopausal women.[20]

Endocrinology of the Menopausal Transition

Changes in the ratio and concentration of the reproductive hormones begin many years before menopause.[13] Smoking, [21] low socioeconomic status,[22] ionizing radiation, medically treated depression, [15] and possibly galactose consumption[23] reduce the reproductive life span of women. In addition, as women age, their menstrual cycles increase in length, become more irregular (menstrual cycles are most regular during middle reproductive life), and are often anovulatory.[13]

Rising concentration of FSH and a declining concentration of inhibin B is the first detectable hormonal change of the perimenopause.[13] In the early perimenopausal phase, the concentration of LH remains in the normal range while FSH is increasing and inhibin B is decreasing.[13]Late in the perimenopause, LH concentrations increase slightly but at a slower rate than those of FSH. Concentrations of LH, FSH and decreased concentrations of estradiol and progesterone can be detected before ovarian function ceases permanently.[13]

Progesterone appears to have a negative effect on mood, mainly as a result of the occurrence of increased irritability and dysphoria; however, hypnotic, anxiolytic, and antiepileptic effects have also been described.[24] It has become increasingly evident that gonadal steroid hormones, such as progesterone, affect not only the hypothalamus but also the hippocampus and cortex.[25] Estrogen acts in concert with progesterone to regulate multiple brain functions, such as cognition and neuroprotection.[25]

Psychiatric Morbidity Associated With Perimenopause:

During perimenopause there is a significant increase in mood lability for women. The majority of research conducted on perimenopausal mental disorders has focused on unipolar depression, while some evidence points toward an exacerbation of bipolar mood symptoms and an increase in

schizophrenic psychosis during perimenopause.[4] Increased susceptibility may be due to the subjective experience of somatic symptoms resulting from this hormonal decline, neuroendocrine effects of declining estrogen levels, and/or the more frequent occurrence of "exit" or "loss" events for females during this period.[4] Other factors contributing to psychiatric morbidity in women entering perimenopause may be facing additional stress from dealing with adolescents, caring for an aging parent, onset of a major illness, career change, divorce or widowhood, or retirement.

Mood Disturbances

Menopause fosters a unique biopsychosocial challenge. This phase of life does not necessarily herald depression but studies have identified the occurrence of irritability, poor mood and other depressive symptoms, and anxiety disorders are seen in some women.[26]

Prior depression and sensitivity to premenstrual and postpartum changes are possible risk factor. Sociocultural connotations, and not menopause itself, may be a direct cause of psychiatric symptoms. Lower education and socioeconomic status, role changes, stressors of aging may contribute to increased symptoms.[26] Depressive disorders and symptoms are frequent over a lifetime, especially in the middle-aged.[27]Major depression& minor depression are two very important sources of incapacity in developed countries. There is an 8% to 40% rate of depressive symptoms in middle-aged women. [27] Women are at higher risk for depression at specific points in their life when reproductive hormones fluctuate: in puberty, when estrogen is first rising; in the premenstrual phase; in pregnancy or the postpartum period and/or during the perimenopause [28] Some of the women are at greater risk than others, including midlife women with a history of depression, premenstrual syndrome, or postpartum depression.

However, even a woman with no history of depression is almost twice as likely to experience an onset of MDD when she enters perimenopause as women of the same age who remain premenopausal.[28] The high level of symptom overlap between perimenopausal symptoms and depression confounds the diagnosis of perimenopausal MDD.[28]

Genetic factors

It is likely that the genetic factors interact with the environment so that perimenopausal depression occurs in some women and not in others. It has been reported that women as compared to women who have the long allele those who have a short allele (SS) of the cytosine-adenine repeat polymorphism of the estrogen receptor-beta gene have a seven times greater risk of vasomotor symptoms and 13 times greater one of psychological symptoms.[27]

Possible Mechanisms Underlying Mood Disorders Associated with the Perimenopause :

The "domino theory" proposes that discomfort caused by somatic symptoms of the perimenopause provokes physical changes, which, in turn, affect mood stability.[29] Vasomotor symptoms (VMS) such as hot flushes and night sweats leads to sleep disturbance and an increasing level of irritability and fatigue.[29] The decrease in estrogen levels could also contribute to mood changes by affecting neuronal function (Estrogen withdrawal theory)[29] Neuronal function is impacted by estrogen through the serotonergic, dopaminergic, noradrenergic, cholinergic systems and γ-amino buytric acid.[29] Women with first onset depression during the perimenopause, do not show differences in in basal levels of gonadotropins, estrogens or testosterone. [30] This indicated that hormonal deficiency may not be the cause of perimenopausal depression.[29]

Risk Factors for the Development of Mood Disorders During the Perimenopause

The MWHS which included women on hormonal replacement therapy (HRT), reported that a long perimenopausal period of at least 27 months was linked to an increased risk of depression.[29, 31] Thus the menopausal period, especially if it is prolonged, may be associated with an increased susceptibility for depression.[29]

Bipolar Mood Disorder

The menopause may improve, aggravate, or not affect the course of affective symptoms in women with bipolar disorder.[32] One study of postmenopausal women with bipolar disorder reported that 20% of patients suffered severe emotional disturbances during perimenopause.[33]

Anxiety

Studies of anxiety symptoms or distress in menopausal transition have reported inconsistent results which are similar to studies of depressive symptoms and the menopausal transition. Most of these studies failed to use standard scales assessment of anxiety and anxiety symptoms as part of symptom checklists to study perimenopausal symptoms.[34]

Symptoms vary from study to study and reflect those symptoms characterizing generalized anxiety, social phobia or panic disorder.[34]

Sexual Dysfunction

Women in perimenopause, approximately 10–15% report no sexual desire and less than 5% report never, or almost never, experiencing arousal; about 20% report occasional and 5% frequenct dyspareunia.[35]

Non-hormonal factors contributing to sexual difficulties

In midlife women who are highly educated, in a significant relationship, having depression, experiencing poor personal health, having concurrent urinary incontinence or who have a past history of sexual abuse; sexual difficulties are more commonly seen.For some women, home, work or relationship stress may be a factor.[35]Other causes related to sexual impairment during the perimenopause may be economic problems, bereavements, children leaving home, retirement, divorce and personal illness, or illness of their partner or close relative.Loss of self-esteem and poor body image due to weight gain can contribute to a woman's reluctance to engage in sexual activity.[35]

Hormonal factors influencing sexual function

The hormonal changes in perimenopause adversely affect the woman's sexual interest and capacity to become aroused and/or achieve orgasm.[35] Women often complain of the vaginal dryness in relation to sexual activity during the perimenopause. This is a result of failure to be aroused and lubricate and probably not due to oestrogen insufficiency. There is a precipitous fall in oestrogen levels following menopause, but testosterone levels fall gradually from the mid reproductive years. Treatment of women in late reproductive period with testosterone resulted in increased arousal and vaginal lubrication. However, such studies have not been conducted in perimenopausal women.[35]

Schizophrenia

In women, late-onset psychosis is much more prevalent than in men for reasons that are imperfectly understood.[36] Women, to some degree are protected against schizophrenia by their relatively high gonadal estrogen production between puberty and menopause, according to the estrogen hypothesis. With the onset of perimenopause and reduced oestrogen levels, women lose this protection. This explains their second peak of illness onset after age of 45.[36] Epidemiologic studies showing a second peak of schizophrenia onset in women around the age of menopause support this hypothesis.[36]

Cognitive Dysfunction

KIWI (Kinmen Women-Health Investigation) and SWAN are the only published longitudinal studies assessing cognitive performance during perimenopause. They did not find reduction in test scores during yearly measurements.[37.] However, cognitive functions may be affected by the increases in depressive and anxiety symptoms that may accompany perimenopause. Decline in estradiol level may stem directly long term cognitive consequences of perimenopause. Estrogen protects against cognitive decline following cholinergic reduction in middle aged women. Studies suggest that at midlife, the loss of estrogen results in changes in serotonergic and cholinergic function which in turn contribute to mood problems and cognitive deficit.[37]

Eating Disorders

In middle and late life eating disorders are getting more common but frequently go unrecognized. Restrictive dieting significant weight loss, preoccuation with body image and purging behaviours, such as utilizing appetite suppressants or drugs of abuse, excessive exercise, may herald overt or subclinical eating disorder in middle-aged or elderly patients.[38.]

Drive for thinness and excessive dieting may be the harbinger of an eating disorder in the older woman. Significant weight loss may often present itself in clinical depressed patients. Both anorexic patients and depressed patients complain of having poor concentration, memory difficulties, anhedonia, low energy and other preoccupations[38] Comprehensive physical examination in all eating disorder patients who present in middle or later life should be done to rule out physiological problems associated with the eating disorder (e.g. electrolyte imbalance, pancreatitis). Diabetes mellitus, substance abuse, malignancy and infection must all be ruled out as a cause of weight loss and/or appetite disturbance.[38]

Sleep Disturbances

Initial insomnia is a major symptom of menopause. During menopause 25% to 50% of women report sleep disturbances. Arousals and disruption of sleep architecture is associated with VMS.

Insomnia and Depression

Mood disorders are associated with menopause. Sleep disruption has been associated with depression. The "domino" theory of sleep disruption proposes that sleep is disturbed by hot flashes or other menopause related reasons which results in insomnia and subsequently depression.[39] Hot flashes themselves could result in sleep disruption, an increased sensitivity to disrupting events or a loss of some other sleep maintaining quality of estrogen. The disruptions then can create insomnia.[39]

Sleep Disordered Breathing and Menopause

Women have approximately 1/3 the frequency of sleep disordered breathing than men prior to menopause. Shortly after menopause this disparity drops for unclear reasons. Weight gain is common during menopause which leads to associated concomitant increase in neck circumference which adds to the development OSA.[39]

Other Sleep Disorders and Menopause

The most significant sleep related disorders that are directly associated with menopause are insomnia, depression, sleep disordered breathing, however, other sleep disorders that may be affected secondarily. Restless legs syndrome (RLS) is not directly correlated with menopause, although the frequency of this disorder increases with age which very common and often is under-recognized for many years by the patient and physician. With the onset of menopause associated sleep disruption, a pre-existing disorder may become more evident.[39] In the perimenopausal period the loss of sleep efficiency and insomnia worsens pre-existing sleep problems. Phase delay or inadequate sleep syndrome patients may therefore suddenly seek out treatment or evaluation as part of the menopause transition.[39] Due to social or work requirements phase delay may be associated with inadequate sleep. With onset of menopause related insomnia and loss of sleep efficiency there may be exacerbation of pre-existing sleep inadequacies which results in patients need for more time in bed to attain restorative sleep.[39]

Factors Associated with Psychiatric Morbidity

Although psychiatric morbidity encompasses multiple symptoms and disorders, individual studies typically focus on specific symptoms or disorders as outcomes. Variation in results may be due to differences in measures used to assess various outcomes.

Socio-demographic Factors

Studies have indicated that in midlife women, higher risk for depressive and anxious symptoms is seen in women who are separated, widowed, or divorced and single as compared to women high school education or less, or financial strain.[34,40]

Life Stressors

Psychosocial stress is referred to as environmental demands that tax or exceeds the resources of the individual.[79]Studies have reported inconsistent findings with respect to whether number of stressful events varies during menopausal transition and whether this may account for differences in rates of depression during menopausal transition. Stressful events may provoke depressive episodes but large majority of individuals who experience stressful situations or events do not become significantly depressed. A range of individual and social factors may explain differences in response to stress.[34]

Social Relations

Inadequate social support among midlife women may be associated with depression, anxiety, and negative mood and in some cases, the association is independent of other relevant factors such as stressful life events.[34]

Vasomotor Symptoms

The most prevalent symptoms during the menopausal transition and early postmenopause are hot flushes and night sweats which are consistently associated with negative mood symptoms.[40,41] which may affect quality of life among women with VMS.

The associations between negative mood symptoms and physical symptoms, including hot flushes and pain, for example, are bidirectional.[34] Negative affect can influence perception and reporting of physical symptoms and as noted above, the latter can lead to depressed and anxious symptoms and disorder.[34] The longitudinal studies of menopause and some preclinical studies suggest that anxious and depressive symptoms may induce disturbing or frequent vasomotor symptoms in some women.[34]

Health Behaviours, Physical Symptoms and Conditions

High-risk health behaviours during midlife, like smoking, poor diet, inactivity, disturbed sleep and lack of adherence to medical regimens are often associated with depression and anxiety. Medical

illnesses including arthritis, diabetes and cardiovascular conditions are also associated with depression and anxiety disorders. Studies have documented significant associations between physical symptoms in midlife women and depressive and anxious symptoms) [34,41]

Psychiatric History

A past history of psychiatric disorders is the best predictor of psychiatric disorders during perimenopause.[34,42] Prospective studies of middle-aged premenopausal and early perimenopausal women have found that a history of an anxiety disorder or depressive disorder was a significant predictor of incident major depression, stressful events, and role functioning.[43]

Conclusion

Perimenopause is the period preceding and following menopause. The gradual decline in estrogen is accompanied by physical symptoms, physiological changes and psychiatric disorders. Studies strongly suggest an association between perimenopause and depression.

There is a need to carry out prospective studies to estimate the temporal association between hormonal changes with physical and mood symptoms during perimenopause.

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