



Effect of Biological Factors on Postpartum Depression Evidence from Routine Examination Results

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Abstract

Background: Postpartum depression (PPD) is a common mental health issue that affects women after giving delivery. Despite extensive research into the effect of socio-psychological, demographic, and obstetric factors on PPD, the biological factors of pregnant women remain incompletely elucidated. Thus, the purpose of this study is to look at the connection between biological variables discovered through standard testing and PPD. **Method:** We recruited a total of 187 pregnant women who underwent routine examinations at a hospital between October 2022 and December 2023. Their

biological factors, such as complete blood count results, liver and kidney function test results, and infectious disease test results were collected. We investigated the relationship between biological variables and PPD using univariate and multivariate methods. **Results:** There were 36 participants (19.25%) diagnosed with PPD. Univariate analysis unveiled significant associations between hematocrit levels, creatinine levels, hepatitis B surface antigen, hepatitis B e antibody, and hepatitis B core antibody with PPD. Multivariate analysis further substantiated a notable correlation between lower hematocrit levels and PPD (coef = -0.07 , 95% CI: $-0.15-0.01$). **Conclusion:** Pregnant women with lower hematocrit levels appear to have an elevated risk of developing PPD. Thus, it is essential to pay heightened attention to the risk of PPD during routine examinations, particularly among individuals with lower hematocrit levels.

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1 Introduction

Postpartum depression (PPD) is a serious public health issue, with symptoms including decreased attention and memory, irritability, and feelings of despair [1–4]. It can also result in self-harm, with suicide accounting for 20% of deaths in the postpartum period [5]. Mothers experiencing PPD may unintentionally strain their relationship with children, which could potentially compromise the children's emotional well-being and obstruct their comprehensive growth and development, as indicated by multiple studies [5, 6]. Due to the limited resources and weak healthcare systems, PPD rates in developing nations range from 5% to 35%, which is 2 to 3 times higher than that in developed countries (range from 10% to 15%) [4, 7].

There are four primary kinds of characteristics that have been linked in previous research to an elevated risk of PPD: (1) demographic factors including age, residence, education, occupation, and economic status [8–12], (2) psychosocial factors such as antenatal depression, negative life events, high stress, postnatal fatigue, and pre-pregnancy mental illness history [8, 9, 11–14], (3) obstetric factors such as planned pregnancy, obstetric history, delivery mode, and pregnancy complications [10, 12, 15], and (4) biological factors including estradiol, progesterone, cortisol, 5-hydroxytryptamine, dopamine, and norepinephrine [16]. In comparison to the first three categories of factors, research on biological factors has been relatively limited, yet they are essential to comprehending the intricate connection between human biology and illness. [17]. Individuals may experience physiological disruptions triggering chronic stress responses, immune-endocrine imbalances, mild inflammation, and other physiological changes before clinical symptoms of psychological stress appear [18, 19]. Therefore, detecting changes in biological factors before clinical symptoms manifest can help achieve a more precise, quantified, and objective assessment for PPD diagnosis, facilitating early recognition and effective intervention.

Currently, in addition to traditional focuses on the neuroendocrine hormones and monoamine neurotransmitters, the role of routine examination indicators on PPD during pregnancy and after childbirth is becoming increasingly recognized. Research has shown that biological factors such as hemoglobin, hematocrit, and blood glucose levels are closely associated with the risk of PPD onset, providing valuable insights for prediction and intervention [20, 21]. In contrast to specialized and costly biochemical analyses, routine examinations such as complete blood counts, liver and kidney function tests can offer broader applicability and convenience

with lower costs [10]. Therefore, it is crucial to investigate biological factors from routine examinations for developing feasible early intervention strategies of PPD.

We conducted a cross-sectional study in Changsha, China, aiming to comprehensively explore the biological factors associated with PPD by analyzing data from complete blood counts, liver and kidney function tests, and infectious disease tests. Our findings hold the potential to uncover the underlying connections between PPD occurrence and biological factors identified through routine examinations, thereby providing a more scientifically grounded basis for the prevention and treatment of PPD.

2 Methods

2.1 Study participants

187 pregnant women who visited Central South University's Xiangya Third Hospital for routine checkups between October 2022 and December 2023 were included in this study. Eligibility criteria included current singleton pregnancy, normal thyroid function, normal pre-pregnancy serum lipid levels, and the ability to understand and independently complete the study questionnaire. Exclusion criteria included history of depression or mental illness, severe physical illness or head trauma prior to pregnancy, adverse obstetric outcomes during pregnancy (such as miscarriage, fetal abnormalities, stillbirth), inability to participate or withdrawal from the study due to physical discomfort, or having more than 20% missing data. Written informed permission was acquired by each subject. The Third Xiangya Hospital Ethics Committee at Central South University approved the study protocol (2022-S270).

2.2 Data collection

Data collection was carried out at the 6th week postpartum by a research team comprised of professionally trained personnel. Personal information of the participants, including age, height, weight, ethnicity, address, occupation, and household income, was collected through questionnaires. Additionally, biological data from postpartum complete blood count, liver and kidney function tests, and infectious disease tests were obtained from the hospital databases (as displayed in Table 1).

2.3 Postpartum depression

PPD was assessed six weeks after delivery using the Edinburgh Postnatal Depression Scale (EPDS), which is available in Chinese. [22]. The EPDS has ten items with a total score range of 0 to 30, each item having a score between 0 and 3. A higher probability of PPD is indicated by higher scores. With a stated sensitivity of 0.82 and specificity of 0.86, the Chinese version of the EPDS has proven to be valid and reliable and is comparable to the original scale's diagnostic accuracy [23]. PPD was defined in this study as having an EPDS score of 10 or above in relation to postnatal women.

2.4 Statistical analysis

Sample statistical properties are described using descriptive statistics, and continuous variable normality is assessed using the Shapiro-Wilk test. The terms mean (standard deviation) and median (interquartile range) are used to characterize continuous variables

Table 1: Biological factors collected from routine examinations.

Routine examination	Biological factor
Complete blood counts	RBC (red blood cell)
	Hb (hemoglobin)
	HCT (hematocrit)
	ABO (ABO blood group)
	Rh (Rhesus blood group)
Liver and kidney function tests	GLB(Globulin)
	A/G (albumin/globulin ratio)
	Cr (creatinine)
	ALB (albumin)
	BUN (blood urea nitrogen)
	ALT (alanine aminotransferase)
	AST (aspartate aminotransferase)
	UAL (uric acid)
	TBA (total bile acid)
	TP (total protein)
	GLU (glucose)
Infectious disease tests	HBsAg (hepatitis B surface antigen)
	HBsAb (hepatitis B surface antibody)
	HBeAg (hepatitis B e antigen)
	HBeAb (hepatitis B e antibody)
	HBcAb (hepatitis B core antibody)
	HBcAb-IgM (hepatitis B core antibody IgM)
	TPPA (treponema pallidum specific antibody)
	Anti-HCV (hepatitis C antibody)
	Anti-HIV (human immunodeficiency virus antibody)

that are regularly distributed and non-normally distributed. Using frequency (%), categorical variables are explained. We looked at the risk factors for PPD using univariate and multivariate logistic regression analysis. Using coefficients and 95% confidence intervals (CIs) for continuous variables and odds ratios (OR) and 95% CIs for categorical variables, the relationship between exposure and PPD is assessed. First and foremost, variables deemed statistically significant in identifying factors impacting PPD in the univariate analysis are those with a p-value of less than 0.1. Subsequently, the correlation between variables and PPD is then evaluated by collinearity analysis, which makes use of the variance inflation factor (VIF) as a diagnostic tool [24]. A VIF value below 5 signifies an absence of collinearity. Lastly, to ascertain the combined effect of variables chosen through univariate analysis on PPD, we utilize multivariate analysis, and variables that have a significance level of $p < 0.1$ are deemed statistically significant. Python 3.9 and Jupyter Notebook 6.4.8 were used for all statistical studies.

3 Results

3.1 Population characteristics

Among the 187 participants, 36 pregnant women (19.25%) are diagnosed with PPD. In addition to comparing the depression group (PPD) and the non-depression group (Non-PPD), Table 2 displays the demographic information for each participant. The participants' average age is 30.19 ± 3.51 years, with the majority (75.40%) having a household monthly income exceeding 6,000 yuan and nearly all

(99.47%) possessing an education level of high school or higher. Nationality and location of residence show substantial statistical differences from the depression and non-depression groups, however age, education level, occupation, and income do not show statistically significant differences.

3.2 A univariate logistic regression study of the biological variables that affect PPD

Table 3 displays the findings of the univariate analysis and descriptive statistics for the biological components causing PPD. It is found that factors associated with PPD include the Cr levels (coef = 0.03, 95% CI: 0.00-0.07), the HCT levels (coef = -0.07, 95% CI: -0.15-0.01), the presence of HBsAg (OR = 3.58, 95% CI: 1.16-11.06), the presence of HBeAb (OR = 2.55, 95% CI: 0.87-7.42), and the presence of HBcAb (OR = 2.88, 95% CI: 0.88-9.41). The VIF for collinearity analysis of these related variables, namely Cr, HCT, HBsAg, HBeAb, and HBcAb, are 1.06, 1.01, 1.79, 1.27, and 1.81, respectively, indicating low levels of multicollinearity among these factors.

3.3 A multivariate logistic regression study of the biological variables that affect PPD

Table 4 presents the findings of the multivariable analysis for the biological parameters that are of concern. The results show a significant connection between HCT levels and PPD (coef = -0.07, 95% CI: -0.15-0.01). After adjusting all variables, other factors such

Table 2: Sample characteristics.

Characteristics	ALL(N=187)	Non-PPD(N=151)	PPD(N=36)	P-value
Age, year	30.19±3.51	30.3±3.65	29.72±2.79	0.37
Nation, n (%)				
Han nationality	178 (95.19%)	147 (97.35%)	31 (86.11%)	0.02 **
Minority	9 (4.81%)	4 (2.65%)	5 (13.89%)	
Residence, n (%)				
Rural	8 (4.28%)	8 (5.30%)	0 (0.00%)	0.00 ***
Town	19 (10.16%)	9 (5.96%)	10 (27.78%)	
City	160 (85.56%)	134 (88.74%)	26 (72.22%)	
Education level, n (%)				
Undergraduate or above	111 (59.36%)	88 (58.28%)	23 (63.89%)	0.72
Junior college	56 (29.95%)	45 (29.80%)	11 (30.56%)	
High school	19 (10.16%)	17 (11.26%)	2 (5.56%)	
Junior high school and below	1 (0.53%)	1 (0.66%)	0 (0.00%)	
Occupation, n (%)				
Worker	3 (1.60%)	3 (1.99%)	0 (0.00%)	0.68
Farmer	2 (1.07%)	2 (1.32%)	0 (0.00%)	
Administrative workers	29 (15.51%)	25 (16.56%)	4 (11.11%)	
Service workers	24 (12.83%)	19 (12.58%)	5 (13.89%)	
Professional technical workers	44 (23.53%)	37 (24.50%)	7 (19.44%)	
other	85 (45.45%)	65 (43.05%)	20 (55.56%)	
Per capita monthly income of households, n (%)				
≤4000	8 (4.28%)	6 (3.97%)	2 (5.56%)	0.59
4001-6000	38 (20.32%)	28 (18.54%)	10 (27.78%)	
6001-8000	49 (26.20%)	40 (26.49%)	9 (25.00%)	
>8000	92 (49.20%)	77 (50.99%)	15 (41.67%)	

*** <0.01, ** <0.05, * <0.10.

as Cr, HBsAg, HBeAb, and HbCAb, which were significant in the univariate analysis are no longer statistically significant.

4 Discussion and Conclusion

This study employed a cross-sectional design and utilized both univariate and multivariate analysis methods to investigate the correlation between PPD and biological factors obtained from routine examinations. Routine postpartum examinations encompassed complete blood count, liver and kidney function tests, and infectious disease tests. Our findings reveal a correlation between lower postpartum HCT levels and PPD. However, subsequent multivariate analysis adjustments indicated that higher levels of Cr, HBsAg, HBeAb, and HbCAb are not significantly associated with PPD.

In previous studies, the association between HCT levels and PPD has been less extensively explored. A prior study noted that an elevated HCT during late pregnancy serves as a biomarker for postpartum depression and anxiety symptoms [20]. However, our findings demonstrate that pregnant women with lower levels of HCT have a higher risk for PPD. One possible explanation is that low HCT levels imply a reduced oxygen-carrying capacity in the blood, leading to insufficient oxygen supply, which may impact brain function and emotional regulation [25]. Additionally, a low HCT level may be correlated with other physical and psychological

factors such as anemia, nutritional deficiencies, and poor postpartum physical recovery, all of which could potentially increase the risk of PPD [26]. Thus, preserving optimum HCT levels may help lower the risk of PPD. However, more study is necessary to fully comprehend the precise mechanisms at play.

5 Limitations and Future Research

Although this study yielded some preliminary results about the association between hematocrit levels and PPD, it has a number of shortcomings that need to be investigated further in further investigations.

Firstly, the small sample size is a significant limitation. When identifying correlations between variables, a limited sample size might result in significant mistakes, which can compromise the conclusions' robustness and generalizability. Subsequent research endeavors ought to contemplate augmenting the sample size through extensive sample procurement across various centers and regions. This approach would enhance statistical power and increase the reliability and generalizability of the results, ensuring that the findings can be widely applied to diverse populations.

Secondly, the lack of longitudinal data collection limits the exploration of causal relationships. It is challenging to demonstrate causality because this study uses a cross-sectional methodology, which can only show the relationship between hematocrit levels

Table 3: The relationship between a few chosen variables and PPD as determined by univariate logistic regression.

Variables	Non-PPD(N=151)	PPD(N=36)	Odd Ratio/Coefficient (95% CI)	P-value
Liver and kidney function tests				
GLB	24.90 [23.00, 26.80]	24.75 [23.13, 26.35]	-0.03 (-0.15, 0.09)	0.64
A/G	1.30 [1.20, 1.45]	1.35 [1.20, 1.50]	0.28 (-1.76, 2.32)	0.79
Cr	46.00 [40.00, 51.00]	46.00 [42.50, 53.25]	0.03 (0.00, 0.07)	0.09*
ALB	33.70 [31.60, 35.75]	34.40 [31.08, 36.18]	-0.03 (-0.10, 0.04)	0.40
BUN	3.12 [2.63, 3.59]	3.36 [2.73, 4.04]	-0.01 (-0.08, 0.06)	0.79
ALT	10.00 [7.50, 12.50]	10.00 [8.00, 13.00]	-0.02 (-0.08, 0.03)	0.42
AST	18.00 [15.00, 22.00]	19.50 [16.00, 22.00]	-0.01 (-0.05, 0.03)	0.77
UAL	315.00 [270.50, 360.50]	320.00 [282.25, 359.50]	0 (0.00, 0.01)	0.45
TBA	3.10 [2.20, 4.60]	3.25 [1.88, 5.13]	-0.01 (-0.04, 0.03)	0.73
TP	58.70 [55.60, 62.50]	58.69 [54.58, 61.20]	-0.01 (-0.03, 0.02)	0.57
GLU	4.00 [3.62, 4.42]	4.02 [3.70, 4.36]	-0.01 (-0.54, 0.52)	0.97
Complete blood count				
RBC	3.75 [3.46, 4.10]	3.73 [3.49, 3.95]	-0.27 (-1.11, 0.58)	0.53
HCT	35.80 [33.10, 38.10]	35.00 [32.53, 37.23]	-0.07 (-0.15, 0.01)	0.08*
Hb	116.00 [106.50, 125.00]	113.00 [104.75, 123.50]	-0.01 (-0.02, 0.01)	0.44
ABO, n (%)				
A	50 (33.11%)	11 (30.56%)	1.16 (0.46, 2.9)	0.75
B	35 (23.18%)	10 (27.78%)	1.51 (0.58, 3.91)	0.40
O	58 (38.41%)	11 (30.56%)	Reference	
AB	8 (5.30%)	4 (11.11%)	2.64 (0.68, 10.3)	0.16
Rh, n (%)				
Rh+	148 (98.01%)	36 (100.00%)	Reference	
Rh-	3 (1.99%)	0 (0.00%)	0 (0, inf)	1.00
Infectious disease tests				
HBsAg, n (%)				
No	143 (94.70%)	30 (83.33%)	Reference	
Yes	8 (5.30%)	6 (16.67%)	3.58 (1.16, 11.06)	0.03**
HBsAb, n (%)				
No	53 (35.10%)	12 (33.33%)	0.92 (0.43, 2)	0.84
Yes	98 (64.90%)	24 (66.67%)	Reference	
HBeAg, n (%)				
No	148 (98.01%)	34 (94.44%)	Reference	
Yes	3 (1.99%)	2 (5.56%)	2.90 (0.47, 18.05)	0.25
HBeAb, n (%)				
No	140 (92.72%)	30 (83.33%)	Reference	
Yes	11 (7.28%)	6 (16.67%)	2.55 (0.87, 7.42)	0.09*
HBcAb, n (%)				
No	143 (94.70%)	31 (86.11%)	Reference	
Yes	8 (5.30%)	5 (13.89%)	2.88 (0.88, 9.41)	0.08*
HBcAb-IgM, n (%)				
No	146 (96.69%)	35 (97.22%)	Reference	
Yes	5 (3.31%)	1 (2.78%)	0.83 (0.09, 7.37)	0.87
TPPA				
No	151 (100.00%)	36 (100.00%)	-	-
Yes	0 (0.00%)	0 (0.00%)	-	-
Anti-HCV, n (%)				
No	150 (99.34%)	36 (100.00%)	Reference	
Yes	1 (0.66%)	0 (0.00%)	0 (0, inf)	1.00
Anti-HIV, n (%)				
No	151 (100.00%)	36 (100.00%)	-	-
Yes	0 (0.00%)	0 (0.00%)	-	-

*** <0.01, ** <0.05, * <0.10.

Table 4: The relationship between a few chosen variables and PPD as determined by multivariable logistic regression.

Variables	Odd Ratio/Coefficient (95% CI)	P-value
HBsAg		
No	Reference	
Yes	1.70 (0.34, 8.64)	0.52
HBeAb		
No	Reference	
Yes	1.93 (0.53, 6.98)	0.32
HBcAb		
No	Reference	
Yes	1.28 (0.23, 6.98)	0.78
Cr	1.03 (0.99, 1.07)	0.13
HCT	-0.07 (-0.15, 0.01)	0.08**

*** <0.01, ** <0.05, * <0.10.

and PPD at particular point in time. Future research should consider implementing a longitudinal study design, tracking changes in hematocrit levels and their relationship with PPD development over time within the same cohort. This would enable a more precise explanation of the causative function of hematocrit levels in PPD, as well as a better knowledge of the direct influence of biological factors on the progressive development of PPD over time.

Additionally, the study's failure to adequately control for confounding variables is another important limitation. Confounding factors such as nutritional status and pre-existing medical conditions, which may influence the relationship between hematocrit levels and PPD risk, were not sufficiently controlled in the analysis. These confounders might obscure or exaggerate the true impact of hematocrit levels on PPD risk. Future research should employ more rigorous statistical models and control methods, such as propensity score matching, to effectively manage these confounding variables. This would allow for a more precise isolation of the specific impact of hematocrit levels on PPD risk.

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