Iran J Public Health, Vol. 54, No.10, Oct 2025, pp.2212-2222

Original Article

Causal Relationship between Immune Cells and Postpartum Depression: A Bidirectional Two-Sample Mendelian Randomization Study

†Yingjia Zhu [1], †Feng Cheng [2], Wenhui Wang [3], Xinyun Yang [4], Mingjie He [5], Zhiyin Zhang [1], *Linling Zhu [1]

1. *Department of Gynecology, Hangzhou Women's Hospital, Hangzhou, Zhejiang, 310000, China*
2. *Department of Orthopedics, The Third Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou, Zhejiang, 310000, China*
3. *Department of Pathology, Hangzhou Women's Hospital, Hangzhou, Zhejiang, 310000, China*
4. *Department of Reproductive Endocrinology, Women's Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, 310000, China*
5. *Department of General Practice, Yiqiao Community Health Service Center, Hangzhou, Zhejiang 310000, China*

***Corresponding Author:** Email: vvzoo@163.com
†These authors contributed equally to this

(Received 17 Feb 2025; accepted 26 Apr 2025)

Abstract

Background: Postpartum depression (PPD) is influenced by immune factors, particularly immune cells. The causal relationship between these cells and PPD is unclear.

Methods: Bidirectional two-sample Mendelian randomization (TSMR) analysis was performed to determine the causal relationship between immune cell characteristics and PPD. The main analysis method used was the inverse variance weighted (IVW) method. To ensure the robustness, heterogeneity, and horizontal pleiotropy of the results, a comprehensive sensitivity analysis was conducted.

Results: Overall, 28 immune cell phenotypes were identified as causally related to the onset of PPD. Most of them were distributed in the B cell group and the Treg cell group. Further analysis revealed that 13 types of immune cells had a promoting effect on PPD, whereas 15 types of immune cells had a protective effect. In addition, the incidence of PPD was found to be causally related to CD62L on granulocyte [IVW: OR (95%): 1.183 (1.037 to 1.348), P = 0.012].

Conclusion: The study unveils the causal link between immune cells and susceptibility to postpartum depression from a genetic standpoint, providing new directions for drug development and precision medicine for PPD treatment.

Keywords: Postpartum depression; Immune cells; Causal inference; Genetic variation; Mendelian randomization

Introduction

Postpartum depression (PPD) is an emotional disorder occurring after childbirth, characterized by low mood, loss of interest, anxiety, irritability, sleep issues, appetite changes, difficulty concentrating, and feelings of helplessness (1). About 10%-15% of postpartum women may be diag-

DOI: https://doi.org/10.18502/ijph.v54i10.20139

nosed with PPD, with over half experiencing symptoms within the first week (2). PPD can adversely affect physical and mental health and, in severe cases, pose a life threat (3). Therefore, finding new early diagnostic methods and novel therapeutic targets is currently a research focus (4).

PPD is associated with immune cell activation and increased inflammatory response, although our understanding of this relationship is still incomplete (5). Research has found that women with PPD show increased activation of the immune system and inflammatory response (6). Excessive immune activation can cause body-wide inflammation and contribute to diseases. In PPD, immune cell activation may influence neurotransmitters and brain function, leading to emotional and behavioral changes. In the context of PPD, activation of immune cells may affect neurotransmitters and brain function, resulting in emotional and behavioral changes (7). While more research is needed to establish the exact link between the immune system and PPD, these findings provide us with a new perspective to understand this mood disorder and offer new insights for future prevention and treatment strategies (8).

Mendelian randomization (MR) is a powerful method that uses genetic variation as instrumental variables (IVs) to establish causal relationships between risk factors and diseases (9). This approach helps overcome inherent biases in observational studies and provides reliable and representative results (10). MR is preferred over randomized controlled trials (RCTs) due to its ethical acceptability, ease of experimental control, and the interpretability of data. By randomly assigning conditions at the genetic level and eliminating the influence of other factors, MR ensures more reliable outcomes. Therefore, previous research has utilized MR to investigate the causal impact of opioid drugs on PPD in order to explore early diagnostic methods (11), as well as to uncover the causal relationship between PPD and cognitive impairment, demonstrating cognitive impairment as a key aspect of PPD and highlighting its independent role in addressing cognitive impairments and alleviating symptoms associated with PPD (12). MR analysis has confirmed a causal relationship between age at first birth (AFB) and PPD, with severe depression, family income level, and marital stress identified as potential mediators of this association (13). However, few studies have evaluated the causal relationship between circulating immune cell counts and the onset of PPD, particularly using MR analysis to explore the causal link between 731 immune cells as the exposure factor and PPD.

We aimed to investigate the causal relationship between immune cell characteristics and PPD using bidirectional two-sample MR analysis, providing insights for drug development and precision medicine in PPD treatment.

Materials and Methods

Study design

The causal relationship between 731 immune cell features and PPD was assessed by employing a two-sample bidirectional MR analysis. Firstly, the immune cell features were treated as the exposure factors, utilizing the single nucleotide polymorphisms (SNPs) of each immune cell as IVs, with PPD as the outcome. MR analysis was performed for each immune cell and PPD, using the results from the inverse variance weighted (IVW) method as the primary statistical analysis, with a significance threshold of $P < 0.05$. Secondly, PPD was treated as the exposure factor and immune cells showed positive results as the outcome, performing reverse MR analysis. Sensitivity analyses were conducted for all results to ensure their robustness. All data used in this study were acquired from publicly available databases, and the research studies included in our analysis had obtained approval from the relevant institutional review boards.

Genome-wide association study (GWAS) data sources for PPD

The PPD-related GWAS data used in this study were obtained from the FinnGen public database (https://gwas.mrcieu.ac.uk), with the dataset identified by the ID "finn-b-

O15_POSTPART_DEPR". The study included a total of 13,657 PPD patients and 59,601 European ancestry controls. PPD was defined as the occurrence of depression within a short period after childbirth (within 4 weeks or at 3, 6, or 12 months) (14). Finding a sufficient number of SNPs for instrumental variable analysis posed a challenge due to the limited number of SNPs that met the threshold of 5×10^{-8}. Therefore, all relevant SNPs were screened in the GWAS data based on a selection threshold of $P < 1 \times 10^{-5}$ and the following criteria: distance between SNPs greater than or equal to 10,000 kbp and linkage disequilibrium (R2) ≤ 0.001. The association between these SNPs and the exposure factor was evaluated using the F-statistic (F = beta2/se2), and SNPs with low statistical power (F-statistic < 10) were excluded (15).

Immunity-wide GWAS data sources

Each GWAS summary statistic of immune traits can be obtained from the GWAS catalog (registration numbers ranging from GCST0001391 to GCST0002121) (16). A total of 731 immune phenotypes were included, encompassing absolute cell counts (AC) (n=118), median fluorescence intensity (MFI) reflecting surface antigen levels (n=389), morphological parameters (MP) (n=32), and relative cell counts (RC) (n=192). Specific proteins and molecules on the surface of immune cells can be used to distinguish different types of immune cells and are used for diagnosing and monitoring immune system function (17). The four immune features of immune cells include surface markers, cell population counts, cell activity, and MP, all of which are essential for assessing normal immune system functioning and widely applied in immunological research and diagnosis. Specifically, the MFI, AC, and RC features encompass B cells, conventional dendritic cells (cDCs), mature stage T cells, monocytes, bone marrow cells, T-cell/B-cell/NK-cell (TBNK), and regulatory T (Treg) cells, while the MP feature includes cDC and TBNK cells. When immune cells are treated as exposure factors, the P-value was set at 1×10^{-5} (18).

Sensitivity and Statistical Analysis

The IVW method was used as the primary approach to estimate causal relationships between exposure and outcome. The IVW method calculates the ratio of the effect size of the SNP associated with the outcome to the effect size of the SNP associated with the exposure (19). To ensure the reliability of our conclusions, sensitivity analyses were conducted, including heterogeneity tests and analysis of differences among individual IVs. If there are substantial differences among the IVs, it indicates high heterogeneity. An important test is the test for horizontal pleiotropy. If the P-value is greater than 0.05, it suggests the absence of horizontal pleiotropy. If horizontal pleiotropy exists, our conclusions are considered unreliable. Other tests include leave-one-out (LOO) and Pleiotropy Residual Sum and Outlier (PRESSO) tests. The LOO test evaluates the influence of each observation by excluding one individual from the analysis dataset in each iteration and assessing the impact on the results. PRESSO is a statistical tool used to detect potential shared genetic effects (pleiotropy) on the genotype and outcome (20).

Summary statistics were harmonized from two datasets to ensure that the SNPs' effects on exposure and outcome corresponded to the same alleles. To infer causal associations, a two-sample Mendelian randomization (TSMR) analysis was performed using multiple methods, including IVW, weighted median, MR-Egger regression, simple model, and weighted model. IVW method was used as the primary method for MR, which combines the Wald ratio estimates from different SNPs to provide a consistent estimate of the causal effect of exposure on outcome (21). The reliability of the IVW method depends on the assumption of no horizontal pleiotropy (22). When at least half of the SNPs are valid IVs, the weighted median method provides a consistent estimate of the causal effect (23). MR-Egger regression is used to confirm the presence of horizontal pleiotropy, with the intercept representing the estimated effect of horizontal pleiotropy (24). Even in the presence of horizontal pleiotropy, MR-Egger regression can still provide an unbi-

ased estimate of the causal association. Compared to MR-Egger, the weighted median method improves the accuracy of results (25). Supplementary analyses were also conducted using a simple model and weighted model (26). In addition, scatter plots and funnel plots were used to demonstrate the robustness and absence of heterogeneity. All analyses were performed using R software version 4.3.1 with the packages TSMR and MR-PRESSO (27). The plotting was done using the random Forest and ggplot2 packages in R.

Results

The causal relationship between immune cells and PPD pathogenesis.

To explore the causal relationship between immune cells and PPD pathogenesis, data from 731 immune cells were employed as exposure and utilized immune cell SNPs as IVs in a two-sample MR analysis with PPD. The primary analytic method used was IVW, with a significance threshold of $P < 0.05$ for inclusion. Through this analysis, a total of 28 immune cell phenotypes were identified that exhibited causal associations with PPD incidence. Among these associations, the majority were observed in B cells and Treg cells, with 7 and 10 phenotypes respectively. Additionally, 2 associations were found in the cDC group, 4 in the Myeloid cell group, 2 in the Maturation stages of the T cell group, 2 in the TBNK group, and 1 in the Monocyte group (Supplementary Table 1) (Not published).

To further refine our findings, the immune cells' impact on PPD development was further differentiated based on the odds ratio (OR) values obtained from the IVW statistical analysis. OR values greater than 1 are generally considered to promote disease progression, while values less than 1 indicate a protective effect against disease occurrence. Among the 28 immune cell types that yielded positive results, 13 were found to promote disease incidence, while 15 exhibited a protective role. The immune cell phenotypes that contributed to PPD occurrence included 6 types in the Treg cell group, 3 types in the B cell group, 2 types in the TBNK group, and 1 type each in the Monocyte and Myeloid cell groups (Supplementary Table 1) (Fig. 1). On the other hand, out of the 15 immune cell types that showed a protective effect against PPD, there were 4 types in the B cell group, 4 types in the Treg cell group, 3 types in the Myeloid cell group, 2 types in the cDC cell group, and 2 types in the Maturation stages of T cell group (Supplementary Table 1) (Fig. 2).

Exploring the causal relationship between PPD onset and immune cells

To further investigate the causal relationship between PPD incidence and immune cells, a TSMR analysis was conducted, using PPD as the exposure factor, immune cells with positive results (n=28) as the outcome, and SNPs influencing PPD as IVs. The main analysis was performed using the IVW method, with a significance threshold set at $P < 0.05$ for inclusion. Through this approach, a causal relationship between PPD incidence and one specific immune cell phenotype was identified. Our research findings indicate that in the forward MR analysis, where immune cells serve as the exposure and the disease as the outcome, the immune cell CD62L on granulocytes has a protective effect on PPD (Fig. 3A-B). In the reverse MR analysis, where the disease acts as the exposure and immune cells as the outcome, PPD exhibits a promoting effect on the immune cell CD62L on granulocytes (Fig. 3C-D). The results from TSMR were consistent with the primary IVW analysis, providing further reliability to our findings. To enhance the robustness of our results, sensitivity analyses were also performed, which showed consistent estimates with the main IVW analysis, and all associations were non-significant. There was no evidence of heterogeneity in the genetic instrumental estimates. Furthermore, based on the MR-Egger intercept test and the MR-PRESSO global test, no significant evidence of pleiotropy was found (Supplementary Table 1).

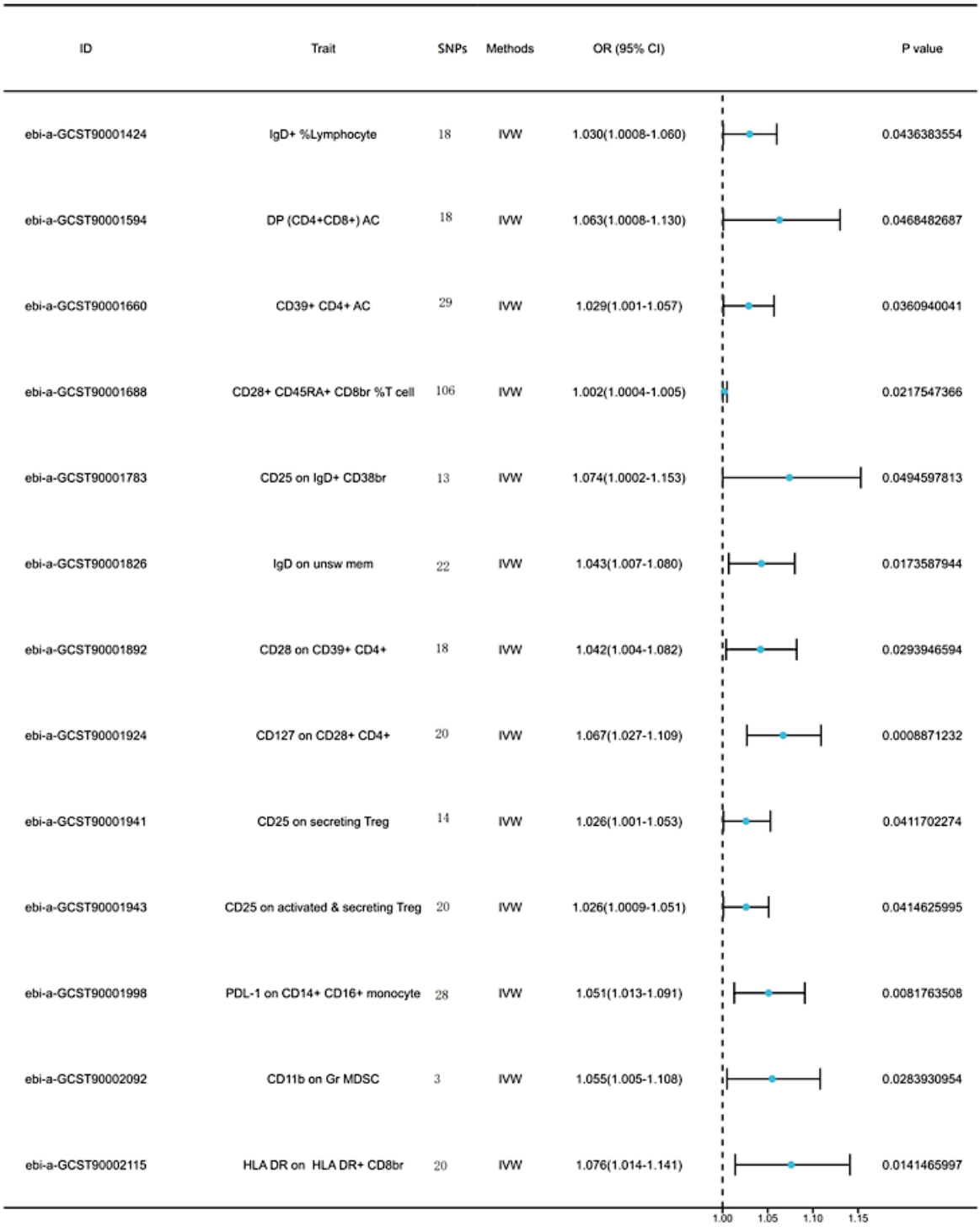

Fig. 1: The causal associations between PPD and 13 immune cells with promoting effect. Note: OR, odds ratio; CI, confidence interval; IVW, inverse variance weighted

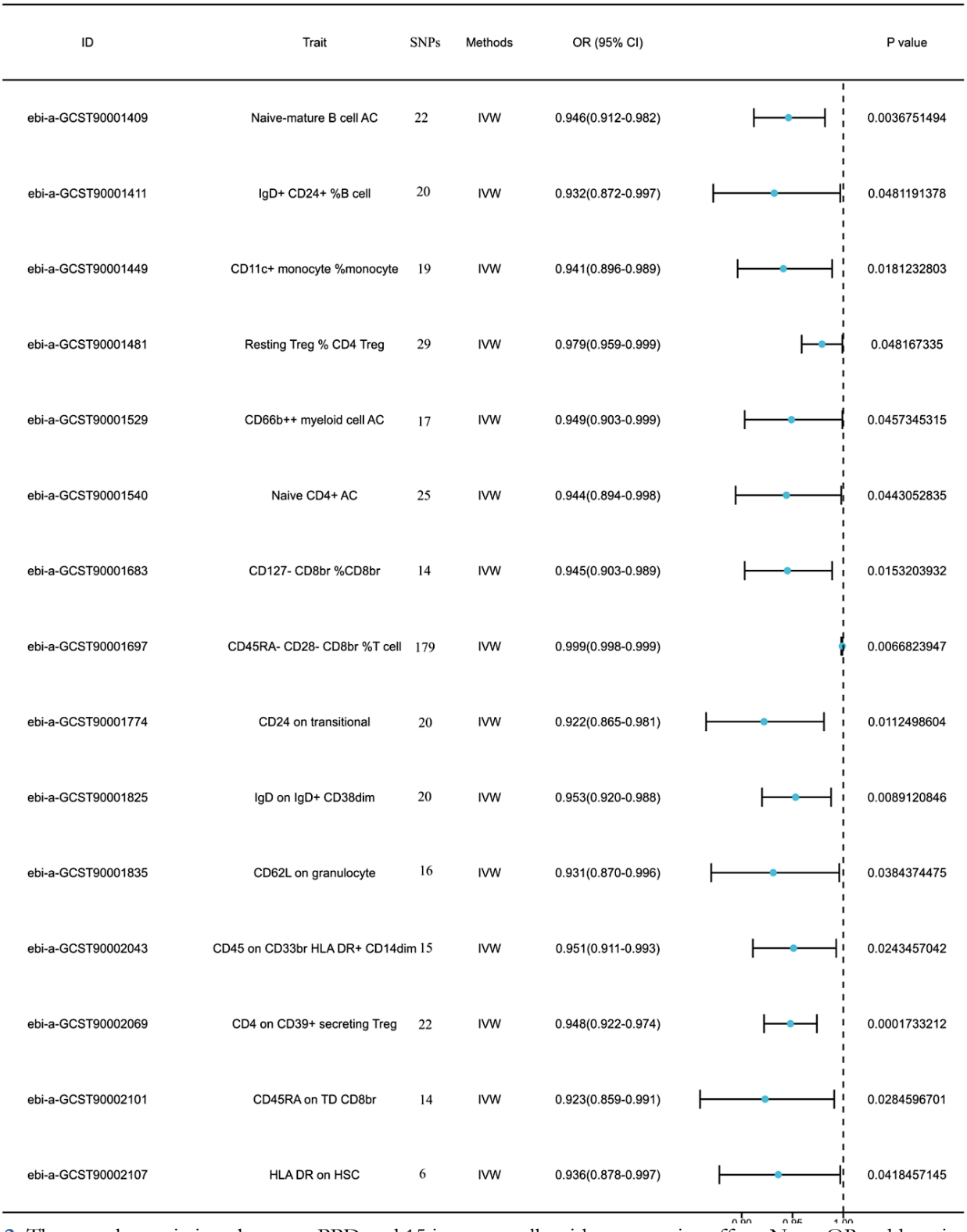

Fig. 2: The causal associations between PPD and 15 immune cells with a protective effect. Note: OR, odds ratio; CI, confidence interval; IVW, inverse variance weighted

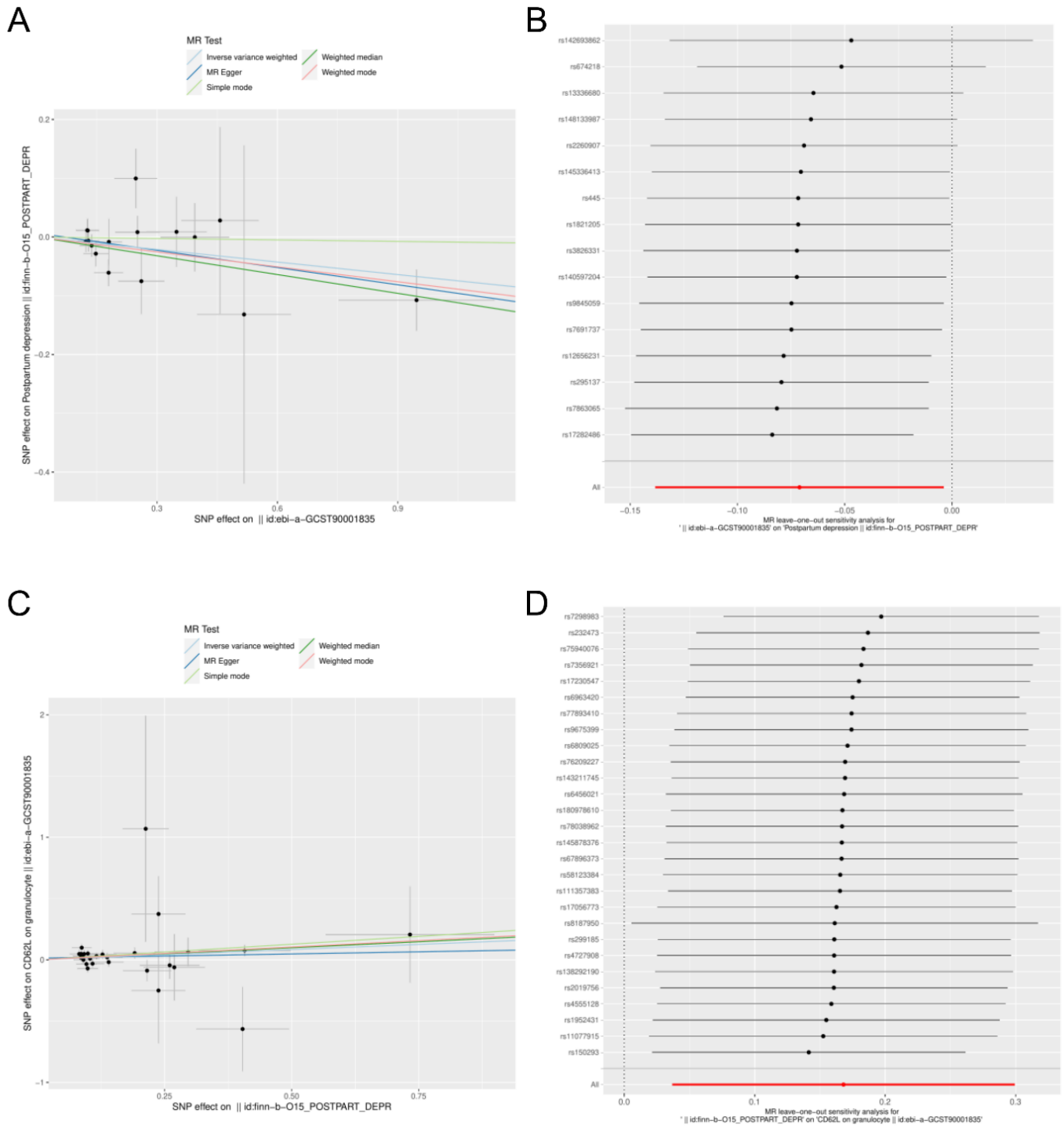

Fig. 3: The causal relationship between PPD incidence and immune cell CD62L. (A) Scatter plot with CD62L on granulocyte immune cells as exposure and PPD as outcome. (B) LOO plot with CD62L on granulocyte immune cells as exposure and PPD as outcome. (C) Scatter plot with PPD as exposure and CD62L on granulocyte immune cells as outcome. (D) LOO plot with PPD as exposure and CD62L on granulocyte immune cells as outcome. Note: PPD, postpartum depression. MR, mendelian randomization; SNPs, single nucleotide polymorphisms

Discussion

PPD has a serious negative impact on maternal health, and maternal depression adversely affects the behavior, emotions, and development of infants (28). Therefore, exploring the etiology and early diagnosis of PPD is crucial.

In this study, 28 immune cells were found to have a causal relationship with PPD, of which 13 immune cells had a promoting effect on PPD and 15 immune cells had a protective effect on PPD. Through data analysis, the majority was comprised of cDC and Myeloid cell groups in our findings, which may indicate that these two types of immune cells play a crucial role in promoting the development of PPD. cDCs are essential for antigen presentation and immune activation. In PPD patients, reduced cDC numbers and impaired function lead to immune dysregulation (29). Myeloid cells are essential for antimicrobial and anti-inflammatory responses. In PPD, they exhibit functional abnormalities, such as reduced macrophage phagocytosis and pathogen killing, which may lead to immune imbalance and contribute to the development of PPD (30). In PPD patients, macrophages and dendritic cells secrete elevated levels of inflammatory factors (such as TNF-α, IL-1β) and cytokines (such as IL-6), which can disrupt neurotransmitter metabolism and contribute to symptoms like low mood and anxiety (31).

Immune cells with protective effects on PPD are mainly concentrated in three types: B cells, Treg cells, and myeloid cells. Studies have shown that changes in B cell homeostasis and excessive activation of B cells may lead to the production of excessive autoantibodies and immune complexes, increasing the risk of depression (32). The number and function of Treg cells in PPD patients are abnormal, manifested as decreased numbers and reduced inhibitory function. This may lead to immune imbalance and inflammatory reactions, harming the nervous system (5). Myeloid cells control infections and reduce inflammation by phagocytosing pathogens and releasing cytokines (33). They also assist in Treg cell differentiation and function, inhibiting immune over-activation (34), and influence neurotransmitter balance and signal transduction, affecting emotions and behavior (35). Identifying the normal fluctuations in immune cells and further exploring the immune regulation mechanisms postpartum can help better promote immune stability and health, potentially playing a role in preventing PPD.

During reverse MR analysis, PPD was used as the exposure factor and focused on 28 positive results of immune cells as the outcome. Our analysis uncovered a causal relationship between the onset of PPD and a specific immune cell phenotype, CD62L, also known as L-selectin. CD62L, a cell surface molecule in the selectin family, is primarily found on white blood cells and is essential for regulating immune cell migration and adhesion (33). Under normal circumstances, CD62L is expressed on the surface of resting granulocytes, allowing weak adhesion with endothelial cells and helping granulocytes to roll on the inner wall of blood vessels. When granulocytes are sufficiently stimulated, such as by inflammatory mediators, the expression of CD62L is downregulated, allowing granulocytes to bind more tightly to endothelial cells and remain at the site of inflammation. CD62L mediates the process of granulocyte migration and transfer by binding to ligands on the surface of endothelial cells. It helps granulocytes move through the endothelial cell layer from the bloodstream into the tissue gap and participate in the inflammatory response and immune response (34). A study of new mothers six weeks after delivery found that the expression level of CD62L on CD4+ T cells decreased significantly, while the expression level of CD62L on CD8+ T cells increased significantly, and this change was associated with the occurrence of PPD (35). Another study found a negative correlation between the expression level of CD62L on CD4+ T cells in the early postpartum period and the severity of PPD (36). Abnormal levels of CD62L may indicate immune system dysfunction and could be related to the pathogenesis of PPD, but further exploration is needed.

Numerous studies have employed MR to explore various factors associated with PPD. These studies have contributed to a better understanding of the causal relationships between different biological and environmental factors and the onset of PPD. For instance, several studies have investigated the role of the gut microbiome in PPD, highlighting the potential link between dysbiosis and mental health outcomes (37, 38). In addition, MR studies have suggested that immune dysregulation may be closely associated with the development of PPD (39). Furthermore, MR-based investigations have provided evidence that genetic variations in reproductive traits, may influence susceptibility to PPD (40). While these studies provide valuable insights into various risk factors for PPD, our study adds a unique dimension by focusing specifically on the causal relationship between immune cell characteristics and PPD. By using a bidirectional two-sample MR approach, we aim to better understand the relationship between specific immune cell and PPD, which may provide new avenues for targeted prevention and treatment strategies.

MR still has some limitations**.** First, MR is limited by the sample size and quality of GWAS because it can only be performed based on known genetic variations. Second, MR cannot completely eliminate the impact of confounding bias, which may lead to incorrect inferences about causality. Finally, because MR can only analyze existing datasets, it does not apply to newly identified or unobservable variables. To more accurately determine the causal relationship between two variables, multiple methods should be used to corroborate each other and incorporate different types of evidence.

Conclusion

Our study highlights the causal relationship between immune cells and PPD through bidirectional TSMR analysis, identifies key cells, suggests potential targets, but deeper research needed to elucidate fully mechanisms.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

Grant support was provided by the Zhejiang Provincial Medical and Health Technology Plan (2023KY205); Zhejiang Provincial Natural Science Foundation of China (Q24H040012); Foundation of Zhejiang Provincial Education Department (Y202351214); Administration of Traditional Chinese Medicine of Zhejiang Province, China (2024ZL740); Medical Health Science and Technology Project in Hangzhou (A20220164).

Data Availability Statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Conflict of Interest

The authors have no conflicts of interest to declare.

References

1. Larsen SV, Mikkelsen AP, Lidegaard O, et al (2023). Depression associated with hormonal contraceptive use as a risk indicator for postpartum depression. *JAMA Psychiatry,* 80: 682-689.
2. Deligiannidis KM, Meltzer-Brody S, Maximos B, et al (2023). Zuranolone for the treatment of postpartum depression. *Am J Psychiatry,* 180: 668-675.
3. Steenland MW, Trivedi AN (2023). Association of medicaid expansion with postpartum

depression treatment in arkansas. *JAMA Health Forum,* 4: e225603.
4. Ma JH, Wang SY, Yu HY, et al (2019). Prophylactic use of ketamine reduces postpartum depression in chinese women undergoing cesarean section. *Psychiatry Res,* 279: 252-258.
5. Osborne LM, Gilden J, Kamperman AM, et al (2020). T-cell defects and postpartum depression. *Brain Behav Immun,* 87: 397-403.
6. Rudzinskas SA, Goff AC, Mazzu MA, et al (2023). Intrinsically dysregulated cellular stress signaling genes and gene networks in postpartum depression. *Mol Psychiatry,* 28: 3023-3032.
7. Worthen RJ, Beurel E (2022). Inflammatory and neurodegenerative pathophysiology implicated in postpartum depression. *Neurobiol Dis,* 165: 105646.
8. Eid RS, Gobinath AR, Galea LAM (2019). Sex differences in depression: Insights from clinical and preclinical studies. *Prog Neurobiol,* 176: 86-102.
9. Sanderson E, Glymour MM, Holmes MV, et al (2022). Mendelian randomization. *Nat Rev Methods Primers,* 2:6.
10. Birney E (2022). Mendelian randomization. *Cold Spring Harb Perspect Med,* 12(4):a041302.
11. Jiang Y, Wei D, Xie Y (2023). Causal effects of opioids on postpartum depression: A bidirectional, two-sample mendelian randomization study. *Front Psychiatry,* 14: 1043854.
12. Li J, Li J, Shen L, et al (2023). Investigating the causal association of postpartum depression with cerebrovascular diseases and cognitive impairment: A mendelian randomization study. *Front Psychiatry,* 14: 1196055.
13. Ou Z, Gao Z, Wang Q (2023). Association between age at first birth and postpartum depression: A two-sample mendelian randomization analysis. *Heliyon,* 9: e20500.
14. Wisner KL, Sit DK, McShea MC, et al (2013). Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. *JAMA Psychiatry,* 70: 490-8.
15. Deng MG, Liu F, Liang Y, et al (2023). Association between frailty and depression: A bidirectional mendelian randomization study. *Sci Adv,* 9(38):eadi3902.
16. Bowden J, Davey Smith G, and Burgess S (2015). Mendelian randomization with invalid instruments: Effect estimation and bias detection through egger regression. *Int J Epidemiol,* 44: 512-25.
17. Orru V, Steri M, Sidore C, et al (2020). Complex genetic signatures in immune cells underlie autoimmunity and inform therapy. *Nat Genet,* 52: 1036-1045.
18. Burgess S, Butterworth A, Thompson SG (2013). Mendelian randomization analysis with multiple genetic variants using summarized data. *Genet Epidemiol,* 37: 658-65.
19. Sang N, Gao RC, Zhang MY, et al (2022). Causal relationship between sleep traits and risk of systemic lupus erythematosus: A two-sample mendelian randomization study. *Front Immunol,* 13: 918749.
20. Bae SC, Lee YH (2018). Vitamin d level and risk of systemic lupus erythematosus and rheumatoid arthritis: A mendelian randomization. *Clin Rheumatol,* 37: 2415-2421.
21. Huang S, Tian F, Yang X, et al (2022). Physical activity and systemic lupus erythematosus among european populations: A two-sample mendelian randomization study. *Front Genet,* 12: 784922.
22. Sidore C, Busonero F, Maschio A, et al (2015). Genome sequencing elucidates sardinian genetic architecture and augments association analyses for lipid and blood inflammatory markers. *Nat Genet,* 47: 1272-1281.
23. Bowden J, Davey Smith G, Haycock PC, et al (2016). Consistent estimation in mendelian randomization with some invalid instruments using a weighted median estimator. *Genet Epidemiol,* 40: 304-14.
24. Burgess S, Thompson SG (2017). Interpreting findings from mendelian randomization using the mr-egger method. *Eur J Epidemiol,* 32: 377-389.
25. Xiang K, Wang P, Xu Z, et al (2021). Causal effects of gut microbiome on systemic lupus erythematosus: A two-sample mendelian randomization study. *Front Immunol,* 12: 667097.
26. Sun W, Zhang L, Liu W, et al (2021). Stroke and myocardial infarction: A bidirectional mendelian randomization study. *Int J Gen Med,* 14: 9537-9545.

27. Hemani G, Zheng J, Elsworth B, et al (2018). The mr-base platform supports systematic causal inference across the human phenome. *Elife,* 7:e34408.
28. Oyetunji A, Chandra P (2020). Postpartum stress and infant outcome: A review of current literature. *Psychiatry Res,* 284: 112769.
29. Lewkowitz AK, Whelan AR, Ayala NK, et al (2024). The effect of digital health interventions on postpartum depression or anxiety: A systematic review and meta-analysis of randomized controlled trials. *Am J Obstet Gynecol,* 230: 12-43.
30. Bassler K, Schulte-Schrepping J, Warnat-Herresthal S, et al (2019). The myeloid cell compartment-cell by cell. *Annu Rev Immunol,* 37: 269-293.
31. Ng LG, Liu Z, Kwok I, et al (2023). Origin and heterogeneity of tissue myeloid cells: A focus on gmp-derived monocytes and neutrophils. *Annu Rev Immunol,* 41: 375-404.
32. Guintivano J, Aberg KA, Clark SL, et al (2022). Transcriptome-wide association study for postpartum depression implicates altered b-cell activation and insulin resistance. *Mol Psychiatry,* 27: 2858-2867.
33. Zitti B, Hoffer E, Zheng W, et al (2023). Human skin-resident cd8(+) t cells require runx2 and runx3 for induction of cytotoxicity and expression of the integrin cd49a. *Immunity,* 56: 1285-1302 e7.
34. Momeni A, Eagler L, Lo CY, et al (2021). Neutrophils aid cellular therapeutics by enhancing glycoengineered stem cell recruitment and retention at sites of inflammation. *Biomaterials,* 276: 121048.
35. Kagamu H, Kitano S, Yamaguchi O, et al (2020). Cd4(+) t-cell immunity in the peripheral blood correlates with response to anti-pd-1 therapy. *Cancer Immunol Res,* 8: 334-344.
36. Pernaa N, Keskitalo S, Chowdhury I, et al (2022). Heterozygous premature termination in zinc-finger domain of kruppel-like factor 2 gene associates with dysregulated immunity. *Front Immunol*, 13: 819929.
37. Zhang J, Wei L, Tan H, et al (2024). Gut microbiota and postpartum depression: a Mendelian randomization study. *Fron Psychiatry*, 15: 1282742.
38. Sun Y, Fan C, Lei D (2024). Association between gut microbiota and postpartum depression: A bidirectional Mendelian randomization study. *J Affect Disord*, 362: 615–622.
39. Yu W, Su B, Wang C, et al (2024). Postpartum depression and autoimmune disease: a bidirectional Mendelian randomization study. *Front Psychiatry*, 15: 1425623.
40. Kang Z, Wu Q, Cao J, et al (2024). Causal relationship between Women's reproductive traits and postpartum depression: a multivariate mendelian randomization analysis. *Front Genet*, 15: 1434762.