Review Article: Anxiety and Depressive Disorders in Pregnancy

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Abstract

Background: *For most expectant mothers and their partners, pregnancy is a time of joy and expectations even more so in African cultures. Sadly, even though a significant number of women face emotional challenges during pregnancy, there was little interest in studying emotional health of pregnant women as it was thought that pregnancy was protective. Several factors may have contributed to this notion. It was widely held that hormonal changes like sudden withdrawal of 'protective pregnancy hormones' were responsible for the high 'incidence' of emotional disorders in the early post-partum period.*

Objectives: *In this article, we intend to review journal articles on anxiety and depressive disorders in pregnancy with specific references to epidemiology of anxiety and depressive disorders, pregnancy and emotional health, neurobiology of anxiety and depressive disorders in pregnancy, psychosocial origins of anxiety and depressive disorders in pregnancy, overview of perinatal mental health disorders, anxiety and depression in pregnancy, and finally risk factors for anxiety and depression in pregnancy. Method: PubMed, google, Crossref, Medline were searched using several combinations of the following search terms: pregnancy, anxiety and depressive disorders, etiology, neurobiology, and epidemiology.*

Study Selection: *All relevant papers published in English and reporting original data related anxiety and depressive disorders in pregnancy were included.*

Data Extraction: *Studies were examined for data related to the prevalence, presentation, predictors/risk factors, new onset, course, and treatment of anxiety disorders during pregnancy.*

Data Synthesis: *Anxiety and depressive disorders are common during pregnancy with varying reported rates of prevalence, incidence, and severity.*

Conclusions: *New cases of anxiety and depressive disorders do occur in pregnancy. Burden of distressing symptoms may be higher in early pregnancy. More community studies are needed to generate findings that are more representative of all pregnant women. Women should be encouraged to book for antenatal care in early pregnancy and screening measures should be instituted to detect those with clinically significant symptoms so they can be helped.*

1. Introduction

Anxiety and depression has been variously defined. Anxiety disorders differ from normal feelings of nervousness or anxiousness, and involve excessive fear or anxiety [1]. Anxiety disorders can also be said to be a group of mental disorders characterized by feelings of anxiety and fear. These disorders include generalised anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD) [1].

The World Health Organization (WHO) has defined depression as a common mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration [2]. The American Psychiatric Association (APA) has also defined depression or major depressive disorder as a common and serious medical illness that negatively affects how you feel, the way you think and how you act [3].

Pregnancy has been defined by the WHO as the period of nine

months or so for which a woman carries a developing embryo and foetus in her womb [4]. A cohort can be described as a group of people with defined characteristics who are followed up to determine incidence of, or mortality from, some specific disease, all causes of death, or some other outcome [5].

1.1 Epidemiology of Anxiety and Depressive Disorders

Findings from the research literature before 1980 are likely to be of limited use because of absence of operational criteria guiding research [6]. Cultural differences in symptom presentation may also limit generalizability of conclusions across cultures [7]. Also most epidemiological research is based on DSM-III criteria, until just recently, and most work has been done in high-income countries [8].

Anxiety disorders are one of the most common mental disorders [9]. They have been reported globally as illustrated by a cross-national study consisting of independently conducted community surveys in 10 different countries, high-, moderate- and low income inclusive [10]. The life-time prevalence of Panic disorder based on DSM-III criteria ranged from 0.4 per 100 in Taiwan to 2.9 per 100 in Italy [10]. The World Mental Health Survey (WMHS) initiative recently reported a prevalence of 3.6% in both sexes (4.6% in females, 2.6% in males) [2]. A recent systematic review and meta-analysis [9] of 87 studies across 44 countries reported a global point prevalence of 7.3% and a 12-month prevalence of 11.6% [9]. The lifetime prevalence of anxiety disorders has been reported in another systematic review to be 16.6% [11].

Some socio-demographic characteristics have been very frequently associated with anxiety disorders in the literature. Increasing age has been associated with lower risk of developing an anxiety disorder [9]. Females are 2-3 times more likely to develop an anxiety disorder than males [9]. Living in an urban city was found to also increase the risk when compared to residing in a rural area [12]. Being married has been reported in the literature to predict lower likelihood of developing an anxiety disorder [13]. Other factors that have been reported to increase the risk of having an anxiety disorder include psychosocial stressors like socioeconomic disadvantage and relationship difficulties, exposure to violence, trauma, conflict [14-18]. Anxiety disorders have been found to rank 6th among the contributors to non-fatal health loss globally as at 2015 having led to a global total of 24.6 million years lived with disability (YLD) [2].

There is paucity of literature on anxiety disorders in Africa and the West African sub region. Most of the literature in the West African sub region is from Nigeria. The WHO estimates that the lowest proportion (10%) of the 264 million suffering from an anxiety disorder, are in Africa [2]. Country estimates of percentage of the population with anxiety disorders are available with the WHO, and as at 2015, Niger has the lowest prevalence of 2.5%. Nigeria's is 2.7%, Ghana 2.8%, Liberia 2.7%, to mention just a few.31 The Nigerian survey of mental health and well-being (NSMHW) re-

ported a 12-month prevalence of anxiety disorders to be 4.1% and lifetime prevalence, 5.7% [19].

The incidence and prevalence of depressive disorders also varies widely across countries and cultures. Lowest annual and lifetime rates in a cross-national study using DSM-III-R criteria were reported from Taiwan, a country with higher rates of psycho-physiologic disorders like Neurasthenia [20]. The lifetime prevalence in the aforenamed study [20]. ranged from 2.9 per 100 to 17.1 per 100. Prevalence rates were reported to be twice higher in females than in males, a difference not explained by a greater tendency of women to report distress or to seek help [21]. ECA follow-up also showed that females have a higher risk of new onset major depression but no higher rates of recurrence and no longer episodes compared to males [22]. A psychiatric epidemiological study on Chinese-Americans also reported that Chinese-American women with high acculturation scores were 2.16 times more likely to develop a major depressive episode in their lifetime compared to their male counterparts [23]. On the other hand, those women with low acculturation scores did not have any significant difference in life-time risk of having a major depressive episode when compared to the Chinese-American men [23]. The risk of developing major depression is increased 2-3 times among relatives of probands with the disorder compared to normal controls [24]. Klerman and Weiss man in a paper published in 1989 concluded that there is an increase in cumulative lifetime rates of major depression with each successive younger birth cohort [25].

The most recent world mental health survey reported an average prevalence of depressive disorders of 5.5% for developed countries and 5.9% for developing countries [26]. The 12-month prevalence ranged from 2.2% in Japan to 10.4% in Brazil [26]. A more recent systematic review and meta-analysis reported a point prevalence of major depressive disorder (MDD) to range from 0.05% among males aged 65 years or more in Japan to 73% among females aged 15 years or older in Afghanistan [27]. The aforementioned systematic review also noted that very few incidence studies on depressive disorders were found in their search and among the few found, the incidence ranged from 1.6% to 7.1%. They generated a pooled point prevalence for MDD of 4.7% after adjusting for methodological differences, and pooled annual incidence of 3% [27].

In Africa, the WHO has estimated the prevalence of depressive disorders to be 5.9% for females and 4.9% for males [2]. These figures are among the highest in the world. The Nigerian survey of mental health and well-being (NSMHW) found a lifetime prevalence of MDD of 3.3% and 12-month prevalence of 1% [19]. The researchers in this survey admitted that this might be an underestimation of the true prevalence due to stigma in admitting to mental health symptoms among other factors.48 Some researchers working in sub-Saharan Africa have also reported prevalence for depression using self-rating instruments to be 14% in hospital settings and 17% in the community [28,29].

Major depression has also been shown to be the fourth most disabling illness globally as at the 1990s [30]. Unipolar depressive disorders now rank first globally among the contributors to years lived with disorder (YLDs) contributing over 50 million YLDs globally to the burden of non-communicable conditions. Over 80% of this burden is in low and middle-income countries where a huge treatment gap still exists [31]. Twenty-one per cent of those with depressive disorders globally i.e. 66.21 million people, live in Africa [31].

Approximately 50-60% of individuals with a lifetime prevalence of major depression have also been found to also have a lifetime history of one or more anxiety disorders [32]. More recently, a report from the Netherlands study of depression and anxiety reports that 67% of those with a depressive disorder had a current comorbid anxiety disorder while 75% had lifetime comorbid anxiety disorder [33]. Of those with a current anxiety disorder, 63% had a current and 81% had a lifetime depressive disorder [33].

1.2 Neurobiology of Anxiety and Depressive Disorders In Pregnancy

Research into neurobiology of anxiety and depressive disorders, including basic biological and translational research is rapidly evolving. A lot has been found and a lot remains to be learnt [34,35]. So much has been reported on the biological underpinnings of mood regulation, fear, anxiety, aetiology of anxiety and depressive disorders, biological effects of treatments, biological explanations for the consequences of non-treatment, and so much more. There are many relationships between the neurobiology of anxiety disorders and that for depressive disorders [36-38]. These findings also hold true for pregnant women.

With regards to the neurobiology of anxiety disorders, Margis et al, using animal models reported that the amygdaloid complex and septo-hippocampal system are involved in novel situations of a real threat or when the experience of such is relieved [39]. They concluded that the septo-hippocampal system acts as the center of analysis of circumstances comparing the actual experience with previously stored memories. The periaqueductal gray matter (PAG) is also thought in their report to promote typical defense reactions like freezing and fight or flight response, when the danger is real, explicit but distant [39]. This is similar to what has been found by other researchers [40-42]. Some researchers, however, report that the PAG may have a more central role in the control of fear responses while the amygdaloid complex may be downstream [43]. Yet, others have opined that uncertainty and anticipation sub served by some of the afore mentioned structures are more central to understanding the pathophysiology of anxiety disorders [38,44,45].

A lot of data exists on the major neurotransmitters and neuropeptides that aforementioned structures use to communicate with each other, derangements of which result in anxiety disorders [39,42]. These include hormones from the hypothalamic-pituitary-adrenal axis (HPA), cholecystokinin (CCK), monoamines such as serotonin, and the amino acids L-glutamate, γ-aminobutyric acid (GABA) and glycine [42]. This explains why drugs such as those acting as agonists at GABA receptors e.g. benzodiazepines (BDZ), drugs acting on monoamine transmission like the selective serotonin reuptake inhibitors (SSRI), antagonists at brain CCK receptors, and the like all play different roles in the pharmacotherapy of anxiety disorders [39,42]. There's a lot of interaction between these chemical systems and the endocrine system, as in a gravid woman, through the hypothalamus. A better understanding of how the different neuroanatomical structures interact in normal states and in anxiety disorders, using the different neurotransmitters and neuropeptides will drive the search for better drugs, improve the knowledge of the biological basis for psychological theories thus improving psychotherapy, and refine our understanding of their pathophysiology in pregnancy [34,46].

The neurobiology of depressive disorders is another engaging area of research. Post et al as far back as 1986 suggested that the 'kindling hypothesis' may be applied to depressive illness to explain the tendency to recurrence and progression [47]. Since then, more evidence has been reported in support of this model [48,49]. Anderson et al in 2017, on the other hand, has called this 'kindling hypothesis' into question in a longitudinal study where after correcting for Slater's fallacy, they found absence of shorter intervals between depressive episodes [50,51].

Several functional and structural changes have also been reported in depressive disorders as seen on functional magnetic resonance imaging (fMRI) [52]. Regional blood flow studies suggest hyperactivity in the ventromedial prefrontal cortex (VMPFC) and lateral orbital prefrontal cortex (LOPFC), while hypoactivity in dorsolateral prefrontal cortex (DLPFC) [52]. The DLPFC maintain executive function, effortful sustained attention and working memory processes [53]. The VMPFC also plays a role in regulation of mood by mediating pain, aggression, sexual functioning and eating behaviour, while the LOPFC assesses risk and modulates maladaptive, perseverative affective states [53]. In a meta-analysis of 12 studies, hippocampal volume was found to be consistently and significantly reduced in patients with MDD when compared with controls [54]. These and other similar findings are not consistent enough to be pathognomonic [53]. Molecular processes mediating these neurobiological changes have also been reported in the literature [53,55-57] and summarized in Figure 2.1. Research literature has also demonstrated that effective treatments restore functioning of the neurochemical system and prevent further structural changes in the brain especially if activity in multiple monoaminergic systems is increased [53,58,59].

Most researchers working on the neurobiology of perinatal anxiety have studied its effects on offspring mental health. For instance, it has been reported that early life stress causes persistent sensitization of CNS circuits which are integrally involved in the regulation of stress and emotions, thus increasing the individual's vulnerabil-

ity to subsequent stress and the development of an anxiety disorder [37]. Some unique fMRI findings have been documented for perinatal anxiety disorders. Low neural responses in the amygdala and low connectivity between the amygdala and insula in response to non-infant emotional cues were reported in women with perinatal anxiety disorders [60,61]. Non-pregnant females with anxiety disorders usually show the opposite, hyperactivity in the amygdala and increased connectivity between the amygdala and insula when presented with similar cues [62,63].

Anxiety disorders in pregnancy have also been associated with changes in foetal arousal and physiology, increased rates of spontaneous preterm births, abnormal child emotional and behavioural development, developmental problems and lower cognitive functioning, as well as structural brain changes in their offspring from the in-utero period [60,64]. Many propose different mechanisms for the developmental consequences of perinatal anxiety disorders. An example is the developmental origins of health and disease hypothesis, which suggests that adaptations made by the developing foetus to a detrimental intra-uterine environment (e.g. resulting from maternal anxiety) lead to permanent changes in structure and function [65]. Others have focused on whether the effects of maternal stress-related hormones on foetal development either through direct effects on brain cells, or through effects on programming of certain biological systems responsible for the regulation of foetal development, explain these developmental outcomes [66]. It has also been suggested in the literature that the mechanisms underlying these effects are associated with or mediated by epigenetic regulation, i.e. alterations in gene function in the absence of changes in the DNA sequence (due to DNA methylation, histone modifications, or non-coding RNAs) [66].

A lot has been reported in the literature in an attempt to explain the development of perinatal depressive disorders. Among the implicated endocrine mediators include cortisol which is usually increased up to 100-fold throughout pregnancy until after the delivery of the placenta when its levels fall abruptly [67]. There has been no consistency in the literature however, showing that cortisol or any other HPA axis marker is significantly different in women with antenatal depression [68]. Neuroactive progesterone metabolites e.g. allopregnanolone and pregnanolone, have also been studied as some of them enhance GABAergic transmission with attendant sedative, anxiolytic and anticonvulsant properties [69]. The evidence has also been inconclusive with some showing an association between low levels of such metabolites and antenatal depression, while others have reported high or unchanged levels [70-72]. The immune system is postulated to be a possible contributor to antenatal depression just as it is thought to be in pre-eclampsia [73]. It has been suggested that a predominant proinflammatory activity is responsible for changes in monoaminergic systems, immune function, neurosecretory activity, and placental function, associated with preterm labour [73]. Another systematic review found 4 studies reporting immune cytokines in antenatal depression with 3 reporting an association with at least one cytokine while 1 did not [74].

1.3 Psychosocial Origins of Anxiety and Depressive Disorders in Pregnancy

Neurobiology alone is not sufficient to explain the etiology and clinical aspects of these disorders. A lot of different psychological and sociological theories have been postulated in attempt to better understand anxiety and depressive disorders. Psychoanalytic theories are among the earliest of these theories and they propose that anxiety arises from intrapsychic conflict [75]. This happens when the ego is overwhelmed by excitation from the outside world (realistic anxiety), the basic instincts of the id (neurotic anxiety) or the standards of the superego (moral anxiety) [75]. The ego may have been weakened by a developmental failure in childhood, which may be from separation or loss, making it vulnerable to being overwhelmed when faced with stressful situations, like pregnancy [76,77]. These theories have not been confirmed by more recent scientific studies [78].

Cognitive and behavioral theories have also been postulated. Some have proposed that generalized anxiety disorders arise when there is an inherited predisposition to excessive responsiveness of the autonomic nervous system, together with generalization of the responses through conditioning of anxiety to previously neutral stimuli [79]. Others have opined that generalized anxiety disorders arises from a tendency to worry unproductively about problems and to focus attention on potentially threatening circumstances like childbirth [80]. These theories have probably exerted the greatest influence on management of anxiety disorders [79,80].

Research has also linked the social environment to the development of anxiety disorders. Brown and Harris studied a population of 404 working-class and single mothers, and reported that adverse experiences in childhood and adolescence (involving parental indifference, and sexual and physical abuse) considerably raise risk of both depression and anxiety conditions (with the exception of mild agoraphobia and simple phobia) in adult life [81]. Other researcher have added to the evidence that the environment, especially early childhood environment contributes to aetiology of anxiety and depressive disorders [82].

As early as 1911, Abraham published a paper on the psychoanalytic investigation of manic-depressive insanity [83]. This was further developed by Freud in 1917 in a paper called 'Mourning and Melancholia' [84]. In it, he drew attention to the similarities between phenomena of mourning and the symptoms of depression, suggesting similarities as well in causation (loss of an 'object' in melancholia). Klein related the loss to weaning in early childhood while Bowlby emphasized the role on the care-giver's rearing ability on the development of 'secure' or 'insecure' attachment relationships, with consequent effects on ability in adulthood to access appropriate emotional support when in difficulties [85,86].

The cognitive model to the understanding of depressive disorders has also been supported in the literature. Beck suggested the cognitive approach to depressive and other disorders based on his clin-

ical observations of cognitive distortions in depression [87]. This model has undergone progressive revisions with further research and today has resulted in the generic cognitive model, which is being applied to many clinical situations [88].

1.4 Anxiety and Depression in Pregnancy

Anxiety in pregnancy is gradually receiving the attention it deserves by researchers. A recent systematic review that pooled data from 70 studies reporting on antenatal anxiety yielded a prevalence of self-reported anxiety symptoms to be 18.2% for the first trimester, 19.1% for the second trimester and 24.6% for the third trimester [89]. They also reported an overall pooled prevalence for self-reported anxiety symptoms across the three trimesters to be 22.9%. The prevalence for a clinical diagnosis of any anxiety disorder was 18.0% for the first trimester, 15.2% for the second trimester and 15.4% for the third trimester. Overall, the prevalence of any anxiety disorder across the three trimesters was 15.2%. The review also found the self-reported anxiety rates were significantly higher in LALMICs when compared to HICs, a view shared by other researchers [89-91]. One of the earliest Nigerian studies to specifically study anxiety in pregnancy was by Fatoye et al [92]. Pregnant women (N=156) attending an antenatal clinic in a teaching hospital were matched with controls and assessed using among other instruments, the state form of the State-Trait Anxiety Inventory (STAI-state). They found that the pregnant women had significantly higher prevalence of anxiety symptoms than the controls [92]. Only screening instruments were used in this study and it was a cross-sectional study. One of the first Nigerian studies to use a diagnostic instrument to study anxiety in pregnancy was by Adewuya et al [93]. It was also a controlled study and they reported a prevalence of any DSM-IV anxiety disorder in the pregnant group as 39.0% compared to 16.3% in the non-pregnant group [93]. This study assessed only women in late pregnancy.

It can be observed so far that most of the studies on anxiety disorders in pregnancy report prevalence. Longitudinal studies in pregnancy are few. One of these by Martini et al was carried out in Dresden, Germany among 306 expectant mothers followed up from early pregnancy to the post-partum period.94 Among the 109 women in their cohort who did not have an anxiety or depressive disorder prior to recruitment into the study, they reported an incidence of any anxiety disorder to be 8(7.3%) during pregnancy [94]. No incidence, to the knowledge of the researcher, has been reported in the West African sub-region.

Anxiety during pregnancy is usually studied together with depression though less commonly studied compared to antepartum depression. Anxiety disorders are the second most common mental disorder in pregnancy and postpartum [95]. Heron et al. reported in 2004 that antenatal anxiety occurs frequently, overlapping with depression, and increases the likelihood of postnatal depression [90]. A positive correlation has also been reported in a Turkish population between anxiety and depression in pregnancy [96]. Sutter-Dallay et al. in 2004 found a prevalence of GAD, the most

prevalent anxiety disorder in pregnancy, to be 8.5% among pregnant women in the third trimester of pregnancy [97]. Two studies conducted in Nigeria reported very disparate prevalence rates in the third trimester, 5.8% and 39.0% [93,98]. The former used a screening instrument while the latter used a diagnostic interview. Esimai et al. also reported figures for the first and second trimesters, 13.0% and 4.3% respectively, suggesting that anxiety disorders are more prevalent in the first trimester while depression is more prevalent in the third trimester [98].

Depression is the more studied disorder in the antenatal period compared to anxiety. It is also the most frequently found mental health condition both during pregnancy and after childbirth [95]. Epidemiological studies in western societies reported rates of antenatal depressive episodes ranging between 5 and 33% [99,100]. A meta-analysis found the point prevalence of depression to range from 8.5% to 11% at different times during pregnancy suggesting similar rates as post-natal depression [101]. Another study conducted in Africa found the mean prevalence of depression during pregnancy to be 11.3%, a figure similar to that in the west [102]. Similar figures have been obtained by other researchers in the West African sub region [103,104].

However, higher prevalence rates have more often than not been reported in low-income settings. For instance, researchers in Addis Ababa, Ethiopia, a low income country, reported a prevalence of antenatal depression to be 24.94% among 393 pregnant women attending antenatal care service in Addis Ababa public health centres [105]. This finding of higher prevalence of antenatal depression in low-income settings has been reported by many researchers, especially when symptom scores are used for diagnosis rather than diagnostic instruments [104,106,107]. The incidence of antenatal depression has been reported to range from 2.2 – 2.5% [108,109].

The age ranges reported in most studies on anxiety and depression in pregnancy in the West African subregion, are similar. Researchers in the Niger delta area of Nigeria reported an age range of 14-44 years in a community study [110]. In Ife(western Nigeria), Akinsulore and his team also reported an age range of 15-45 years in a hospital based population [29]. Even in northern Nigeria where child marriages may be common, researchers reported a range of 17-40 years in a rural antenatal population [111]. Alami et al reported an age range of 19-43 years for an antenatal population in Morocco [106].

Research papers on anxiety and depression in pregnancy have also reported on progression of symptoms through pregnancy. There's been a common believe in a U-shaped pattern of scores, high in first trimester, lowest scores in the second trimester and high again in the third trimester. This has been illustrated in a longitudinal study of 357 pregnant women in an antenatal clinic in Hong Kong [112]. They found that both prevalence and mean scores of anxiety and depression follow a non-linear pattern through pregnancy with higher scores in first and third trimesters, and lowest scores in sec-

ond trimester [113]. One of the earliest prospective studies on this subject, however, reported that there was no significant change in psychiatric morbidity scores in the antenatal period [114]. A report from the AVON longitudinal study, in contrast, suggest that mean depression scores increased between 18 weeks of pregnancy and 32 weeks [115].

Maternal symptoms of anxiety and depression during pregnancy are also associated with poor obstetric outcomes108,109 as well as adverse foetal and developmental consequences [116-118]. The effect of depression on the fetus and pregnancy may be directly mediated by the neurobiological substrates of depression such as glucocorticoids that cross the placenta, or the fetus may be indirectly affected by neuroendocrine mechanisms in which depression modulates physiological maintenance of pregnancy [119]. The indirect effect is hypothesized to be related to hyperactivity of the pituitary-adrenal axis, which induces placental hypersecretion of corticotropin-releasing factor and in turn increases myometrial contractility, leading to preterm delivery or pregnancy loss [120,121]. Depression may also have an indirect impact on the fetus through poor health behaviors, such as poor eating and poor weight gain, and poor sleep and subsequent use of over-the-counter medication, alcohol, tobacco, or caffeine [118].

A variety of pharmacological and psychological interventions have been found to be effective for anxiety and depression occurring in pregnancy [121]. Antidepressant use has increased in recent years, and the increase has been attributed primarily to the newer antidepressants, Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) [122,123]. Psychological interventions are generally the most favoured modality of treatment of these disorders in pregnancy. They can even be delivered effectively by non-specialist health workers in community settings [122,124,125].

1.5 Risk Factors for Anxiety and Depression in Pregnancy

Majority of research examining mental health in pregnant women in LALMICs to date are cross-sectional making it difficult to infer causality from their findings. However, they provide an overview of factors associated with maternal mental health [100]. Longitudinal studies on antenatal anxiety and depression are still few even in HICs. One of such published in 2015 is the Maternal Anxiety in Relation to Infant Development (MARI) study in which 306 expectant mothers in Germany were followed up to 16 months postpartum [126]. They were assessed for anxiety and depressive disorders using a version of CIDI, as well as for potential risk factors using the medical records and additional questionnaires. It was reported in the MARI study that the strongest predictors for peripartum anxiety and depressive disorders were anxiety and depressive disorders prior to pregnancy. It was also found that psychosocial (e.g. maternal education), individual (e.g. low self-esteem), and interpersonal (e.g. partnership satisfaction, social support) factors were significantly related to peripartum anxiety and depressive disorders [126].

A recent systematic review including 97 papers published in English between 2003 and 2015, from a variety of countries including LALMICs reported on the relationship between a myriad of factors in the literature with antenatal anxiety and depression [127]. The most relevant factors were: lack of partner or of social support; history of abuse or of domestic violence; personal history of mental illness; unplanned or unwanted pregnancy; adverse events in life and high perceived stress; present/past pregnancy complications; and pregnancy loss [127]. Some of these risk factors in anxiety and depression in pregnancy are discussed in more detail in this section.

Sociodemographic and economic risk factors have been examined in relation to antenatal anxiety and depression, but the results have been equivocal [127]. A significant correlation has been found with young age and adolescence by some researchers, while others have found older age to be significantly related, and yet some others reported that age was not associated with anxiety or depression during pregnancy [90,93,104,126-128]. Low educational achievements have been observed to be more common in women with anxiety and depressive disorders in pregnancy and a significant relationship between them has been reported in many studies [126,129]. Nevertheless, two studies conducted in LALMICs reported that women with more years of schooling were more likely to experience symptoms of anxiety and depression during pregnancy [130,131]. A few studies did not find education to be significant predictor of antenatal anxiety and depressive disorders [129,132]. A similar equivocal picture in the literature is observed for unemployment, low income and ethnicity [126].

Social support and marital relationship risk factor have also been reported in the literature to be associated with antenatal anxiety and depressive disorders. Perceived lack of partner and of social support have been reported as important risk factors [103,129,132,133]. On the other hand, perceived social support and marital satisfaction are protective against anxiety and depressive disorders in pregnancy [112]. A poor relationship with partner has also been reported to be a significant risk factor for the onset of these disorders during pregnancy [126]. Being single is another reported risk factor in the literature predicting antenatal anxiety and depressive disorders, probably working with other risk factors [103,104]. Other researchers, however, did not find that marital status was always a significant predictor of antenatal anxiety and depressive disorders [132]. Being in a difficult marital relationship may better predict antenatal anxiety and depressive disorders than being a single mother [127].

Another group of risk factors studied are obstetric and pregnancy-related risk factors. Unplanned or unwanted pregnancy is one of these that increase the risk of developing anxiety and depressive disorders in expectant mothers [104,129,133]. Some researchers have reported that this effect is only true in the first trimester while others have not found a relationship [112,134,135]. The role of parity in increasing the risk of antenatal depressive and anxiety

disorders is not clear [127]. Multiparous women are at increased risk of developing antenatal anxiety and depressive disorders according to some studies, while other studies found nulliparous or primiparous women as more at risk than multiparous women, and yet others did not find any significant association between parity and antenatal mental health [90,128,136-138]. Current or past pregnancy/delivery complications have been reported in some papers to be a significant predictor of antenatal anxiety and depressive disorders, and in others no such association was found [103,138-140].

2. Conclusions

New cases of anxiety and depressive disorders do occur in pregnancy. Burden of distressing symptoms may be higher in early pregnancy. More community studies are needed to generate findings that are more representative of all pregnant women. Women should be encouraged to book for antenatal care in early pregnancy and screening measures should be instituted to detect those with clinically significant symptoms so they can be helped.

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