



# Mental Health in Pregnant Adolescents: Focus on Psychopharmacology

J. Rebecca Weis, MD<sup>1,2</sup>, and Judy A. Greene, MD<sup>3,4</sup>

Prevention of teen pregnancy is one of 6 top priorities set by the Centers for Disease Control,<sup>1</sup> yet the US teen pregnancy rate remains higher than other western industrialized nations.<sup>2</sup> In 2013, the live birth rate for mothers age 15-19 was 26.5 per 1000.<sup>3</sup> Teens with mental health diagnoses may experience higher rates of pregnancy. Two studies have found increased rates of pregnancy and early parenthood among bipolar teens,<sup>4,5</sup> and young adults diagnosed with attention deficit hyperactivity disorder (ADHD) in childhood had a significantly higher rate of early parenthood (26%).<sup>6</sup> Inversely, pregnant teens appear to have a high rate of mental health problems. In Brazil, teenagers reported a high prevalence (32.5%) of psychiatric illness during the 12 months preceding the birth of their child including substance use disorders, psychotic disorders, major depressive disorder, bipolar disorder, anxiety disorders (15.7%) including posttraumatic stress disorder (PTSD), and eating disorders.<sup>7</sup> A study in Iowa identified high rates of depression during pregnancy (16%).<sup>8</sup> A program in Michigan serving teen parents found that prior to birth, teen parents had experienced an average of 5 traumatic events. Almost one-half of the teenagers met criteria for PTSD, and fully one-half met criteria for major depressive disorder.<sup>9</sup>

Given this data, medical professionals working with teen girls are extremely likely to treat pregnant teens also struggling with mental illness. Unfortunately, the medical literature provides little guidance especially when dealing with psychotropic medication management for pregnant teens. This article will provide a synthesis of what is known regarding psychotropic medication in teens along with information extrapolated from the adult reproductive psychiatry literature.

## Identification of Mental Health Problems in Pregnant Teens

Many pregnant teens have psychiatric symptoms that have not been previously identified or treated. One study from Brazil noted that in adolescents admitted for obstetric care, 22.5% had some mental disorder but only but only one-fifth of those young women had their psychiatric disorder detected during prenatal care.<sup>10</sup> Even without the confounder of pregnancy, a recent study demonstrated that clinicians failed to identify at least one-half of their pediatric patients

with moderate mental health symptoms and 28% of those with high symptoms when compared with parent report of symptoms.<sup>11,12</sup> The American Academy of Pediatrics recommends routine screening with validated measures for mental health problems,<sup>13</sup> and the American Congress of Obstetricians and Gynecologists recommends screening for perinatal depression and anxiety at least once “in the perinatal period.”<sup>14</sup> Although beyond the scope of this commentary, the use of a generalized screening instrument followed by a more specific screening tool will help to guide treatment referrals.<sup>15</sup>

## Treatment of Mental Health Problems in Pregnant Teens

Most of the research looking at treatment of mental illness during adolescent pregnancy has involved psychoeducational or supportive interventions. Recent reviews have provided overviews of these interventions, many of which have successfully improved prenatal care follow-up and several postnatal outcomes.<sup>16-19</sup> Several studies also examined standardized psychotherapy interventions for depression or PTSD in pregnant adolescents. Given the current evidence base, any pregnant teen experiencing significant mental health symptoms should be referred to programs that increase social support and/or for psychotherapy.

To date, there are no studies examining use of psychotropic medications specifically in pregnant adolescents, but we know that pregnant teens are taking these medications. One study looking at 506 pregnant teens in Iowa found that 3.4% of the teens were taking antidepressants.<sup>20</sup> Unfortunately, the majority of teen pregnancies are unintended,<sup>21</sup> so teens on medication often expose the fetus during the first trimester before realizing they are pregnant. Because embryologic development is most active in the first trimester, counseling about elective termination of pregnancy when there have been early high risk exposures will play a role in management. Because the available data on safety of medications is constantly changing, databases such as Reprotox are helpful.<sup>22</sup> In addition, clinicians may wish to review the Food and Drug Administration (FDA) pregnancy labeling for medications, which has changed as of June 30, 2015.<sup>23</sup>

ADHD	Attention deficit hyperactivity disorder
FDA	Food and Drug Administration
PTSD	Posttraumatic stress disorder
SSRI	Selective serotonin reuptake inhibitor

From the <sup>1</sup>Department of Child and Adolescent Psychiatry, New York University School of Medicine; <sup>2</sup>Early Childhood Mental Health, Bellevue Hospital Center; <sup>3</sup>Department of Psychiatry, New York University School of Medicine; and <sup>4</sup>Women's Mental Health, Bellevue Hospital Center, New York, NY

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## Antidepressants

Antidepressants are the most widely used psychotropic medications during pregnancy averaging 6.5% in the US,<sup>24</sup> not surprising given that depression and anxiety are the most prevalent mental health problems during pregnancy. Although postpartum depression has received much attention, some studies now suggest that prenatal depression is more common.<sup>25,26</sup>

The impact of untreated depression and anxiety on the mother include the symptoms experienced and also related adverse outcomes: decreased school/work/social functioning, decreased energy and motivation (which could impair follow-up for prenatal care), and suicidal ideation. In addition, some studies have now linked prenatal depression to moderately increased risk for pre-eclampsia and operative delivery.<sup>27</sup> Depression and anxiety also increase the risk that women will drink alcohol, smoke cigarettes, or use illicit drugs during pregnancy.<sup>28</sup> Among women with a history of major depression, those who discontinue antidepressants just prior to or during pregnancy have a high risk of relapse into major depression. In 1 study, those who continued antidepressants had a relapse rate of 26%, and those who discontinued had a relapse rate of 68%.<sup>29</sup>

An accumulating body of evidence also suggests untoward effects for the fetus when depression and anxiety are present prenatally such as decreased fetal growth, increased prematurity, disorganized sleep after birth, and decreased responsiveness to stimulation in the neonate as well as attentional and behavioral problems in childhood and chronic illnesses in adulthood.<sup>30</sup> Studies attempting to elucidate the etiologic factors linking prenatal depression to child outcomes have examined fetal heart rate variability (which is in turn linked to autonomic nervous system development),<sup>31</sup> cortisol reactivity and hypothalamic-pituitary-adrenal axis dysregulation in infancy,<sup>32</sup> and epigenetics.<sup>33</sup>

Only some antidepressants are approved by the FDA for use in adolescents with only escitalopram and fluoxetine spe-

cifically approved for treatment of depression.<sup>34</sup> Prescribers must be aware of and notify families of the FDA black-box warning about increased risk of suicidal thinking and behavior in adolescents and document having done so; however, this warning has been challenged including most recently by a meta-analysis that found “no evidence of increased suicide risk ... in youths receiving active medication.”<sup>35</sup> It is still wise in practice for adolescent patients to be seen within 1-2 weeks after initiating an antidepressant for review of side effects and any suicidal thoughts.

Other potential adverse effects of selective serotonin reuptake inhibitors (SSRIs) in general include headache, nausea, insomnia or drowsiness, and agitation. Citalopram and fluoxetine have been associated with QTc prolongation, so caution should be used in patients with underlying cardiac pathology or hypokalemia/hypomagnesemia. Combination with other serotonergic medications (such as triptans) should proceed carefully because of the potential risk for serotonin syndrome. Findings related to SSRI use during pregnancy specifically are summarized in **Table I**.<sup>36-40</sup>

There are also some data regarding use of tricyclic antidepressants and newer antidepressants bupropion, venlafaxine/duloxetine (serotonin norepinephrine reuptake inhibitors), nefazodone/trazodone, and mirtazapine. To date, no major congenital malformations have been associated with these antidepressants, but, given relatively small numbers of patients in studies, reproductive safety cannot be clearly established. Monoamine oxidase inhibitors are rarely used, and there is a risk that a hypertensive crisis could be triggered when tocolytic medications are administered.<sup>41</sup>

In conclusion, based on the current evidence, when a pregnant teen is presenting with mild depression or anxiety, referral for psychotherapy and social support services would be the first step. For teens struggling with more severe depression and/or anxiety symptoms, a trial of SSRI in combination with other referrals may be warranted after a careful risk-benefit analysis. Finally, it is worth noting that in PTSD, antidepressants have not been found as effective in adolescents

**Table I.** SSRI use during pregnancy

Category of finding	Concerns raised	Counter evidence decreasing concern
Congenital malformations	Several studies suggested increased risk of certain cardiovascular malformations	Recent study with very large cohort with SSRI exposure during first trimester failed to find substantial increased risk <sup>36</sup>
Adverse pregnancy outcomes	Linked to preterm delivery, low birth weight, decrease in Apgar scores but possibly because of prenatal depression rather than medication	Recent meta-analysis: (1) no significant association with spontaneous abortion; (2) statistically significant association with shorter gestation (but mean difference only about 3 d); (3) increased risk of prematurity (OR 1.55); (4) significant association with lower birth weight (but mean difference was only 74 g); and (5) significant association with lower Apgar scores (less than one-half point) <sup>37</sup>
Neonatal outcomes	With exposure in third trimester, “serotonergic over activity” for 1-4 d (tremors, restlessness, increased muscle tone) <sup>38</sup> One study found association with persistent pulmonary hypertension of newborn at rate of 1% <sup>38</sup>	No residual symptoms after this 4-d period <sup>38</sup> Subsequent studies have found no association or much lower risk than the original report <sup>38</sup>
Long-term outcomes for child	Contradictory findings in research about whether antidepressant exposure is associated with long-term neurobehavioral effects such as developmental delay, autism	Longitudinal studies found no impact at point of evaluation in preschool and 1 study found IQ and language development was adversely associated with maternal depression <sup>40</sup>

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