

ORIGINAL RESEARCH ARTICLE

Changes in core depressive symptoms over time
in peripartum women: A network analysisYuqun Zhang¹, Ju Gao², Meixia Qin³, Weiying Zhao³, Yi Ding⁴, and Xin Yue^{4*}¹Department of Humanities and Nursing, School of Nursing, Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China²Department of Psychiatry, Institute of Mental Health, Suzhou Psychiatric Hospital, the Affiliated Guangji Hospital of Soochow University, Suzhou, Jiangsu, China³Department of Obstetrics and Gynecology, Jiangbei Campus, Zhongda Hospital, Southeast University, Nanjing, Jiangsu, China⁴Department of Obstetrics and Gynecology, The Second Hospital of Nanjing, Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China

Abstract

Perinatal depression (PND) is a prevalent mental health condition that affects women during pregnancy and after childbirth. Distinct clinical subtypes of PND exist, with the timing of symptom onset being a pivotal element in the classification of these subtypes. However, the specific manifestations of PND across the various stages of pregnancy and the postpartum period remain to be elucidated. This study aimed to explore the changes in depression symptoms with the stage of pregnancy. Women in their second ($n = 161$) and third trimesters ($n = 248$) of pregnancy as well as those in their first 6 weeks of the postpartum period ($n = 110$) were recruited. Each patient was evaluated using the Edinburgh Postnatal Depression Scale. A network analysis approach was used to explore the interconnections among depressive symptoms across the different time periods. Women in the postpartum period exhibited the most pronounced prevalence of PND and severity of depressive symptoms. In the second and third trimesters, "sadness and misery" was the most central symptom. However, its prominence diminished after childbirth. "Fear and panic" was the predominant symptom in the postpartum network. The structural integrity of PND symptom networks was maintained across all three periods, with consistent strength and closeness. This study demonstrates the temporal evolution of PND's central symptoms in women during and after pregnancy, transitioning from depression-centric to anxiety-centric manifestations. These findings advocate for symptom-specific interventions to enhance the mental well-being of mothers and their offspring. Furthermore, this study offers clinical insights into the biological underpinnings of PND subtypes, facilitating precise diagnosis and targeted treatment strategies.

Keywords: Perinatal depression; Different periods; Central symptoms; Network analysis; Subtype

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Citation: Zhang Y, Gao J, Qin M, Zhao W, Ding Y, Yue X. Changes in core depressive symptoms over time in peripartum women: A network analysis. *J Clin Basic Psychosom.* 2024;2(4):4089. doi: 10.36922/jcbp.4089

Received: June 30, 2024**Accepted:** September 3, 2024**Published Online:** October 17, 2024

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1. Introduction

Perinatal depression (PND) is characterized by depressive episodes experienced by women during pregnancy (antenatal depression [AND]) as well as in the initial 12 months

postpartum (postpartum depression [PPD]).¹ According to epidemiological studies, the prevalence of PND among women ranges from 13.3% to 19.7%.^{2,3} However, according to a meta-analysis, the incidence of AND is higher at 20.7%,⁴ and patients in their second and third trimesters are particularly vulnerable to AND.¹ Globally, PPD is projected to impact approximately 17.22% of women,⁵ and it usually manifests within 6 weeks of childbirth.⁶ Women with PND face an elevated risk of self-harm and suicide as well as challenges in parenting and marital relationships. The risk is particularly pronounced among women who have utilized donor sperm for conception, possess restricted educational and financial means, lack sufficient social support, and have experienced previous episodes of depression disorders.^{1,7,8} Furthermore, PND can impact the early brain development of infants, with effects on cognition becoming apparent in primary schooling.⁹ PND also increases the risk of depression in the spouse,¹⁰ thus placing a significant burden on families and society.

PND represents a diverse clinical entity, encompassing various subtypes that exhibit distinct symptom profiles and onset patterns at different stages of pregnancy and the postpartum phase.^{11,12} Investigating the onset timing is crucial for delineating more accurate phenotypic classifications as well as for biological and genetic studies of PND. For example, although PND typically emerges either in the final trimester of pregnancy or within the first 6 weeks following childbirth,¹ the underlying contributing factors differ. PND onset in the postpartum period is a subtype sensitive to sex hormone fluctuations, as sex hormone levels decline rapidly from high peaks after childbirth. Conversely, PND onset in the third trimester is not hormone-sensitive.¹³

The biological mechanisms underlying the variance in the central symptoms and severity of PND in different periods of pregnancy remain to be elucidated. Previous studies have only addressed the differences in depression severity between AND and PPD.^{11,14} In these studies, individuals from different trimesters were grouped together in the AND group, and the core symptoms of PND at each stage were not clarified. Identifying the core symptoms associated with PND subtypes is essential because it can enhance the development of more efficacious intervention strategies.

Employing a novel network analysis approach can provide deeper insights into the pivotal symptoms of PND and their interplay with other symptoms across various time frames. Network theory posits that central symptoms, due to their extensive connections with other symptoms, are instrumental in the etiology, perpetuation, and resolution of mental health disorders.¹⁵ This methodology

circumvents the limitations of conventional methods by identifying the most salient symptoms of psychiatric conditions.¹⁶⁻¹⁸ For example, network analysis has revealed that the most central symptoms in individuals diagnosed with obsessive-compulsive disorder are compulsive behaviors and obsessive thoughts.¹⁹ Wang *et al.*¹⁸ applied network analysis to discern shifts in the central symptoms of depression and anxiety from the onset to the post-peak period of the COVID-19 pandemic; their findings highlighted the evolving central characteristics over time. Consistent with network theory, these symptoms exhibit intricate causal interconnections, which are best understood from a causal systems perspective.²⁰ Thus, the identification of network characteristics through this innovative analytical instrument may yield significant clinical benefits for the diagnosis, treatment, and prevention of mental disorders. However, studies on PND have only analyzed the relationships between specific risk factors and depressive symptoms during pregnancy and the postpartum period,^{21,22} or have only exhibited the network structure of depression in the second trimester.²³ The changes in network characteristics in the different trimesters and postpartum period remain to be explored.

The current study aimed to assess the variations in the depressive severity among women in their second trimester, third trimester, and postpartum period to better understand how the core symptoms of PND change over time, especially during high-risk periods for depression. Furthermore, we aimed to estimate the networks of depressive symptoms of PND at different time periods to collect evidence for the precise diagnosis and treatment of PND subtypes. In addition, we aimed to propose recommendations for enhancing the psychological well-being of women throughout pregnancy and the postpartum period. This study is the first to employ network analysis on a cohort of women across various pregnancy stages and the postpartum period, aiming to explore symptom interactions of depression and examine symptom evolution over time. We hypothesized that the network characteristics of depression symptoms would change over the three time periods and that depression severity would significantly differ between the three groups.

2. Methods

2.1. Participants and procedure

The Wenjuanxing platform (Zhongyan Network Technology Co., Shanghai, China) was utilized to facilitate an online survey. The QR code for the online survey was disseminated across platforms such as Intent, WeChat, and Tencent QQ. Women aged 19–49 years who could read and operate a computer or smartphone were recruited from two centers

(Zhongda Hospital, affiliated to the Southeast University, and Nanjing Hospital, affiliated to the Nanjing University of Chinese Medicine) between May 2022 and March 2023. The participants were categorized into three groups based on their pregnancy phase: the second-trimester group (161 women), third-trimester group (248 women), and postpartum group (110 women). This study was approved by the Ethics Committee of Zhongda Hospital (No. 2020ZDSYLL230-P01; October 27, 2020). All participants had to provide and sign a written informed consent available online.

2.2. Instrument

The Edinburgh Postnatal Depression Scale (EPDS)²⁴ is a well-established instrument for detecting depressive symptoms in both pregnant and postpartum women. This 10-item questionnaire utilizes a self-assessment scale wherein each item is rated from 0 (most of the time) to 3 (not at all). The total score can vary from 0 to 30. A total score of ≥ 10 suggests the presence of depression, and an elevated total score is indicative of more pronounced depressive symptoms.²⁵

2.3. Statistical analyses

Statistical analyses were conducted using SPSS software (version 21.0; IBM Corporation, Armonk, NY, USA). One-way analysis of variance (ANOVA) was used to compare the age and EPDS scores among groups. Bonferroni correction was used to perform a post-hoc analysis of the groups. The Chi-square test was employed to assess differences in depression prevalence. A p -value of < 0.05 was indicative of statistical significance. All network analyses were performed using R (version 4.2.1).

2.3.1. Network estimation

The symptom networks were depicted through network diagrams, including the overall EPDS network for all participants as well as the EPDS networks specific to each time period. Within these diagrams, “nodes” corresponded to the variables, whereas “edges” signified the correlations existing between them.²⁶ A least absolute shrinkage and selection operator Gaussian graphical model was applied to infer the structure of the symptom networks, and pairwise correlations delineated the associations among the variables.²⁷ The selection of the optimal network configuration was guided by the extended bayesian information criterion.²⁸ For executing this analysis, the “bootnet” R package’s “estimateNetwork” function was used, employing “EBICglasso” as the standard approach for network estimation.²⁹

2.3.2. Network centrality

The “qgraph” package in R, specifically its “centrality plot” function, was used to ascertain the network’s centrality

metrics.³⁰ These metrics included strength, betweenness, closeness, and expected influence (EI), which are integral to characterizing the network’s architecture.¹⁸ Strength was calculated as the aggregate weight of edges connected to each node. Betweenness quantified the frequency with which a node lay on the shortest path between pairs of nodes. Closeness was determined as the inverse of the mean distance from a particular node to all other nodes. EI represented the cumulative weight of the edges emanating from a given node.

2.3.3. Network stability

The resilience of the network solution, including the precision of edge weights and the reliability of centrality measures, was assessed using the “bootnet” R package.²⁶ Network stability was gauged through a bootstrapping procedure that involved 2500 resampling iterations, with 95% confidence intervals (CIs).¹⁶ A wider CI indicated a lower precision in edge weights, whereas a narrower CI indicated a more dependable network structure.²⁹ The inclusion of “0” within the range of the constructed CIs signified the absence of statistically significant differences in edge weights (or node strength) among distinct symptoms.

To assess the stability of the centrality indices using a case-dropping subset bootstrap method,¹⁶ the correlation stability (CS) coefficient was determined. The network’s structure was deemed stable if the CS coefficient remained high even after eliminating a subset of cases. An exemplary CS value should approach 0.7, indicating a 95% likelihood that the correlation would remain 0.7 even after removing the maximum allowable proportion of cases.²⁹ Furthermore, the CS value should not drop below 0.25, and it should ideally be > 0.5 .

3. Results

3.1. Demographic characteristics and depressive symptoms

Figure 1 and Table S1 depict the age and EPDS scores during the three time periods. No significant difference in age was found between the three groups ($P > 0.05$). The prevalence of depression in all participants was 32.18%, with the highest prevalence in the postpartum group (45.45%), followed by the second trimester (27.33%) and third trimester (29.44%) groups. Similarly, the postpartum group exhibited the highest total scores, both depression and anxiety scores, and the highest scores for each item of the EPDS (all $P < 0.05$, Bonferroni correction), except for items 5, 7, and 10 ($P > 0.05$).

3.2. Network estimation and centrality

Figure 2 depicts the depression network and the EI of all participant data. Except for EPDS10 (“self-harm”)

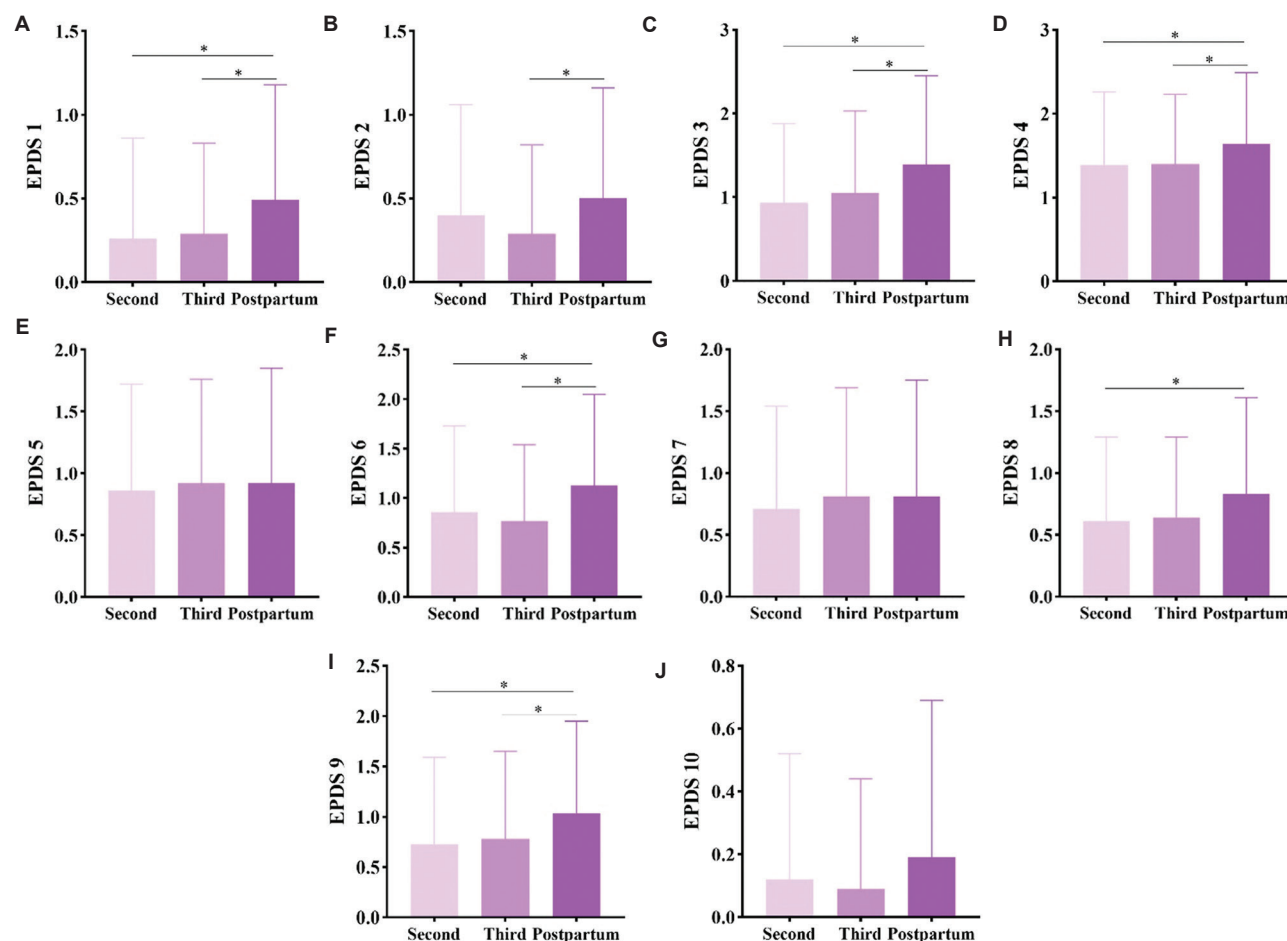


Figure 1. Score of each item on the EPDS in the three study groups. (A-J) Represent comparison of scores at different stages of the EPDS for items 1 to 10, respectively.

Note: * $P < 0.05$ (Bonferroni correction), when compared with the postpartum group.

Abbreviation: EPDS: Edinburgh Postnatal Depression Scale.

and EPDS3 (“self-accusation”), the other depressive symptoms were strongly interconnected within this network, as evidenced by their elevated EI. The networks for the three time periods displayed varied configurations (Figure 3A-C), as reflected by the quantity and intensity of the edges. Figure 3D shows the EI for the networks corresponding to the second trimester, third trimester, and postpartum period. The node EPDS8 (“sadness and misery”) emerged with the highest EI in the depression network models for both the second and third trimesters. However, the node EPDS5 (“fear and panic”) exhibited the highest EI in the postpartum network model. In addition, almost all nodes, especially the nodes EPDS8 (“sadness and misery”), EPDS5 (“fear and panic”), and EPDS4 (“worrying”), exhibited a relatively high strength in all the time periods (Figure S1), indicating the critical role of these symptoms in the networks.

The detailed edge weights are enumerated in Tables S2-S4. In the second trimester network, the most robust correlation was observed between EPDS4 (“worrying”) and EPDS5 (“fear and panic”), followed by correlations between EPDS1 (“laughter and interest”) and EPDS2 (“looking forward to the future”) and between EPDS7 (“unhappiness and insomnia”) and EPDS8 (“sadness and misery”). Similarly, the strongest association in the third-trimester network was observed between EPDS4 (“worrying”) and EPDS5 (“fear and panic”), followed by the associations between EPDS8 (“sadness and misery”) and EPDS9 (“unhappiness and crying”) and between EPDS1 (“laughter and interest”) and EPDS2 (“looking forward to the future”). In the postpartum network, the most significant association was identified between EPDS4 (“worrying”) and EPDS5 (“fear and panic”), followed by the associations between EPDS1 (“laughter and interest”)

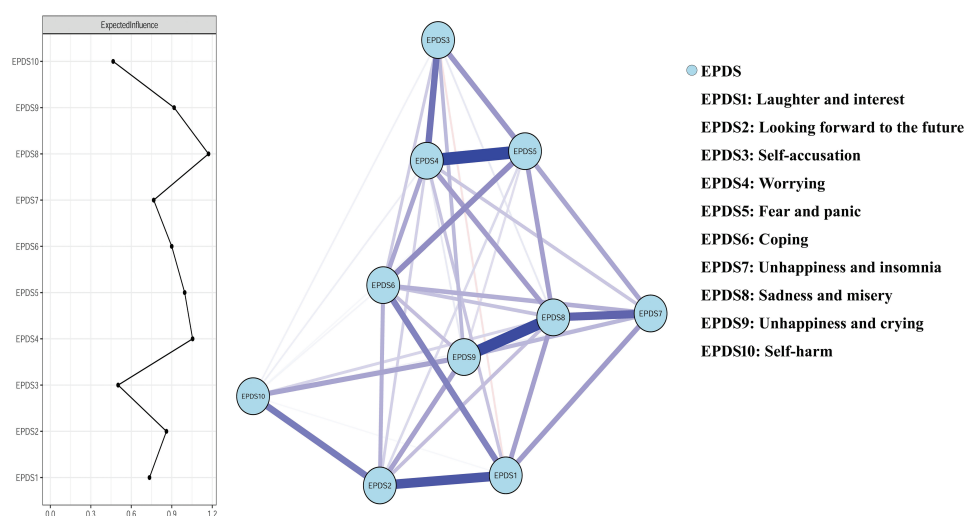


Figure 2. The network of all participants. The expected influence statistics and the network model of depressive symptoms in all participants are shown. Blue nodes represent EPDS items. Blue edges represent positive correlations between nodes, and red edges represent negative associations between nodes. Abbreviations: EPDS: Edinburgh Postnatal Depression Scale.

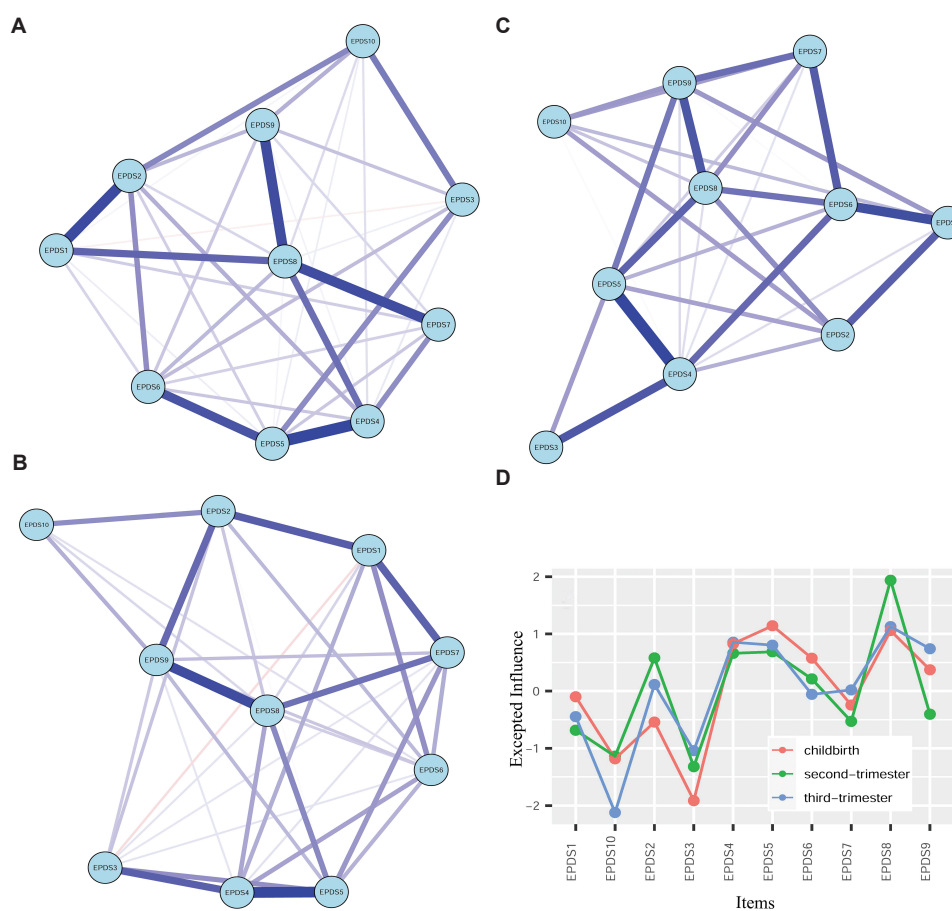


Figure 3. Depressive symptom networks and the expected influences in the 3 time periods. Depressive symptom networks during the (A) second trimester, (B) third trimester, and (C) postpartum period. Blue nodes represent EPDS items. Blue edges represent positive correlations between nodes, and red edges represent negative associations between nodes. (D) The graph depicts the differences in expected influence between the three time periods. Abbreviations: EPDS: Edinburgh postnatal depression scale.

and EPDS6 (“coping”) and between EPDS8 (“sadness and misery”) and EPDS9 (“unhappiness and crying”).

3.3. Network stability

Figure 4 depicts the stability of the depressive symptom networks in the second trimester, third trimester, and postpartum period, indicating that both the strength and closeness of the networks were relatively consistent. In the second trimester network, the strength ($CS_{cor=0.7} = 0.441$) exhibited an acceptable level of stability, whereas the closeness ($CS_{cor=0.7} = 0.205$) exhibited poor stability. In the third trimester network, the strength ($CS_{cor=0.7} = 0.516$) exhibited good stability, and the closeness exhibited acceptable stability. In the postpartum network, the stability of both strength ($CS_{cor=0.7} = 0.364$) and closeness ($CS_{cor=0.7} = 0.364$) were acceptable. However, the betweenness exhibited great instability at all time periods (second trimester: $CS_{cor=0.7} = 0.13$; third trimester: $CS_{cor=0.7} = 0$; and postpartum: $CS_{cor=0.7} = 0$). Furthermore, the stability of the edge-weights precision was validated using the bootstrap method (Figure S2).

4. Discussion

The current study investigated the prevalence and severity of PND across various pregnancy stages and the postpartum phase. It also aimed to identify and elucidate the PND subtypes by evaluating the central depressive symptoms and their associations with other symptoms. We found that women in the postpartum period exhibited the highest rates and most intense manifestations of depression and anxiety compared to those in the second and third trimesters. The network analysis revealed that “sadness and misery” (EPDS8) exhibited the most pronounced centrality in the second and third-trimester networks as well as in the network that included all participants. However, “fear and panic” (EPDS5) emerged as the most central symptom in

the postpartum network. The stability of the strength and closeness in all three PND networks was maintained.

Depression was most prevalent in the postpartum period, which is consistent with the finding of a study from Korea.³¹ Because a proportion of women with PPD may have experienced depressive symptoms during or before pregnancy,⁶ the prevalence of PPD would increase over time. However, other studies have reported a lower prevalence of PPD (11.7 – 23%).^{5,32,33} This may be attributed to the different criteria used to define postpartum. In this study, we used 6 weeks postpartum as the criteria of PPD, which is according to the International Statistical Classification of Diseases (10th Revision), and more specifically to refer to the high-risk time period for PPD. However, previous studies have employed the World Health Organization criteria, which extends the postpartum period to 12 months.¹⁴ The diagnostic definition of PPD remains controversial because its complex mechanisms results in diverse clinical features. Furthermore, there may be specific PPD subtypes, which would account for the variation in prevalence. For example, rapid changes in reproductive hormone levels occur only within the first 6 weeks of the postpartum period, which is an important factor that triggers PPD.³⁴ Therefore, the mechanism underlying the onset of the onset of PPD after 6 weeks, which would result in different depressive features and prevalence, should be evaluated.

Similar to the prevalence of PND, most of the items on the EPDS exhibited the highest scores in the postpartum period in our study, indicating that depression is the most severe within 6 weeks after childbirth. In a previous study, depressive symptoms during pregnancy and 4 weeks postpartum were compared in Chinese women; the results suggested that there are more preterm births and lower birth weights in women with depression onset in the postpartum period than in those during pregnancy.³⁵ Infant health, breastfeeding demands, diminished

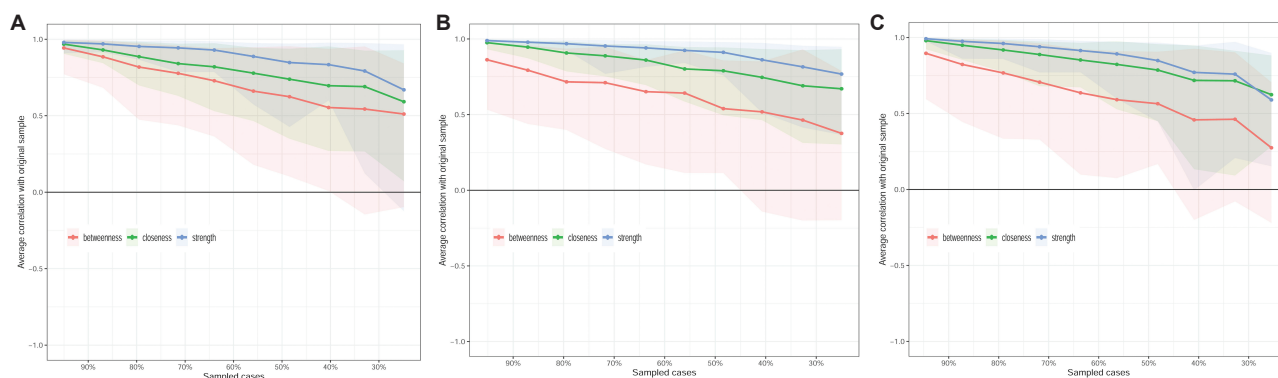


Figure 4. Stability of network structures. The stability of second trimester, third trimester, and postpartum networks is shown in (A–C), respectively. The x-axis represents the included proportion of cases, and the y-axis represents the average correlation between the original and estimated centrality indices after excluding the proportions of cases. Different colored lines indicate different centrality while the shading indicates the 95% confidence interval

personal time, and shifts in the partner relationship, including sexual relationship, may be added stressors in women after childbirth.³⁶ Moreover, approximately 31% of women with PPD have suicidal ideations.³⁷ In addition to environmental risk factors, biological factors play an important role in the development of PPD. For example, the estrogen receptor gene is a trigger for PPD, which has been associated with EPDS scores in women in the postpartum period.³⁸ Furthermore, although more severe depressive symptoms have been observed in women with PPD than in those with AND, the cause remains unclear. However, differences in psychotherapy effectiveness between PPD and AND have been considered as the cause for the difference in depression severity.³⁹ Therefore, the differences in specific depressive symptoms between the different periods should be identified to better understand the biological mechanisms of PND subtypes.

Consistent with a previous study's finding, we found that most symptoms of depression have high centrality during pregnancy.²² In the current study, "sadness and misery" and "looking forward to the future" were the most central depressive symptoms in the second trimester. However, the centrality of these symptoms decreased in the third trimester and the postpartum period, indicating that women experienced lower negative moods during postpartum. Conversely, "fear and panic," as one of the most central anxiety symptoms, exhibited the highest centrality in the postpartum period, indicating an increase in women's anxiety after childbirth. The depression symptoms undergo a temporal shift, transitioning from depression-centric to anxiety-centric manifestations. Depression and anxiety can develop concurrently,⁴⁰ impacting 75% of women during the postpartum period.⁴¹ This comorbidity status may complicate the identification of PND subtypes because depression and anxiety share some biological mechanisms.⁴² Furthermore, depression and anxiety are substantially associated with the genetics of female reproductive system disorders.⁴³ Therefore, it may be more accurate to focus on the individual items or subscales of the EPDS, rather than the entire scale, to assess PND symptoms throughout a woman's pregnancy. Putnam *et al.*¹¹ reported that there are three underlying dimensions and five distinct clinical subtypes of PND that are measured using the EPDS, with different levels of anxious depression being subdivided into these five subtypes.

Depression with features of anxiety is characterized by distinct neurobiological signatures when contrasted with depression without anxiety. Furthermore, individuals with anxious depression are more prone to recurrent major depressive episodes and exhibit an elevated

risk of suicidal thoughts than those with non-anxious depression.⁴⁴ This may account for the central symptoms and higher prevalence and more severe symptoms in the postpartum period than during pregnancy in the present study. Therefore, we propose that more anxiety-centric interventions be administered to women with PPD and more depression-centric interventions be administered to women with AND. A meta-analysis reported that the effect of psychological therapy is highly heterogeneous,³⁹ which may be attributed to the PND subtypes and their different clinical features. However, psychological therapy is effective and should be considered the first-line treatment for PND.⁴⁵ Thus, identifying PND subtypes before the implementation of targeted psychological therapy may improve the consistency of treatment efficacy.

This study had several limitations that warrant recognition. First, the participant pool was not a randomly selected large-scale sample, and symptom data were collected during a particular phase. Moreover, women in their first trimester were not included in this study. Thus, the results may be applicable only to Chinese women in their second or third trimester and those in the postpartum period (within 6 weeks after birth). Future studies should focus on women throughout their pregnancy as well as during the postpartum period to explore the changes in core depressive symptoms. Second, depressive symptoms were not limited to the time of onset in different time periods. The determination of the time of onset may be more indicative of the core symptoms. Third, although this study provides valuable insights into the temporal evolution of the psychological network, the analytical methods employed could not reveal the underlying causal mechanisms. Therefore, the relationships between the networks may be considered bi-directional due to their non-directional nature. However, examining how core symptoms change over time in pregnant and postpartum Chinese women is a novelty of this study. Our study findings have important implications for the identification of PND subtypes and the selection of appropriate interventions for depression during pregnancy and the postpartum period.

5. Conclusion

This is the first study to examine the changes in depressive core symptoms over time in pregnant and postpartum women. The study findings provide valuable information for understanding the interplay between PND symptoms. We identified network configurations between the second and third trimesters and the postpartum period, which revealed a temporal progression in core symptoms from depression-centric to anxiety-centric dominance. Therefore, to improve the mental health of mothers,

fetuses, and infants, more symptom-specific interventions should be used. Collectively, our findings provide clinical evidence for the evaluation of the biological mechanisms of PND subtypes and for the precision in PND diagnosis and treatment.

Acknowledgments

We thank all the participants in this study.

Funding

This work was funded by the Qing Lan Project of Jiangsu Higher Education Institutions, Jiangsu Government Scholarship for Overseas Studies (grant number, 2020-039), National Natural Science Foundation of China (grant number, 82001426), School-based Youth Project Funding (grant number, NZY82001426) and Doctoral Talent Program of Suzhou Guangji Hospital (2022B01).

Conflict of interest

Yuqun Zhang is an Editorial Board Member of this journal but was not in any way involved in the editorial and peer-review process conducted for this paper, directly or indirectly. Separately, other authors declared that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

Author contributions

Conceptualization: Xin Yue

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Writing—review & editing: Xin Yue

Ethics approval and consent to participate

Conducted in adherence to the ethical guidelines of the Declaration of Helsinki, this study received clearance from the Zhongda Hospital Ethics Committee (No. 2020ZDSYLL230-P01). All participants provide written informed consent before their participation.

Consent for publication

All participants gave written consent to publish their data in this study.

Availability of data

The data sets utilized and examined within the scope of this study are accessible upon reasonable request to the corresponding author.

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