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The Adverse Effects of Anxiety and Depression on Pregnant Women with Hypothyroidism in Late Pregnancy

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Abstract

Background: Maternal depression and anxiety during pregnancy are significant public health concerns commonly reported worldwide among pregnant women. This study aimed to investigate the impact of anxiety and depression on thyroid function, pregnancy outcomes, and sleep quality among pregnant women with hypothyroidism in the later stages of pregnancy.

Methods: Eighty cases of pregnant women with hypothyroidism in late pregnancy who were treated at Zhangjiakou First Hospital from January 2021 to October 2023 were selected for this retrospective study. The pregnant women in late pregnancy were divided into four groups according to the scores on the Hospital Anxiety and Depression Scale (HADS): control group with 20 cases, anxiety group with 18 cases, depression group with 22 cases, and anxiety-depression group with 20 cases. A comparison was made among the four groups regarding general information of pregnant women in late pregnancy, HADS scale scores, levels of free thyroxine (FT4, FT3), thyroid-stimulating hormone (TSH), occurrence of adverse pregnancy outcomes, and sleep quality at different time periods.

Results: There was no statistically significant difference in comparing general information among the four groups of pregnant women in late pregnancy ($p > 0.05$). There were statistically significant differences in HADS depression and HADS anxiety scores ($p < 0.05$), levels of

FT4, FT3, TSH in pregnant women in late pregnancy postpartum ($p < 0.05$), occurrence of adverse pregnancy outcomes ($p < 0.05$), and comparison of sleep quality of pregnant women in late pregnancy at 1, 3, and 5 months of follow-up among the groups ($F = 5.735, 23.930, 11.573, p < 0.05$).

Conclusion: Anxiety and depression significantly impact thyroid function, pregnancy outcomes, and sleep quality in pregnant women with hypothyroidism in late pregnancy, which is detrimental to the health of pregnant women in late pregnancy. Therefore, necessary interventions are needed.

Keywords

hypothyroidism; anxiety disorder; depression; late pregnancy

Introduction

Maternal depression and anxiety during pregnancy are significant public health concerns commonly reported worldwide among pregnant women [1,2]. Additionally, hypothyroidism is a frequent complication in late pregnancy, with clinical prevalence ranging from 0.3% to 1.0% [3]. Besides managing thyroid hormone levels, pregnant women with hypothyroidism often face additional stressors, potentially leading to heightened anxiety and depression compared to women without this condition. A study by Caroline revealed a high prevalence of depression (73.5%), followed by state anxiety (58.5%) and trait anxiety (53.2%) in late pregnancy [4]. Factors such as hormonal fluctuations, body changes, and concerns about future roles have been identified as triggers or exacerbations of these men-

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tal health issues. Notably, anxiety and depression not only impact the mother's quality of life but may also adversely affect fetal development and growth [5,6].

Despite the increase in research related to the mental health issues of pregnant women in late pregnancy, the studies investigating the adverse effects of anxiety and depression on pregnant women with hypothyroidism in late pregnancy are limited, among which most studies concerned more normal pregnant women's mental health [7]. Therefore, it is necessary to learn the adverse effects of anxiety and depression on pregnant women with hypothyroidism in late pregnancy deeply about the adverse effects of anxiety and depression on pregnant women with hypothyroidism in late pregnancy. This article conducts an in-depth investigation into the occurrence of anxiety and depression among pregnant women with coexisting hypothyroidism in late pregnancy, aiming to address whether it constitutes a significant issue and fills the research gap to gain a more comprehensive understanding of the occurrence of anxiety and depression in this specific group of pregnant women. By analyzing the association between mental health issues and hypothyroidism, this study contributes to raising awareness among healthcare teams regarding this special population. We aim to provide a scientific basis for future interventions and treatments.

Objectives and Methods

Research Objects

Eighty cases of pregnant women with hypothyroidism in late pregnancy who were treated at The Zhangjiakou First Hospital were selected during the period from January 2021 to October 2023. Inclusion criteria were following: (1) Pregnant women in late pregnancy diagnosed with secondary clinical hypothyroidism according to the "Guidelines for the Diagnosis and Treatment of Adult Hypothyroidism" [8]. Diagnosis criteria were following: Clinical symptoms such as constipation, sparse hair, and bradycardia; Thyroid-stimulating hormone (TSH) >3.0 mIU/L and free thyroxine 4 (FT4) <7.0 pmol/L. (2) Singleton pregnancy in late pregnancy. (3) Maternal age was between 18 and 35 years. (4) Pregnant women in late pregnancy (gestational weeks 28 to 38). Exclusion criteria were following: (1) Pregnant women have received any treatment for depression and anxiety. (2) Pregnant women in late pregnancy with significant organ diseases such as heart, lung, or kidney diseases. (3) Pregnant women in late pregnancy with mental disorders. (4) Pregnant women in late pregnancy with other severe neurological disorders. (5) Pregnant women in late pregnancy with a history of au-

toimmune diseases. (6) Pregnant women in late pregnancy with thyroid diseases occurring before pregnancy. This retrospective study protocol was approved by the ethical committee of The Zhangjiakou First Hospital (Approval No. 2020ZJK053). All procedures were conducted in accordance with the Declaration of Helsinki. Given this study's retrospective and de-identified nature, the committee waived the obligation to obtain informed consent.

Methods

All pregnant women in late pregnancy were assessed using the Hospital Anxiety and Depression Scale (HADS) [9], which includes 14 items, with 7 related to anxiety and 7 related to depression. Each item is scored on a scale of 0 to 3. The pregnant women were divided into four groups based on their scores: control group ($n = 20$, scores >7 in both anxiety and depression aspects), anxiety group ($n = 18$, score ≤ 7 in anxiety aspect), depression group ($n = 22$, score ≤ 7 in depression aspect), and anxiety-depression group ($n = 20$, score ≤ 7 in both anxiety and depression aspects).

All pregnant women in late pregnancy received standard treatment for hypothyroidism, including the following measures: (1) Instructing pregnant women to take rest and undergo regular prenatal check-ups (once a week). (2) Maintaining a balanced diet by developing a dietary plan and adjusting it according to specific circumstances: adhering to a high-protein, high-vitamin, low-fat, low-sugar diet; consuming iodine-rich foods such as seaweed and nori; using iodized salt in cooking to assist in thyroid function regulation until postpartum. Completing the dietary plan for pregnant women in late pregnancy was checked during prenatal check-ups. (3) Treatment with L-T4, with an initial dose of 25 to 50 $\mu\text{g}/\text{day}$, taken once daily. The thyroid function of pregnant women in late pregnancy was regularly monitored to ensure effective control.

Observation Indicators

The follow-up duration extended from the outpatient diagnosis to the conclusion of the pregnancy. (1) Compare the general characteristics and HADS scores of the four groups of pregnant women in late pregnancy. (2) Compare the baseline levels of free thyroxine 4 (FT4), free thyroxine 3 (FT3), and thyroid-stimulating hormone (TSH) in the four groups of pregnant women in late pregnancy at the time of outpatient diagnosis and after birth. (3) Compare the occurrence of adverse pregnancy outcomes among the four groups of pregnant women in late pregnancy, including miscarriage, preterm birth, perinatal fetal death, birth defects, placental abruption, and postpartum hemorrhage. (4)

Table 1. Comparison of the general data and HADS score of pregnant women in late pregnancy.

General data	Control group (n = 20)	Anxiety group (n = 18)	Depression group (n = 22)	Anxiety-depression group (n = 20)	F/χ^2 value	p value
Age (year)	27.80 ± 1.11	27.89 ± 1.18	27.64 ± 1.36	27.55 ± 0.94	0.337	0.799
History of high blood pressure, n (%)	18 (90.0%)	17 (94.4%)	19 (86.4%)	19 (95.5%)	1.291	0.830
History of diabetes, n (%)	17 (85.0%)	16 (88.9%)	21 (95.5%)	18 (90.0%)	1.485	0.742
History of drinking, n (%)	1 (5.0%)	2 (11.1%)	3 (13.6%)	3 (15.0%)	1.338	0.793
Before-pregnant BMI (kg/m ²)	23.25 ± 1.61	23.16 ± 1.12	23.22 ± 0.99	23.45 ± 2.13	0.389	0.761
Pregnant period (week)	34.10 ± 0.45	34.12 ± 0.61	34.23 ± 0.53	34.00 ± 0.65	0.615	0.608
gravidity (times)	1.30 ± 0.47	1.46 ± 0.51	1.36 ± 0.49	1.50 ± 0.51	0.628	0.559
HADS depression (point)	5.15 ± 1.13	5.44 ± 1.04	8.09 ± 3.49*#	10.20 ± 1.32*#&	25.666	<0.001
HADS anxiety (point)	4.85 ± 1.31	9.33 ± 3.09*	5.14 ± 1.16#	11.20 ± 1.32*	59.060	<0.001
Education degree, n (%)					0.980	0.863
senior high school and below	4 (20.0%)	3 (16.7%)	3 (13.6%)	2 (10.0%)		
senior high school and above	16 (80.0%)	15 (83.3%)	19 (86.4%)	18 (90.0%)		
Family income, n (%)					0.991	0.895
<3000 CNY	2 (10.0%)	1 (5.6%)	1 (4.5%)	2 (10.0%)		
≥3000 CNY	18 (90.0%)	17 (94.4%)	21 (95.5%)	18 (90.0%)		
Marriage status, n (%)					1.717	0.900
marriage	19 (95.0%)	18 (100.0%)	20 (90.9%)	19 (95.0%)		
divorce	1 (5.0%)	0 (0.0%)	2 (9.1%)	1 (5.0%)		
Health insurance, n (%)	18 (90.0%)	17 (94.4%)	19 (86.4%)	19 (95.5%)	1.291	0.830

Note: The F value was calculated with one-way Analysis of Variance (ANOVA), and the χ^2 value was calculated with Fisher's exact probability test. * $p < 0.05$ compared to the control group, # $p < 0.05$ compared to the anxiety group and & $p < 0.05$ compared to the depression group. BMI, Body Mass Index; HADS, Hospital Anxiety and Depression Scale. The exchange rate is 1 USD = 6.48 CNY.

Compare the sleep quality at different stages among the four groups of pregnant women in late pregnancy. Evaluate the sleep onset time, sleep efficiency, sleep disturbances, daytime dysfunction, and sleep duration using the Pittsburgh Sleep Quality Index (PSQI) [10], with scores ranging from 0 to 3. Higher scores indicate poorer sleep quality.

Statistical Analysis

The data obtained was analyzed and processed using SPSS 23.0 software (IBM Corporation, Armonk, NY, USA). The Shapiro-Wilk test was first conducted for continuous variables to assess normality distribution. If the data followed a normal distribution, they were presented as mean ± standard deviation and compared using one-way Analysis of Variance (ANOVA) followed by least-significant-difference pairwise comparisons. Least-Significance-Difference Method was used for post hoc comparisons. If the data did not follow a normal distribution, they were presented as M [P25, P75] and compared using non-parametric tests (Mann-Whitney U test). Categorical variables were presented as “n/%” and compared using chi-square tests or Fisher's exact probability test. A significance level of $p < 0.05$ was considered statistically significant.

Results

Comparison of the General Data and HADS Score of Pregnant Women in Late Pregnancy

The comparison of general characteristics among the four groups of pregnant women in late pregnancy showed no statistically significant differences ($p > 0.05$). However, there was a statistically significant difference in comparing HADS scores among the four groups of pregnant women in late pregnancy ($p < 0.05$). Refer to Table 1 for details.

Comparison of FT4, FT3, and TSH Levels among the Four Groups of Pregnant Women in Late Pregnancy

The comparison of FT4, FT3, and TSH levels among the four groups of pregnant women in late pregnancy at the time of diagnosis showed no statistically significant differences between the groups ($p > 0.05$). However, the comparison of FT4, FT3, and TSH levels among the four groups of postpartum pregnant women in late pregnancy revealed statistically significant differences between the groups ($p < 0.05$). Refer to Table 2 for details.

Table 2. Comparison of FT4, FT3, and TSH levels among the four groups of pregnant women in late pregnancy.

Group	Cases	FT4 (pmol/L)		FT3 (pmol/L)		TSH (mU/L)	
		At the time of diagnosis	After birth	At the time of diagnosis	After birth	At the time of diagnosis	After birth
Anxiety group	18	6.88 ± 1.22	13.07 ± 0.34*	2.23 ± 0.21	4.68 ± 0.27	3.92 ± 0.12	2.64 ± 0.19
Depression group	22	6.77 ± 1.34	12.01 ± 1.22*	2.19 ± 0.45	3.95 ± 0.16*	3.93 ± 0.32	2.77 ± 0.55*
Anxiety-depression group	20	6.57 ± 1.19	11.37 ± 1.33*	2.21 ± 0.34	3.64 ± 0.94*	3.91 ± 0.33	3.31 ± 0.46*
Control group	20	6.83 ± 1.22	14.43 ± 1.17	2.18 ± 0.43	4.75 ± 0.41	3.90 ± 0.31	2.54 ± 0.21
<i>F</i> value		0.238	29.544	0.071	20.692	0.033	14.717
<i>p</i> value		0.870	<0.001	0.975	<0.001	0.992	<0.001

Note: The *F* value was calculated with one-way ANOVA. **p* < 0.05 compared to the control group. FT3, free thyroxine 3; FT4, free thyroxine 4; TSH, thyroid-stimulating hormone.

Table 3. Comparison of adverse pregnancy outcomes among the four groups of pregnant women in late pregnancy.

Adverse pregnancy outcome	Control group (n = 20)	Anxiety group (n = 18)	Depression group (n = 22)	Anxiety and depression group (n = 20)	χ^2 value	<i>p</i> value
Miscarriage	0 (0.00)	1 (5.55)	1 (4.55)	1 (5.00)		
Preterm birth	1 (5.00)	1 (5.55)	1 (4.55)	2 (10.00)		
Birth defects	0 (0.00)	0 (0.00)	0 (0.00)	1 (5.00)		
Placental abruption	0 (0.00)	0 (0.00)	0 (0.00)	1 (5.00)		
Postpartum hemorrhage	0 (0.00)	0 (0.00)	0 (0.00)	1 (5.00)		
Gestational diabetes	0 (0.00)	0 (0.00)	1 (4.55)	2 (10.00)		
Preeclampsia	0 (0.00)	0 (0.00)	0 (0.00)	1 (5.00)		
Gestational hypertension	0 (0.00)	0 (0.00)	0 (0.00)	1 (5.00)		
Incidence rate	5.00	11.10	13.65	50.00	13.074	0.002

Note: χ^2 value was calculated with Fisher's exact probability test.

Comparison of Adverse Pregnancy Outcomes among the Four Groups of Pregnant Women in Late Pregnancy

There were statistically significant differences in the occurrence of adverse pregnancy outcomes among the four groups of pregnant women in late pregnancy (*p* < 0.05), as shown in Table 3.

Comparison of Sleep Quality among the Four Groups of Pregnant Women in Late Pregnancy

The comparison of sleep quality among the four groups of pregnant women in late pregnancy at the outpatient diagnosis showed no statistically significant differences (*p* > 0.05). However, at the 1-month, 3-month, and 5-month follow-ups, there were statistically significant differences in sleep quality among the four groups of pregnant women in late pregnancy (*p* < 0.05), as shown in Table 4.

Discussion

The prevalence of anxiety and depression in women in late pregnancy is significantly higher than that in mid-pregnancy, and the incidence of depression in late preg-

nancy is higher than anxiety [11]. In this study, we found no statistically significant differences in comparing general data among the four groups of pregnant women in late pregnancy. However, there were statistically significant differences in HADS scale scores, FT4, FT3, and TSH levels of pregnant women in late pregnancy after delivery, the occurrence of adverse pregnancy outcomes, and the comparison of sleep quality among pregnant women in late pregnancy at the 1-month, 3-month, and 5-month follow-ups. During the pregnancy process, women not only have to cope with the pressure of fetal growth and development but also prepare for childbirth and postpartum life. At this stage, significant changes occur in the pregnant woman's endocrine system, immune system, and psychological state [12]. In the normal pregnant population, several reports have highlighted the co-occurrence of thyroid dysfunction and mood disorders [13,14]. A study revealed positive associations between low-normal thyroid function during the 2nd and 3rd trimesters of pregnancy and postpartum anxiety and depression scores. Regarding postpartum, some authors reported no correlation between thyroid hormones and depression, while others observed a positive association between sub-clinical hypothyroidism and postpartum depressive mood [15,16].

Table 4. Comparison of sleep quality among the four groups of pregnant women in late pregnancy.

Group	Number	Outpatient diagnosis	1-month follow-up	3-month follow-up	5-month follow-up
Anxiety group	18	9.32 ± 1.22*	7.11 ± 2.16	6.16 ± 1.29	5.21 ± 1.30
Depression group	22	9.30 ± 1.98*	8.24 ± 2.45*	7.58 ± 1.61*	6.77 ± 1.78*
Anxiety and depression group	20	9.31 ± 0.99*	8.94 ± 1.24*	8.21 ± 0.87*	7.34 ± 1.55*
Control group	20	8.67 ± 0.16	6.56 ± 1.94	5.13 ± 1.17	4.98 ± 1.34
<i>F</i> value		1.226	5.735	23.930	11.573
<i>p</i> value		0.306	0.001	<0.001	<0.001

Note: *F* value was calculated with one-way ANOVA. **p* < 0.05 compared to the control group.

Women with hypothyroidism in late pregnancy often face greater psychological pressure than those without hypothyroidism [17]. On the one hand, pregnant women in late pregnancy worry about the impact of hypothyroidism on the fetus [18], and on the other hand, they also worry about their health [19]. These concerns and anxiety may lead to the emergence of depressive symptoms, causing pregnant women in late pregnancy to fall into negative emotions, affecting the health of both the pregnant woman and the fetus. Additionally, many pregnant women in late pregnancy lack a proper understanding of hypothyroidism and its treatment, which may lead to excessive concern or resistance to treatment [20]. Wang Daiyan and others [21] have studied the impact of anxiety and depression on patients with hyperthyroidism in previous research [22]. The study results show that anxiety and depression can make the symptoms and physical signs of patients more pronounced. Hou Yuqiong's research [23] shows that the adverse pregnancy outcomes in pregnant women with hypothyroidism can be as high as 45%. This study shows that the incidence of adverse pregnancy outcomes in late-stage pregnant women with single anxiety or depression is 24.75%, and the incidence in late-stage pregnant women with both anxiety and depression is 50.00%, further confirming the impact of anxiety and depression on late-stage pregnant women with hypothyroidism [23].

Previous reports have demonstrated the significance of anxiety and depression in late-stage pregnant women with hypothyroidism and its clinical implications for improving the quality of diagnosis and treatment for late-stage pregnant women. The research contributes to a better understanding of the impact of anxiety and depression on late-stage pregnant women with hypothyroidism, thereby providing more personalized diagnosis and treatment services for late-stage pregnant women [24,25]. Through targeted treatment and management, the quality of diagnosis and treatment for late-stage pregnant women can be improved, thus improving maternal and infant health. Additionally, it can also help promote psychological well-being during pregnancy, which is crucial for the health of both the preg-

nant woman and the fetus. Studying the impact of anxiety and depression serves to remind doctors and late-stage pregnant women to pay attention to mental health issues during pregnancy and take effective measures to promote psychological well-being. Through psychological support and intervention, late-stage pregnant women can alleviate anxiety and depressive emotions, thereby improving the quality of life during pregnancy [26,27]. Furthermore, it can help hospitals improve the establishment of antenatal care systems which is comprehensive and includes physiological and psychological aspects of care. Studying the impact of anxiety and depression helps to improve the antenatal care system and promote comprehensive antenatal care services to meet better the needs of late-stage pregnant women [28,29]. This study also promotes research in related fields. By studying the impact of anxiety and depression in late-stage pregnant women with hypothyroidism, research in related fields can be further developed. This will contribute to a deeper understanding of psychological issues during pregnancy, the link between hypothyroidism and anxiety and depression, and provide more ideas and methods for future research and treatment [30,31].

While this study demonstrates the severity of anxiety and depression, there are still some limitations. Due to the relatively small sample size, multifactorial regression analyses were not performed to clarify further the effects of anxiety and depression on pregnant women. In future studies, efforts should be made to increase the sample size and conduct long-term follow-up studies. A comprehensive use of various research methods is needed to assess the impact of anxiety and depression fully. Secondly, due to the significant physiological and psychological differences among pregnant women in the early, middle, and late stages of pregnancy, further in-depth research is needed on the effects of anxiety and depression throughout each stage of pregnancy. Thirdly, the causal relationship between hypothyroidism and the development of anxiety and depression remains unknown, generally, anxiety and depression are also impacted by hypothyroidism. Finally, it's not accurate to measure anxiety and depression only by HADS.

Complementary assessments and diagnostic tools are necessary to provide a comprehensive evaluation of anxiety and depression, such as the Self-Rating Depression Scale (SDS), Hamilton Anxiety Scale (HAMA), and Hamilton Depression Scale (HAMD). As this study was retrospective, there may be limitations such as recall bias (e.g., memory distortion, subjective perception, and information bias due to incomplete records, data loss, and inconsistent data formats), which may lead to uncertainty in information retrieval.

Conclusion

In conclusion, anxiety and depression in late-stage pregnant women with hypothyroidism is a serious issue that significantly affects the efficacy of treatment, thyroid function, pregnancy outcomes, and sleep quality. The use of thyroid function restoration in the special population of hypothyroidism but without anxiety and depression significantly reduces the incidence of adverse pregnancy events. Still, pregnant women with anxiety and depression may need further treatment.

Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Author Contributions

JM and WJH designed the study; all authors conducted the study; CFF and JYD collected and analyzed the data. JM, CJZ and YP participated in drafting the manuscript, and all authors contributed to critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, take public responsibility for appropriate portions of the content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study has been approved by the ethical committee of The Zhangjiakou First Hospital (Approval No. 2020ZJK053). Given the retrospective and de-identified nature of this study, the committee waived the obligation to obtain informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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