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THE INTERFACE BETWEEN PSYCHIATRY AND WOMEN'S REPRODUCTIVE AND SEXUAL HEALTH

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Respected Chairpersons, Teachers and Colleagues, I thank the Indian Psychiatric Society for giving me the opportunity and honor of delivering this year's Tilak Venkoba Rao Oration.

The topic of today's oration is based on research done by my colleagues and me over the last several years. The canvas of the topic - the interface of psychiatry and women's reproductive health is very wide. It encompasses several areas of study and I have chosen to focus on hormonal and biological variations related to the reproductive cycle, which have an influence on mental health. Wherever relevant, I will also be focusing on psychosocial issues as they relate to reproductive and sexual health in women.

In terms of areas of interface, probably the most important is the influence of reproductive physiology i.e. the menstrual cycle, pregnancy, menopause and the effect of all these three on mood, behaviour and cognition among women with and without psychiatric disorders.

The interface can be broadly divided into three areas

1.The influence of reproductive physiology on mood, behaviour and cognition.
2.The influence of reproductive issues and gonadal hormones on the course of mental illness among women.
3.The impact of major mental illnesses such as schizophrenia and bipolar disorder on reproductive and sexual health issues.
4.Gynecological and reproductive pathology and its relationship to psychiatry.

It is apparent that the areas are very wide and I have chosen to focus on a few of them, based on current areas of study, possibilities of further research and areas of personal interest.

The Menstrual Cycle and Mental Health

The influence of the menstrual cycle can be described under three important headings - the impact of the menstrual cycle on mood, behavior and cognition among normal women; the premenstrual syndrome and subsyndromes and finally, the influence of the menstrual cycle on symptoms among women with severe mental illness.

The PMS and Premenstrual Dysphoric Disorder

The premenstrual syndrome is probably one of the most ill defined syndromes in psychiatry with a lot of sub-syndromes being subsumed under the heading of PMS (Rubinow and Roy-Byrne, 1984; VanDer Akker and Steptoe, 1985). We must recognize that the PMS consists of multiple sub syndromes and one that is particularly relevant to psychiatry is the premenstrual mood disorder otherwise also known as the Late Luteal Phase Dysphoric disorder. The several important methodological issues in the study of PMS include the nature of rating i.e. retrospective or prospective ratings; the need to assess psychopathology in the non-premenstrual phases of the cycle and defining various subsyndromes. It has been concluded that it is important that we do at least prospective ratings for two cycles before we can establish the diagnosis of PMS (Chandra et al., 1994). PMS should not be viewed as a cross-sectional phenomenon as there is enough evidence

to indicate that a large majority of women who have premenstrual mood dysphoric disorder tend to have mood problems in the rest of the menstrual cycle (Yonkers, 1997). Strict criteria have been now established including the DSM IV and the NIMH criteria that focus on the magnitude of the problem by severity assessment and self report of disability (Halbreich et al., 1982; Halbreich et al, 1988).

In an epidemiological study done in Bangalore city which looked at self reports of premenstrual symptoms among 400 normal women i.e. women who did not complain of PMS, some of the commonest reported symptoms were irritability (39 %), sadness (42 %) and mood swings (23 %). A smaller proportion of women also reported feelings of well being in the premenstrual phase, indicating that there might be a sub group of women who have increased positive symptoms in the perimenstrual phase (Chaturvedi et al, 1994).

Severe PMS that was disabling, and resulted in significant occupational and social functioning was observed among 10% of women. Majority of them appeared to have mild symptoms (56 %), while some of them had moderate degree of symptoms (34 %).

A factor analytic study among 112 non-complaining women indicated the presence of four factors - Factor 1 - Negative Mood Changes, Factor 2 - positive mood changes and Well Being, Factor 3 - Water Retention and Libido and Factor 4 - Somatic and Physical changes. These factors are similar to those found by other researchers. In this sample, negative mood changes were seen in 20 % of women, positive changes in 18 % and biphasic changes in 35 %. Positive mood changes have been reported as being commonly found in the premenstrual phase (Chaturvedi et al, 1993; Chaturvedi and Chandra, 1990; Logue and Moos, 1988; Stewart, 1989).

Cognitive Functions Across the menstrual cycle

An important area of research has been the variation of cognitive functions across the menstrual cycle with fairly inconsistent results (Cockerill et al., 1994). Some workers report a high degree of cognitive dysfunction, particularly in memory; new learning and concentration while others have not been able to replicate these findings. The finding that women with PMS seem to have retrieval deficits and problems in new learning has been consistently reported (Keenan et al., 1995). Women without Premenstrual Dysphoric disorder give subjective reports of poor concentration even though objective testing has not substantiated this.

To assess the role of mood and the menstrual cycle phase in normal women we assessed neuropsychological functions in 40 normal women across the premenstrual cycle using a neuropsychological battery. The battery assesses various lobe functions with, higher scores indicating poorer performance. Our findings indicate that women in the premenstrual phase actually seem to do better than women who are in the intermenstrual phase, indicating that normal women may not have cognitive problems in the premenstrual phase.

In addition to cognitive functions, we also assessed anxiety and mood prospectively to discern the relationship of anxiety and mood disturbances to cognitive functions. However this relationship was also not evident from our results. It seems from our research that in normal women cognitive functions do not seem to significantly vary across the menstrual cycle.

Suicide and the Menstrual Cycle

Devi and Rao (1972) analysed 115 cases of attempted suicide and reported that 64 % had made their attempts when in the premenstrual or early menstrual phase. Data from our study indicated premenstrual suicidal ideation in 10 % of 296 women studied. Suicidal ideation was more in younger women and was strongly associated with irritability, mood swings and depression. There was also an association with water retention, which probably has some implication in etiology

(Chaturvedi et al., 1995). We also found that not only the premenstrual phase but also even the menstrual phase seemed to be associated with suicidal ideation.

Mood, Food and the Menstrual Cycle

One area, which has been studied lately, has been the relationship between food, mood and the premenstrual cycle and the role of carbohydrate craving in premenstrual depression. There has been a definite evidence of premenstrual craving that seems to be specific to carbohydrates and has a fairly strong association with premenstrual depression (Bancroft, 1995; Dye et al., 1995).

We studied phase related changes in carbohydrate intake among 40 normal women by rating mood over four phases of the menstrual cycle in the intermenstrual, premenstrual, menstrual and immediate postmenstrual phase by using a food index. The food index evaluated the number of carbohydrate foods that women in our sample consumed. Though not statistically significant, there did seem to be an increase of carbohydrate intake in the premenstrual and menstrual periods compared to the rest of the cycle and this had an association with mood ratings.

Since then much work has been done on the relationship between carbohydrate and premenstrual depression and subjective reports of women who have premenstrual depression. Women have reported an improvement in mood with the consumption of tryptophan containing carbohydrates. There is also experimental evidence in the form of tryptophan free mixtures being given to women who had premenstrual depression and to women in the premenstrual period without premenstrual depression. There was a definite worsening of mood 2 - 3 hours after intake of tryptophan free mixtures among women with premenstrual depression indicating that some association exists between tryptophan containing carbohydrates and regulation of mood, implying an important role of serotonin in premenstrual depression (Menkes et al., 1994).

Can socio-cultural factors actually modify what is otherwise a purely biological phenomenon?

We have looked at the influence of menstrual attitudes and influence of menarcheal experience on the experience of premenstrual distress. Even though it seems clear now that premenstrual dysphoric disorder is definitely a biological phenomenon, there is enough evidence to suggest that many socio-cultural factors might be modifying the perception, the explanation or even help seeking related to it (Chandra and Chaturvedi, 1989; Chandra and Chaturvedi, 1992; Chandra et al., 1995; Johnson, 1987).

Menstrual psychosis

The other area that has been of increasing interest to researchers is that of psychosis occurring exclusively in the premenstrual period. Menstrual psychosis has been classified as - catamenial psychosis i.e. that occuring only during menstruation, the paramenstrual which occurs immediately premenstrual or post menstrual, mid cycle and epochal - i.e. switching of bipolar illness during a specific phase of the cycle (Brockington, 1998). Studies have found a strong association between anovulatory cycles, increasing estradiol levels and menstrual psychosis.

In a prospective study among 12 cases with menstrual psychosis , we found both catamenial and premenstrual psychosis occurring equally. What seems to be interesting however is that subsequent reproductive events seem to be triggers as evidenced by the finding that at one-year follow up, two of these women developed postpartum mania, one developed an independent depressive disorder and one had an abortion related psychosis. Another important finding has been, a strong association of menstrual psychosis with premenstrual migraine, with 75% of the above sample reporting the same.

Premenstrual Depression and Serotonin - the evidence

Several forms of therapy for premenstrual dysphoric disorder have been tried since the early 1970s. These have ranged from progesterone and oral contraceptives to GNRH analogs. However, all these methods of treatment have shown inconsistent results. The bulk of the evidence now seems to be falling on the role of serotonin as evidenced by

a. The association of mood and tryptophan intake in women with premenstrual depression.
b. neuroendocrine challenges i.e. the effect of IV tryptophan on prolactin, GH and cortisol.
c. good response of premenstrual mood disturbances to serotonin modifying drugs.

Majority of the investigations done to study the biology of Premenstrual Dysphoric Disorder involve the serotonergic system. These include measurement of serotonin in whole blood, with symptomatic women having low levels of serotonin, decreased 5HT platelet uptake and blunted prolactin, growth hormone and cortisol response to tryptophan (Bancroft et al, 1991). Menkes et al. (1994) found that depleting the serotonin precursor tryptophan was significantly more likely to provoke premenstrual depression among women with premenstrual dysphoric disorder as compared to asymptomatic controls.

Mental Illness and the Menstrual Cycle

The other area, which has a strong interface, is that of mental illness and the menstrual cycle. In a study on psychiatric admissions related to the menstrual cycle over a two-month period, we assessed all women who were admitted into the hospital either for an emergency or electively. An assessment of the menstrual cycle phase was done in all women. Only women, who had regular cycles, were not on oral contraceptives and who did not have any other gynecological pathology were included. The results indicated a definite increase in the premenstrual admission rates in the emergency group as compared to the elective group but we also found a slight increase in the early luteal phase and some increase in the ovulatory phase (Prema et al., 1991).

Reicher-Rossler (1994) & Kulkarni (1997) have focused on the variation of psychopathology in relation to the menstrual cycle among women with schizophrenia and evidence is now accumulating that there is a premenstrual worsening of psychosis (Thompson et al., 2000). Reicher-Rossler (1994) found a negative correlation between estradiol levels, psychopathology scores, ward behaviour and well being scores indicating an inverse relationship between estradiol levels and severity of psychosis with higher levels of estradiol being associated with less psychopathology and better well being.

PSYCHIATRY OF CHILDBIRTH

I now come to the second area of interface, which is related to psychiatric disorders occurring in the pregnancy and postpartum. Some of the findings reported are from an ongoing collaborative study between NIMHANS, Bangalore and the Queen Elizabeth Hospital, Birmingham, U.K.

Prepartum Psychosis

One entity, which is often missed in clinical settings, is prepartum psychosis. Prepartum psychosis has been described by Brockington et al (1990) as being an episodic illness, with onset at least two weeks prior to delivery, with no non-pregnancy episode.

We have studied 76 consecutive patients who have been admitted to the hospital with pregnancy and postpartum related mental illness and found that 10% had a prepartum onset. Our series indicated an equal distribution of prepartum psychosis between primis and multi whereas the western literature has found a higher incidence in multipara (Brockington et al., 1990). Onset of psychosis occurred in both 2nd and 3rd trimesters and not only in the 3rd trimester.

Among our cases, pure prepartum psychosis was uncommon, i.e. recurrent episodes

occurring only in the prepartum period. Several women had a puerperal worsening and 50% had prepartum relapse in subsequent pregnancies. This finding has definite therapeutic implications. Adequate and vigorous treatment in the prepartum period may prevent fairly severe puerperal worsening.

That active mental disturbance during pregnancy is related to the development of postpartum psychosis within a high risk group has been reported by McNeil (1988). The study had a follow up of 88 women with past postpartum psychiatric disturbance. Mental disturbance during pregnancy was associated with early onset psychosis i.e. onset within 3 weeks after delivery. Women with anxiety and excitement showed an increased risk for early onset postpartum psychosis while depression in pregnancy did not indicate an increased risk.

Bipolar Disorders And Postpartum Psychosis

One of the areas that we have studied has been the association of postpartum psychosis with bipolar mood disorders.

Time of Onset following childbirth

Several studies have found that the nature of postpartum psychosis is determined by the time of onset of the psychosis following childbirth (Dean et al., 1989; McNeil 1988). The latter study reported that with three weeks following childbirth as a cut off point, a high prevalence of affective disorders was found in the early onset group. However, we have not been able to replicate this study and found a higher incidence of affective disorders in the late onset group, taking 3 weeks as the cut off (Yogananda et al., 1997).

Length of episodes of PP and non PP Mania

Length of episodes were compared between postpartum and non-postpartum mania and it was found that post partum mania seemed to be relatively benign in terms of length of episodes, with most episodes ranging between 1-3 months as compared to the duration of non puerperal mania which was in the range of 3-6 months. Postpartum mania in our study had a better prognosis than non-postpartum mania and this is in line with findings of other workers (Dean et al., 1989).

Family History

40% of women in our sample had a family history of psychiatric illness. 75% of the affected family members in the above group had affective disorders. An interesting finding was that 30% of the probands had a mother or a sister who had suffered from post partum psychiatric illness. The literature on genetic factors operating in postpartum psychosis is sporadic and most of the evidence accumulated till now points towards the close association between these disorders and affective illnesses, particularly bipolar disorders. Dean et al. (1989) found a morbidity risk of 50% and also showed that those with pure postpartum episodes (women with psychosis limited to postpartum state only) had higher rates of family illness than those with combined postpartum and non-postpartum episodes.

Aggression in the Postpartum Period

Resnick (1969) in his review on infanticide noted that two-thirds of women who commit filicide have psychiatric problems while only 17% of women in the neonaticide group had psychiatric illnesses. According to him, the most common psychiatric problem in these mothers was schizophrenia. Other psychiatric disorders noted were melancholia, manic-depressive psychosis, neurosis, character disorder, and unspecified psychosis. Brockington (1996) reports depression as the commonest cause of filicide. It often has a component of delusional mercy killing, what is termed as 'libericide'. Filicide is committed in the belief that the child's best interests are being served - delusional altruism. Often the mother kills the child to protect it from the misfortune of being motherless after her intended suicide. The other psychiatric causes include postpartum mania, delusional disorders, menstrual mood disorders

which are particularly associated with rage and violence and trance states seen in epilepsy and somnambulism.

There is often an unusual relationship between postpartum psychiatric disorders and infanticide. One of the common psychopathological themes reported in the literature on postpartum disorders is the mother's fear of harming her baby. Aggression in the postpartum has been an area of interest in world literature now particularly because of the increasing interest in the role of both oxytocin and prolactin in mothering and bonding. As we gain more knowledge about the effect of these hormones on relationship between mother and child, there might be more methods of intervention for this distressing problem.

One of the aims of our study was to study how often mothers with post partum psychiatric disorders hurt their children. We found that 18 (30%), of the total sample of women (60) with postpartum psychosis had infanticidal ideations, one had committed infanticide, while one mother had fatally harmed an older child. Aggression towards the child is one of the many mother child interaction problems, which include hostility, rejection, and lack of bonding. As joint mother and baby admissions become more prevalent, the safety of mother and baby units is a concern. More studies need to be done in this area to assess what factors predict aggression towards the child. These might include, the psychiatric illness, personality factors in the mother, characteristics of the child and circumstances of childbirth. Another issue of interest in the area of aggression has been that of deliberate self-harm. 50 % of those women (12/60) who attempted deliberate self-harm in our sample also tried to harm the child.

With increasing interest in the biology of aggression in postpartum women, this area is worth further investigation.

Hormonal Basis of Postpartum Psychiatric Morbidity

The common hormones implicated in the causation of postpartum psychosis include estrogen, progesterone, adrenal corticosteroids, prolactin, thyroxine, and oxytocin. Cookson (1982) first proposed that a fall in oestrogen levels in postpartum period would result in dopamine receptor supersensitivity, which in turn would precipitate psychosis. Wieck et al. (1991) concluded similar findings from their study. The mechanism of oestrogen modification of dopamine receptors in striatum, hippocampus, substantia nigra and hypothalamus is thought to be due to the alteration in number of binding sites, effects on pre and post synaptic receptors, activation of breakdown enzymes and direct effects on neuronal firing. Sichel et al. (1995) extrapolated these experimental findings into therapeutics. They discovered the so called 'estrogen withdrawal period' and administered decreasing dosages of estrogen in seven women with past history of postpartum psychosis and found that only one patient had a relapse. This low rate of relapse i.e. 9% compared to an expected 35-60% without prophylaxis, suggested that oral estrogen might stem the rapid rate of change in estrogen following delivery.

The evidence about progesterone's involvement in the pathogenesis of postpartum psychosis is fragmentary. Harris (1994) found no association between progesterone and postpartum mood disturbances. There is not much unequivocal evidence for other hormonal systems such as prolactin, tryptophan, beta-endorphin, oxytocin, renin, angiotensinogen and angiotensin in the pathogenesis of postpartum psychosis.

Ahokas et al (2000) studied oestradiol levels among patients with postpartum psychosis and found evidence of oestradiol deficiency with slow recovery in the postpartum. Patients with oestradiol deficiency were then treated with 17-beta oestradiol alone and showed a good clinical response. Putatively, estrogen with its effects on neurotransmitter functions is involved in the regulation of mood and behaviour. The antipsychotic effects of estrogen maybe mediated by serotonin as well as dopamine receptor mechanisms. Though the therapeutic role of oestrogen is still limited to case studies, it is a

fertile area for research as it has important therapeutic implications.

Recent studies have focused on autoimmune thyroid dysfunction occurring in pregnancy and the presence of thyroid antibodies in women who are pregnant. There seems to be a transient hyperthyroidism followed by a transient hypothyroidism in several women including normal women in the pregnancy and postpartum. In women with post partum depression there seems to be a strong association between the presence of thyroid antibodies and mood state rather than thyroid dysfunction (Harris, 1994; Harris et al., 1994; Harris et al., 1996).

In a study on thyroid dysfunction in women with mentally illness over a two-year period we found that of 88 women who had abnormal thyroid functions and were in the reproductive age group, 32 of them, (nearly two thirds) were in the post partum period and majority of them had affective disorders. In 65 % of them, the only abnormality found was high TSH levels (Shantala et al., 1998). Routine T_3, T_4, TSH levels may not be very contributory and probable answers now seem to lie in the detection of thyroid antibodies in order to detect sub clinical hypothyroidism in women with post partum depression.

REPRODUCTION AND SEXUAL HEALTH IN WOMEN WITH SEVERE MENTAL ILLNESS

Family Planning Issues in Women with SMI

An area, which has been of concern to us, has been family planning needs in women with severe mental illness, which are frequently not discussed. There seems to be a high incidence of unplanned pregnancies and poor control of contraception and problems in child rearing.

On interviewing 89 women with severe mental illness we found a fairly high number of unplanned pregnancies (70 %), children of 24 women were being reared by others. It was also found that very few women (1/3rd) had actually discussed these issues with their psychiatrist, probably resulting in a high incidence of unplanned pregnancies. Miller and Finnerty (1996) have reported similar findings in their study of women with schizophrenia spectrum disorders. Coverdale et al., (1992) emphasize that women with severe mental illness have fewer planned pregnancies; more unwanted pregnancies, more abortions and are more often victims of violence during pregnancy. Miller and Finnerty (1996) report that they were more likely to have lost custody of children and to report inability to meet their children's basic needs. It is evident that health care delivery systems must meet the family planning and parenting training needs of women with severe mental illness.

Severe mental illness and Sexual HRSB

High-risk sexual behaviour is commonly under detected among women with mental illness. It is very often related to sexual disinhibition, impaired judgment and lack of knowledge. Research has begun to detail the HIV related risk conferring behaviours among women with severe mental illness. Investigation involving community based samples found high-risk behaviour in women with long standing schizophrenia including multiple sexual partners, engaging in sex in exchange of money, thus posing a high risk of HIV infection. In a study, which investigated factors, associated with risk for HIV infection among chronic mentally ill adults, there were no differences in risk behaviour between the women diagnosed as paranoid schizophrenia, other schizophrenias, schizoaffective disorder or bipolar affective disorder. 29% of women reported multiple sexual partners, 9% reported having had sex with an intravenous drug using sexual partner in the previous year and they were unlikely to use condoms. A history of sexually transmitted diseases was present and they frequently used alcohol and drugs in conjunction with sex. Most reported contacts with persons unfamiliar to them, whom they met in bars and psychiatric clinics, 21% involved coercive partners and were often involved in sex in exchange of money or drugs (Carey & Carey, 1997).

In a study on HIV risk and context of AIDS

among women with severe mental illness by Weinhardt et al (1998), 54% had been sexually active in the past 2 months (of 61 patients). 38% reported atleast one of the risk factors during that period. 23% reported 2 or more risk factors and 16% had three or more risk factors. Among those reporting multiple sexual partners in the past two months, condom use was rare. These data assume importance as they correspond with findings from the limited research done in India and highlight the need to address this behaviour in women with severe mental illness (Chopra et al., 1998; Chandra et al., 1996).

TOWARDS THE FUTURE

The area of Women's mental health in general and specifically the area of the interface between psychiatry and women's reproductive and sexual health is a fertile area of research with far reaching clinical and social consequences.
Some of the specific issues that we need to address in the future include -

- The role of gonadal hormones in modulating mood and behaviour in women with and without psychiatric disorder.
- The influence of drugs used in psychiatry such as antipsychotics and mood stabilizers on reproductive physiology.
- The impact of sociocultural factors such as explanatory models and help seeking on biological aspects of reproduction.
- The influence of mental illness on women's reproductive and sexual health.

I hope that the next few years will see an increase in Indian research in this important field.

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