



Effects of anemia during the third trimester of pregnancy on postpartum depression and pregnancy outcomes in pregnant women older than 35 years: a retrospective cohort study

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Background: There is no study on the impact of anemia on postpartum depression and outcomes in mothers older than 35 years, which makes the nursing of these pregnant women with anemia more difficult.

Methods: We retrospectively collected the demographic and clinical characteristics of pregnant women older than 35 years at conception between August 2014 and December 2019. Hemoglobin less than 110 g/L was defined as anemia. Postpartum depression was assessed according to Edinburgh Postnatal Depression Scale. A subgroup analysis was performed by dividing anemia into mild anemia or moderate and severe anemia. All participants were followed up for at least 3 months postpartum and their pregnancy outcomes were recorded. The existence of postpartum depression was evaluated at 4 weeks postpartum. The risk factors of anemia during the third trimester of pregnancy and the impacts of anemia on postpartum depression and pregnancy outcomes were analyzed using multivariable logistic regression analysis.

Results: A total of 519 pregnant older than 35 years women were included in this study, including 281 without anemia and 238 with anemia. No significant difference was found in the incidence of postpartum depression between anemia and non-anemia groups (18.9% *vs.* 12.8%, $P=0.057$), while the anemia group had significantly higher incidence of preterm delivery, prolonged labor, and caesarean section. The subgroup analysis found that significantly pregnant women with older age in the moderate or severe anemia subgroup had postpartum depression than those in the mild anemia subgroup (23.2% *vs.* 12.5%, $P=0.038$). A higher rate of preterm delivery, prolonged labor, and caesarean section was recorded in the moderate or severe anemia subgroup (8.3% *vs.* 20.4%, $P=0.012$; 30.2% *vs.* 43.0%, $P<0.001$; 20.8% *vs.* 40.1%, $P=0.002$). Moderate or severe anemia, the presence of depression during the first trimester of pregnancy, unplanned pregnancy, and fewer parity were identified as risk factors of postpartum depression in pregnant women older than 35 years with anemia.

Conclusions: Anemia has significant impacts on pregnancy outcomes in pregnant women older than 35 years. Furthermore, moderate and severe anemia will significantly increase the incidence of postpartum depression, which should be corrected at an early stage to minimize its negative effects.

Keywords: Anemia; third trimester of pregnancy; postpartum depression; pregnancy outcomes; retrospective cohort study

Submitted Dec 29, 2021. Accepted for publication Mar 01, 2022.

doi: 10.21037/apm-22-165

View this article at: <https://dx.doi.org/10.21037/apm-22-165>

Introduction

Anemia is a common disease among of people of all ages and is especially prevalent during pregnancy. The main type of anemia among pregnant women is nutrition related anemia, that is, iron deficiency anemia. Due to limited food supply and industrial deficiencies, the reported anemia during pregnancy is higher in developing countries than that in developed countries (1-4). Although the national living standards in China have improved significantly in the past decades, the incidence of anemia during pregnancy has remained high. It has been reported that the overall incidence of anemia among pregnant Chinese women ranged from 36.76% to 43.82% between 2014 and 2018 (5). A single center study showed that the incidence of anemia in pregnant women was 39.8% (6). Incidence of anemia is also different during different stages of pregnancy. Typically, it is the highest during the third trimester of pregnancy, and was reported to be 80.85% in the northeast of China (5). In view of this, it is particularly important to study the risk factors of anemia during pregnancy, its impacts on pregnant women, and determine appropriate preventative measures.

Postpartum depression is one of the common and serious complications affecting postpartum women globally and an important cause of postpartum suicide (7). The causes of postpartum depression are not very clear. A history of prenatal depression, low income, weak social support, poor family relationships, and family and work stress have been reported as associated with the occurrence of postpartum depression (8-10). It has also been reported that postpartum hemorrhage significantly increases the rates of postpartum depression and suicide among postpartum women (11). A meta-analysis comprehensively analyzed the significant correlation between postpartum anemia and postpartum depression in 10 studies (12). However, the relationship between gestational anemia and postpartum depression is not clear. A study combining 2 Chinese samples found that there was no significant correlation between hemoglobin or ferritin levels during pregnancy or postpartum and the incidence of postpartum depression (13). A Japanese study also suggested that postpartum hemorrhage could lead to postpartum depression (14); however, there was no significant correlation between anemia during the second and third trimesters of pregnancy and postpartum depression. On the contrary, Yilmaz *et al.* reported that anemia is associated with higher depressive symptom levels during the last trimester of pregnancy (15). However, apart from these 3 studies, there have been no other relevant

studies to further analyze the relationship between anemia during pregnancy and postpartum depression.

In recent years, the proportion of pregnant women older than 35 years in China has gradually increased (16). It is of increasing clinical significance to study the relationship between anemia during pregnancy and postpartum depression. Compared with younger pregnant women, there are many differences in physiological and psychological states of pregnant women older than 35 years. This study retrospectively reviewed the clinical data of pregnant women older than 35 years in the past 5 years, analyzed the impacts of anemia during the third trimester of pregnancy on their postpartum depression and postpartum outcomes, and assessed the risk factors of anemia during the third trimester of pregnancy. We present the following article in accordance with the STROBE reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-165/rc>).

Methods

Ethical statement

This study was performed in the Department of Obstetrics in Affiliated Hai'an Hospital of Nantong University and approved by the Ethics Committee of the Affiliated Hai'an Hospital of Nantong University (No. 20210031). This study was performed in accordance with the Helsinki Declaration (as revised in 2013) and the written informed consent of participants were not required due to the retrospective nature.

Pregnant women

This study was performed to analyze the impacts of anemia on postpartum depression and postpartum outcomes. The following pregnant women were included: (I) those who were older than 35 years old at conception; (II) those who visited the Affiliated Hai'an Hospital of Nantong University between August 2014 and December 2019 for their first prenatal examination before 12 gestational weeks; (III) those who were expected to deliver at the Affiliated Hai'an Hospital of Nantong University. Pregnant women who had chronic liver disease, chronic kidney disease, chronic lung disease, chronic heart disease, and other life-threatening disease, and those who had a history of depression or were taking antidepressants were excluded from this study.

Demographic and clinical data were retrospectively

collected as follows: maternal age at conception, pre-pregnancy body mass index (BMI), educational status, occupational status, marital status, planned pregnancy, history of drinking and smoking, gestational hypertension, preeclampsia, gestational diabetes mellitus, gravidity, parity, history of cesarean section, the presence of depression during the first trimester of pregnancy, and the level of hemoglobin during the third trimester of pregnancy. The first and third trimester were defined as gestational week of <13 weeks and 28–42 weeks. The level of hemoglobin was routinely measured with an automated hematology analyzer. A hemoglobin level of no less than 110 g/L was defined as no anemia; hemoglobin less than 110 g/L but not less than 100 g/L was defined as mild anemia; hemoglobin less than 100 g/L but not less than 70 g/L was defined as moderate anemia; and hemoglobin less than 70 g/L was defined as severe anemia. A subgroup analysis was performed by dividing pregnant women with anemia into a mild anemia group and a moderate and severe anemia group to determine their different impacts on postpartum depression and pregnancy outcomes.

Outcomes

All participants were followed up for 3 months postpartum and those lost to follow up were excluded. The following pregnancy outcomes were recorded during the follow up: preterm delivery, premature rupture of membranes, placental abruption, prolonged labor, caesarean section, low birth weight, small-for-gestational-age, Apgar score <7 points at 5 min, early neonatal death, and neonatal intensive care unit (NICU) admission.

Postpartum depression

Depression in this study was assessed according to Edinburgh Postnatal Depression Scale (EPDS), which is used widely for the screening of perinatal depression (7). The EPDS consists of a total of 10 items containing depressive and dysphoric mood, loss of pleasure, sleep disorders, reduction of performance, thoughts of death or suicide, and guilt. The scale was translated into simplified Chinese and its sensitivity and specificity was reported to be 0.76 and 0.84, respectively (14). A cut-off value of 9 points represented as depression diagnosis. The existence of depression was evaluated twice, the first during the first trimester of pregnancy and the second at 4 weeks postpartum, which was classified as postpartum depression.

Statistical analysis

The software SPSS 20.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analysis in this study. Continuous data were expressed by mean with standard deviation and compared between 2 groups by Student's *t*-test. Categorical data were expressed by number with percentage and compared between 2 groups by chi-square test. The risk factors of anemia during the third trimester of pregnancy and the impacts of anemia on postpartum depression and pregnancy outcomes were analyzed using multivariable logistic regression analysis. A *P* value less than 0.05 was defined as significantly different.

Results

There were more than 6,000 pregnant women admitted to the Affiliated Hai'an Hospital of Nantong University between August 2014 and December 2019, among whom 541 women were older than 35 years old. A total of 22 women were excluded due to chronic disease which may have affected the results of this study, a history of depression, or were taking antidepressants. Finally, 519 pregnant women were included in this study, including 281 non-anemic women and 238 anemia women (*Figure 1*). According to the level of hemoglobin, 96 participants were diagnosed with mild anemia during the third trimester of pregnancy, 138 with moderate anemia, and 4 with severe anemia.

Participant characteristics are shown in *Table 1*. The mean maternal age at conception of all cases was 37.2 ± 2.4 years old, and the age in anemia group was significantly higher than that in the non-anemia group (37.9 ± 2.2 vs. 36.6 ± 2.4 years old, $P < 0.001$). Also, mean pre-pregnancy BMI of all cases was 22.5 ± 2.5 kg/m², and mean BMI in the anemia group was significantly lower than that in the non-anemia group (21.3 ± 2.7 vs. 23.5 ± 1.7 kg/m², $P < 0.001$). A total of 116 cases (22.4%) had an educational status of college or above and 406 cases (78.2%) were employed. Most participants were married. A total of 464 cases (89.4%) had planned their pregnancies, and there were more planned pregnancies in the anemia group than in the non-anemia group (84.5% vs. 93.6%, $P = 0.001$). Very few participants had a history of smoking or drinking. Gestational hypertension had been diagnosed in 38 women (7.3%), and there was a significant difference between the 2 groups ($P = 0.026$). However, there was no significant difference in the incidence of preeclampsia and gestational diabetes mellitus between

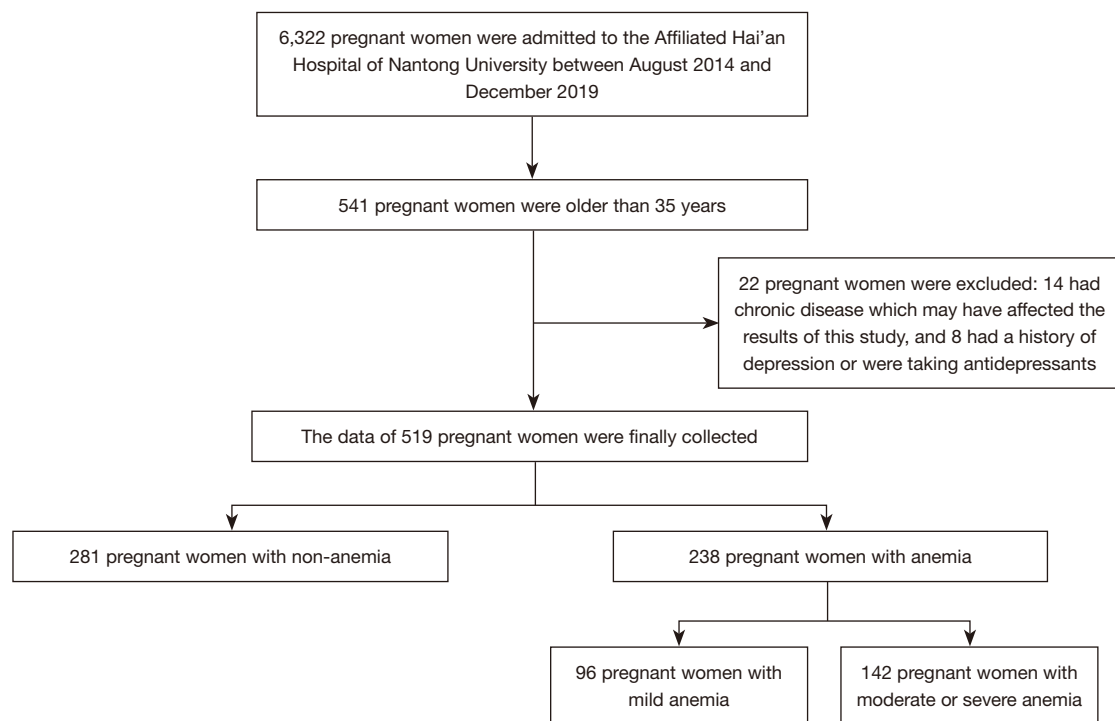


Figure 1 Flow chart of this study.

the 2 groups. Gravidity and parity were also significantly different between the 2 groups (1.7 ± 0.6 vs. 2.0 ± 0.7 , $P < 0.001$; 0.7 ± 0.5 vs. 1.0 ± 0.6 , $P < 0.001$). No differences were found between the 2 groups in the history of cesarean section and the presence of depression during the first trimester of pregnancy.

The risk factors of anemia in pregnant women older than 35 years were calculated by multivariable logistic regression, as shown in *Table 2*. Maternal age at conception, lower pre-pregnancy BMI, unplanned pregnancy, and fewer parity were finally identified as risk factors of anemia. Gestational hypertension was not found to be associated with the incidence of anemia.

Postpartum depression and pregnancy outcomes in pregnant women older than 35 years are summarized in *Table 3*. No significant difference was found in the incidence of postpartum depression between anemia and non-anemia groups, although the incidence of postpartum depression was higher in anemia group (18.9% vs. 12.8% , $P = 0.057$). The anemia group had significantly higher incidence of preterm delivery, prolonged labor, and caesarean section.

A subgroup analysis was performed to assess the impacts of different severities of anemia on the postpartum depression and pregnancy outcomes. Characteristics

of pregnant women in the 2 subgroups are shown in *Table 4*. It was found that mean pre-pregnancy BMI was significantly lower in the moderate or severe anemia subgroup than in the mild anemia subgroup (20.6 ± 2.6 vs. 21.6 ± 2.8 , $P = 0.023$). No significant difference was found in other characteristics between the 2 subgroups. The postpartum depression and pregnancy outcomes in the 2 subgroups are summarized in *Table 5*. Pregnant women with significantly older age in the moderate or severe anemia subgroup had postpartum depression than in the mild anemia subgroup (23.2% vs. 12.5% , $P = 0.038$). More preterm delivery ($n = 29$, 20.4%) occurred in women in the moderate or severe anemia subgroup, much more than the 8 cases (8.3%) of preterm delivery in the mild anemia subgroup ($P = 0.012$). Furthermore, the incidence of prolonged labor and caesarean section was also significantly higher in the moderate or severe anemia subgroup than in the mild anemia subgroup. The risk factors of postpartum depression and pregnancy outcomes were also calculated by multivariable logistic regression, as shown in *Table 6*. Moderate or severe anemia, the presence of depression during the first trimester of pregnancy, unplanned pregnancy, and fewer parity were identified as risk factors of postpartum depression. In addition, moderate or severe

Table 1 Characteristics of included pregnant women

Variables	Total	Non-anemia group	Anemia group	P value
Number	519	281	238	
Maternal age at conception	37.2±2.4	36.6±2.4	37.9±2.2	<0.001
Pre-pregnancy BMI, kg/m ²	22.5±2.5	23.5±1.7	21.3±2.7	<0.001
Educational status (college or above)	116 (22.4%)	66 (23.5%)	50 (21.0%)	0.499
Occupational status (employed)	406 (78.2%)	215 (76.5%)	191 (80.3%)	0.304
Marital status (married)	492 (94.8%)	269 (95.7%)	223 (93.7%)	0.299
Planned pregnancy	464 (89.4%)	263 (93.6%)	201 (84.5%)	0.001
History of drinking	14 (2.7%)	9 (3.2%)	5 (2.1%)	0.440
History of smoking	3 (0.6%)	1 (0.4%)	2 (0.8%)	0.438
Gestational hypertension	38 (7.3%)	14 (5.0%)	24 (10.1%)	0.026
Preeclampsia	20 (3.9%)	7 (2.5%)	13 (5.5%)	0.080
Gestational diabetes mellitus	52 (10.0%)	22 (7.8%)	30 (12.6%)	0.071
Gravidity	1.8±0.7	2.0±0.7	1.7±0.6	<0.001
Parity	0.8±0.6	1.0±0.6	0.7±0.5	<0.001
History of cesarean section	184 (35.5%)	99 (35.2%)	85 (35.7%)	0.909
Presence of depression during the first trimester of pregnancy	51 (9.8%)	26 (9.3%)	25 (10.5%)	0.633
Level of hemoglobin during the third trimester of pregnancy	104.4±12.4	114.0±5.6	93.0±7.9	<0.001

BMI, body mass index.

Table 2 Risk factors associated with anemia

Variables	OR	95% CI	P value
Maternal age at conception	1.316	1.197–1.447	<0.001
Pre-pregnancy BMI	0.642	0.578–0.713	<0.001
Planned pregnancy	0.373	0.184–0.759	0.006
Gestational hypertension	2.180	0.977–4.866	0.057
Parity	0.387	0.258–0.582	<0.001

OR, odds ratio; CI, confidence interval; BMI, body mass index.

anemia, lower BMI, and fewer parity were identified as risk factors of prolonged labor. In moderate or severe anemia, lower BMI, and a history of cesarean section were identified as risk factors of cesarean section.

Discussion

Previously, few studies have investigated the effect of anemia during the third trimester of pregnancy on postpartum depression, and research on pregnant women older than

35 years was even more scarce. To our knowledge, this study was the first to investigate the effect of anemia with different severity on postpartum depression in these pregnant women. Our results showed that anemia had a limited impact on postpartum depression generally and does not statistically increase the incidence of postpartum depression. However, we found in subgroup analysis that moderate and severe anemia significantly increased the incidence of postpartum depression compared with mild anemia. It was also shown that anemia of all severities

Table 3 Pregnancy outcomes in pregnant women older than 35 years

Variables	Total	Non-anemia group	Anemia group	P value
Number	519	281	238	–
Preterm delivery	61 (11.8%)	23 (8.2%)	38 (16.0%)	0.006
Premature rupture of membranes	10 (1.9%)	6 (2.1%)	4 (1.7%)	0.482
Placental abruption	7 (1.3%)	3 (1.1%)	4 (1.7%)	0.409
Prolonged labor	141 (27.2%)	51 (18.1%)	90 (37.8%)	<0.001
Caesarean section	124 (23.9%)	47 (16.7%)	77 (32.4%)	<0.001
Low birth weight	42 (8.1%)	19 (6.8%)	23 (9.7%)	0.227
Small-for-gestational-age	27 (5.2%)	10 (3.6%)	17 (7.1%)	0.067
Apgar score <7 points at 5 min	5 (1.0%)	2 (0.7%)	3 (1.3%)	0.422
Early neonatal death	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
NICU admission	10 (1.9%)	5 (1.8%)	5 (2.1%)	0.791
Postpartum depression	81 (15.6%)	36 (12.8%)	45 (18.9%)	0.057

NICU, neonatal intensive care unit

Table 4 Characteristics of mild anemia and moderate or severe anemia subgroups

Variables	Mild subgroup	Moderate or severe subgroup	P value
Number	96	142	–
Maternal age at conception	38.1±2.2	37.8±2.2	0.310
Pre-pregnancy BMI	21.6±2.8	20.6±2.6	0.023
Educational status (college or above)	24 (25.0%)	26 (18.3%)	0.214
Occupational status (employed)	79 (82.3%)	112 (78.9%)	0.516
Marital status (married)	91 (94.8%)	132 (93.0%)	0.568
Planned pregnancy	81 (84.4%)	120 (84.5%)	0.978
History of drinking	2 (2.1%)	3 (2.1%)	0.678
History of smoking	1 (1.0%)	1 (0.7%)	0.645
Gestational hypertension	14 (14.6%)	10 (7.0%)	0.058
Preeclampsia	6 (6.3%)	7 (4.9%)	0.660
Gestational diabetes mellitus	14 (14.6%)	16 (11.3%)	0.450
Gravidity	1.7±0.6	1.6±0.6	0.624
Parity	0.7±0.4	0.6±0.5	0.170
History of cesarean section	35 (36.5%)	50 (35.2%)	0.844
Presence of depression during the first trimester of pregnancy	14 (14.6%)	11 (7.7%)	0.091
Level of hemoglobin during the third trimester of pregnancy	104.4±4.0	86.0±5.6	<0.001

BMI, body mass index.

Table 5 Pregnancy outcomes in mild anemia and moderate or severe anemia subgroups

Variables	Mild subgroup	Moderate or severe group	P value
Number	96	142	–
Preterm delivery	8 (8.3%)	29 (20.4%)	0.012
Premature rupture of membranes	2 (2.1%)	2 (1.4%)	0.531
Placental abruption	2 (2.1%)	2 (1.4%)	0.531
Prolonged labor	29 (30.2%)	61 (43.0%)	<0.001
Caesarean section	20 (20.8%)	57 (40.1%)	0.002
Low birth weight	10 (10.4%)	13 (9.2%)	0.747
Small-for-gestational-age	5 (5.2%)	12 (8.5%)	0.341
Apgar score <7 points at 5 min	2 (2.1%)	1 (0.7%)	0.349
Early neonatal death	0 (0.0%)	0 (0.0%)	–
NICU admission	2 (2.1%)	3 (2.1%)	0.678
Postpartum depression	12 (12.5%)	33 (23.2%)	0.038

NICU, neonatal intensive care unit.

Table 6 Risk factors associated with adverse pregnancy outcomes

Variables	OR	95% CI	P value
Postpartum depression			
Moderate or severe anemia vs. mild anemia during the third trimester of pregnancy	4.753	1.554–14.539	0.006
Presence of depression during the first trimester of pregnancy	39.863	10.975–144.794	<0.001
Planned pregnancy	0.091	0.012–0.689	0.020
Parity	0.456	0.221–0.939	0.033
Prolonged labor			
Moderate or severe anemia vs. mild anemia during the third trimester of pregnancy	4.681	2.467–8.883	<0.001
Pre-pregnancy BMI	0.760	0.669–0.865	<0.001
Parity	0.556	0.320–0.964	0.037
Caesarean section			
Moderate or severe anemia vs. mild anemia during the third trimester of pregnancy	2.592	1.411–4.760	0.002
Pre-pregnancy BMI	0.868	0.775–0.973	0.015
History of cesarean section	8.649	4.544–16.462	<0.001

OR, odds ratio; CI, confidence interval; BMI, body mass index.

increased the incidence of adverse pregnancy outcomes, including preterm birth, prolonged labor, and caesarean section. These results suggest that anemia during the third trimester of pregnancy should be corrected as soon as possible to reduce the adverse effects in pregnant women older than 35 years.

The presence of anemia in pregnant women may be different during different gestational periods. According to previous studies, the incidence of anemia in pregnant women during the third trimester is the highest, and the incidence of moderate and severe anemia is significantly higher than that of mild anemia (17,18). In our study,

the incidence of anemia was 45.9%, which was similar to previous studies (19), but the proportion of severe anemia was very low, lower than 1% of the total number of pregnant women (20). Then, the risk factors of anemia in pregnant women older than 35 years were investigated. Age, BMI, planned pregnancy, and parity were closely related to the occurrence of anemia. Among these factors, BMI and planned pregnancy may be related to the nutritional status of pregnant women. The BMI directly reflects the physical state and nutritional level of women before pregnancy. Pregnant women who plan to get pregnant should make more preparations before pregnancy, including appropriate exercise, supplementing various nutritional elements, and reducing fatigue. These may promote the physical status of pregnant women and reduce the occurrence of anemia in the third trimester. The age and times of delivery are related to the experience of pregnant women. In this study, the proportion of multiparas was high because the participants were pregnant women older than 35 years. Previous pregnancy experience makes pregnant women more familiar with pregnancy, which may reduce the incidence of anemia.

This study also determined the effect of anemia on pregnancy outcome. The results showed that anemia increased the incidence of preterm birth, prolonged labor, and caesarean section. The effect of anemia on caesarean section has been investigated in many studies previously, and the results have been similar to ours (21,22). Our study further confirmed that the effect of anemia on caesarean section is also applicable to pregnant women older than 35 years. In addition, anemia was also considered to have an impact on the prognosis of infants. The most studied aspect was the impact of anemia on low birthweight infants and small for gestational age infants (23,24). However, our study did not yield significant results because the sample size of included pregnant women was small and the incidence of low birthweight infants and small for gestational age infants was low, which may require more large sample studies to further explore.

The most important purpose of this study was to explore the effect of anemia during the third trimester of pregnancy on postpartum depression in pregnant women older than 35 years. There have been contradictions in the previous research results (12,14,25). Interestingly, our results found that although anemia increased the incidence of postpartum depression to a certain extent, the effect of anemia on postpartum depression was not statistically different. When we divided anemia into mild, moderate, and severe levels,

we found that moderate and severe anemia significantly increased the incidence of postoperative depression. This can be explained by the definition of mild anemia in this study, which was that hemoglobin is in the range of 100–110 g/L, and this mild anemia did not easily cause discomfort symptoms in pregnant women, so that these women were not particularly susceptible to negative emotions. On the contrary, the hemoglobin level of moderate and severe anemia was lower, which may lead to obvious fatigue symptoms during the third trimester of pregnancy, engendering negative emotions in pregnant women. At the same time, combined with the increase of the incidence of adverse pregnancy outcomes, moderate or severe anemia promoted the incidence of postpartum depression.

There were some limitations to this study. First, not all types of demographic and clinical characteristics could be collected due to the retrospective design. For example, intrapartum hemorrhage may also affect postpartum depression and pregnancy outcome, but this study could not accurately collect relevant data. Secondly, there were only 4 pregnant women with severe anemia in the subgroup analysis, thus we could only allocate pregnant women with moderate anemia and severe anemia to one subgroup. The effect of severe anemia on pregnancy outcome requires further study to be verified. Thirdly, due to the small sample size and low incidence of some adverse pregnancy outcomes, the impacts of anemia during the third trimester of pregnancy on some pregnancy outcomes in this study was not very clear, including premature rupture of membranes, low birth weight infants, and NICU admission. Fourthly, postpartum depression is mainly related to psychosocial factors, however, psychosocial factors are inadequately adjusted in this study.

In conclusion, our study identified that anemia in pregnant women older than 35 years had no significant impacts on postpartum depression, while it would increase the incidence of preterm delivery, prolonged labor, and caesarean section. Further analysis indicated that moderate or severe anemia was associated with increased incidence of postpartum depression. Anemia in pregnant women should be promptly corrected to reduce its impacts on the prognosis of pregnant women older than 35 years.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-165/rc>

Data Sharing Statement: Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-165/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-165/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was performed in the Department of Obstetrics in Affiliated Hai'an Hospital of Nantong University and approved by the Ethics Committee of the Affiliated Hai'an Hospital of Nantong University (No. 20210031). This study was performed in accordance with the Helsinki Declaration (as revised in 2013) and the written informed consent of participants were not required due to the retrospective nature.

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(English Language Editor: J. Jones)

Cite this article as: Tian Q, Chen S, Jiang D. Effects of anemia during the third trimester of pregnancy on postpartum depression and pregnancy outcomes in pregnant women older than 35 years: a retrospective cohort study. *Ann Palliat Med* 2022;11(3):1048-1057. doi: 10.21037/apm-22-165