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Original article

Use of antidepressants following hysterectomy with or without oophorectomy: A national sample in the US

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ABSTRACT

Objective: Hysterectomy is one of the most common gynecological surgeries conducted around the world. Previous studies reported inconsistent results on depressive symptoms experienced after hysterectomy. This study explored the association between hysterectomy with or without oophorectomy and the use of antidepressants.
Study design: This cross-sectional study included 4888 subjects between 20 and 80 years old who participated in the US National Health and Nutrition Examination Survey (NHANES) between 2015 and 2018. The associations between hysterectomy with or without oophorectomy and the use of antidepressants were estimated using multivariable logistic regression models.
Main outcome measures: There was a positive relationship between hysterectomy, both with and without oophorectomy, and the use of antidepressants after adjusting for all potential confounders (OR = 2.13, 95 % CI = 1.43–3.17, p = 0.000; OR = 2.04, 95 % CI = 1.35–3.06 p = 0.001). In the subgroup analysis stratified by race, a positive association between hysterectomy without oophorectomy was found among non-Hispanic white women (OR = 1.89, 95 % CI = 1.04–3.44, p = 0.038) and women of other races (OR = 3.14, 95 % CI = 1.30–7.56, p = 0.010), and a positive association between hysterectomy with oophorectomy was found among non-Hispanic black women (OR = 3.09, 95 % CI = 1.15–8.27, p = 0.024). However, no association was found among non-Hispanic black and Mexican American women who had undergone hysterectomy with oophorectomy, and it was not reported in women of non-Hispanic white, Mexican American or other race who underwent hysterectomy with oophorectomy.
Conclusion: This study suggested that hysterectomy was significantly associated with antidepressant use, but the extent of the associations may vary by race.

1. Introduction

Hysterectomy, with or without oophorectomy, is one of the most common gynecological surgeries worldwide [1]. More than 33 % of US women have undergone this operation by the age of 60 years old due to abnormal uterine bleeding, uterine fibroids or other benign gynecological disorders and gynecologic malignancies [2–4]. It has been reported that women living in the Unites States have the highest cumulative risk throughout their lifetime [5], and about 54 % of women who underwent hysterectomy also had their bilateral ovaries removed [6].

Abbreviations: NHANES, National Health and Nutrition Examination Survey; NCHS, National Center for Health Statistics; DLQ, disability questionnaire; PHQ-9, The 9-item Patient Health Questionnaire; OR, odds ratio; CI, confidence intervals; SD, standard deviation; STROBE, The STrengthening the Reporting of OBservational studies in Epidemiology; FSH, Follicle Stimulating Hormone; MHT, menopausal hormone therapy.

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Although hysterectomy is a valid option for treating benign gynecological conditions, it is an intrusive surgical procedure with numerous side-effects, such as bleeding and reduced physical functioning [7–9]. Some studies have shown that hysterectomy was associated with increased long-term coronary heart disease and hypertension [10,11]. Depressive symptoms after hysterectomy have been extensively studied; however, the results reported were inconsistent between studies. For instance, a postoperative cohort study that included 53 women who had undergone hysterectomy reported no association with depressive symptoms at three months after the surgery [12]. Moreover, some authors reported that women who underwent hysterectomy had a better quality of life and a reduced fear of cancer [13]. A prospective multicenter cohort study with 419 women who underwent hysterectomy reported that women experiencing depression before hysterectomy for benign indication were observed to have remarkable improvements on postoperative depression after a year of follow-up [14]. It should be noted that these studies had relatively short follow-up periods.

Previous longitudinal research found that hysterectomy posed a higher risk for depressive symptoms in women after surgery [15–17]. Although the risk of depressive symptoms after hysterectomy has been confirmed in long-term follow-up studies, there has been no literature examining the use of antidepressant therapy among women who had undergone hysterectomy. In addition, a few studies suggested that non-Hispanic black women and women from other racial-ethnic groups were less likely to be diagnosed depression or receive psychotropic medications compared with non-Hispanic white women [18,19]; however, none of these studies focused on the association of race and use of antidepressants after hysterectomy.

Thus, the purpose of this study was to explore whether there is an association between hysterectomy and the use of antidepressants, stratified by bilateral oophorectomy status, among women of different races. We used a nationally representative sample obtained from the National Health and Nutrition Examination Survey (NHANES).

2. Materials and methods

2.1. Study population

The study data were obtained from NHANES (https://www.cdc.gov/nchs/nhanes/index.htm). The NHANES database was designed to assess the health and nutritional status of adults and children in the United States. It is a nationally representative, cross-sectional survey conducted by the U.S. National Center for Health Statistics. Since 1999, a series of large, stratified, multistage probability sampling processes were used to select about 5000 persons every year across the nation to complete the survey; each survey cycle lasts for two years [20]. The contents of the survey include demographic, socioeconomic, dietary, and health-related questions, and the questionnaires consist of questions regarding medical, dental, and physiological health [21].

Data from two cycles of NHANES (2015–2016 and 2017–2018) were used in this study. Among the 23,181 participants, 9776 were females. We further excluded women without information on the use of medication for depression (n = 3720) or those without information on their history of hysterectomy (n = 1098), we also excluded women who underwent oophorectomy without hysterectomy (n = 70). Finally, data from a total of 4888 women between the ages of 20 and 80 years old were analyzed. The Institutional Review Board of NCHS had approved each survey, and each participant provided a written informed consent.

2.2. Major variable assessment

The use of antidepressants was the dependent variable (outcome). Information on antidepressant usage was obtained from the participants' self-reported responses to the following question from the Disability Questionnaire (DLQ): “Do you take medication for depression?” History of hysterectomy was the independent variable. Information about history of hysterectomy and oophorectomy were extracted from the following two questions in reproductive health section of the questionnaire: “Have you had a hysterectomy that is, surgery to remove your uterus or womb?” and “Have you had both of your ovaries removed either when you had your uterus removed or at another time?” We organized the responses to history of hysterectomy into three groups: never had hysterectomy, undergone hysterectomy without oophorectomy, and undergone hysterectomy with oophorectomy.

2.3. Covariates

According to previous reports and availability of records in the NHANES [22,23], the following variables are considered to be possible confounders: (a) demographic characteristics including age (20–80 years old, as a continuous variable), race (non-Hispanic white, non-Hispanic black, Mexican American, and others, including Hispanic, Asian and multi-racial), education (less than high school, high school graduate, more than high school, or missing), marital status (married/living with partner, not married, widowed/divorced/separated, or missing), occupation (employed, unemployed, or missing), (b) socioeconomic status as measured by poverty income ratio (<1.0, 1.0–2.0, >2.0, or missing), (c) alcohol use (≥4 drinks every day, <4 drinks every day, or missing), (d) smoking status (current smoker, former smoker, non-smoker, or missing), (e) body mass index (BMI) (<18.5, 18.5–25.0, 25.0–30.0, 30.0–35.0, ≥35.0, or missing), (f) use of female hormones, ever (hormone replacement therapy) (yes, no, or missing), (g) regular periods in the past year (regular period, undergone hysterectomy, natural menopause), (h) hours of sleep (average number of sleeping hours per day), and (i) current depression; the 9-item Patient Health Questionnaire (PHQ-9) was used to evaluate current symptoms of depression. Poverty income ratio measures the ratio of family income to poverty thresholds at the household level. The poverty income ratio adjusts for household size and geographic region, with lower values equating to higher poverty levels. The score of the PHQ-9 was treated as a covariate for the analysis.

2.4. Statistical analysis

The complex sampling design followed the U.S. National Center for Health Statistics guidelines, and sampling weights were calculated based on the analytical guideline [21]. All analyses were calculated using the R statistical package version 3.4.3 (http://www.R-project.org) and EmpowerStats software (http://www.empowerstats.com). Multivariable logistic regression models were used to estimate the associations of hysterectomy with use of antidepressants. Two models were established: Model 1, with no covariates controlled; and Model 2, with all the covariates controlled. Subgroup analyses by races were also conducted.

This was a type II prognostic study which investigates the relationship between hysterectomy and the use of antidepressants. The sample size calculation required 10 events for each variable in the multivariable logistic regression model [24,25]. In Model 2, we planned to include 14 independent variables; therefore, a minimum of 140 participants reporting use of antidepressants were required. An odds ratio (OR) with 95 % confidence intervals (CIs) was calculated as a measure of association between the independent variable and the outcome (dependent variable). For continuous variables, mean ± standard deviation (SD) was presented, and the p-value was calculated by weighted linear regression model. For categorical variables, the percentage was presented, and the p-value was calculated by weighted chi-square test. The significance level was set at 0.05 ($p < 0.05$). Multiple imputation based on replications and chained equation approach method in the R MI procedure was used to account for missing data. Regression analysis was conducted on the five sets of data and the OR values and 95 % confidence intervals of the five regression models were merged [26]. The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement guideline was followed.

3. Results

The flow chart of history of hysterectomy after ethnic stratification was shown in Fig. 1. Among the 4888 participants, the average age of 1052 women at the time of hysterectomy was 41.49 years old (range: 19–60). Among them, the average age of 564 women at the time of both hysterectomy and oophorectomy was 43.69 years old (range: 19–60). There were 632 participants taking antidepressants and Table 1 provided the characteristics of our study population, stratified by use of antidepressants. The women taking antidepressants were older (54.03 ± 15.65 vs 49.46 ± 17.64 years; $p < 0.001$) and were more likely to be unemployed (65.19 % vs 43.94 %; $p < 0.001$) than those who were not taking antidepressants. Non-Hispanic white women, those who were widowed/divorced/separated, those who had undergone hysterectomy only or both hysterectomy and oophorectomy, those who used female hormones, and who did not have regular periods in the past year due to hysterectomy were more likely to take antidepressants ($p < 0.001$). Women taking antidepressants were more likely to be current smokers (21.99 % vs 10.71 %; $p < 0.001$), drink four or more alcoholic drinks every day (15.51 % vs 5.78 %; $p < 0.001$), have BMI ≥ 35.0 (32.59 % vs 22.25 %; $p < 0.001$), live below the federal poverty level < 1.0 (25.16 % vs 18.70 %; $p < 0.001$), score higher on PHQ-9 (7.97 ± 5.92 vs 3.05 ± 3.90; $p < 0.001$), and experience more sleeping problems (69.15 % vs 25.80 %; $p < 0.001$) than those who were not taking antidepressants.

The results of the logistic regression models are presented in Table 2 (n = 4888). A positive association between hysterectomy without oophorectomy and the use of antidepressants was found in the Model 2 (OR = 2.13, 95 % CI = 1.43–3.17, p = 0.000) after adjusting for potential covariates. The association between hysterectomy with oophorectomy and use of antidepressants was also positive in Model 2 (OR = 2.04, 95 % CI = 1.35–3.06, p = 0.001).

After stratifying by race, a positive association between hysterectomy without oophorectomy and the use of antidepressants were reported in 1650 non-Hispanic white women (Model 1: n = 48 taking antidepressant; OR = 2.08, 95 % CI = 1.44–3.00, p < 0.000; Model 2: n = 48 taking antidepressant; OR = 1.89, 95 % CI = 1.04–3.44, p = 0.038), and 1353 women of other races (Model 1: n = 24 taking antidepressant; OR = 3.73, 95 % CI = 2.25–6.19, p < 0.000; Model 2: n = 24 taking antidepressant; OR = 3.14, 95 % CI = 1.30–7.56, p = 0.010). Also, the positive association between hysterectomy with oophorectomy and use of antidepressants was only reported in 1098 non-Hispanic black women (Model 1: n = 20 taking antidepressant; OR = 1.96, 95 % CI = 1.15–3.35, p = 0.014; Model 2: n = 20 taking antidepressant; OR = 3.09, 95 % CI = 1.15–8.27, p = 0.024) (Table 2), it is worth noting that the estimate of 95 % CI interval has increased after adjustment, so it is likely the result of confounding. No significant association was found in non-Hispanic black and Mexican American women who had undergone hysterectomy without oophorectomy, and no significant association was found in non-Hispanic white, Mexican American women and women of other races who had undergone hysterectomy with oophorectomy.

4. Discussion

This study suggested that hysterectomy was significantly associated with use of antidepressants. Those associations were found in non-Hispanic white women and women of other races (including Hispanic, Asian, and Multi-Racial races) who had undergone hysterectomy without oophorectomy. Associations were not found in non-Hispanic black and Mexican American women who had undergone hysterectomy only, and associations were not found in non-Hispanic white, Mexican American women and women of other races who had undergone hysterectomy with oophorectomy.

In this study, the average age of participants at time of hysterectomy was 41.49 years old, while the average age of participants at time of survey was 54.03 years old, which suggested that it may take a long time for depressive symptoms to appear after undergoing hysterectomy with or without oophorectomy. This result was consistent with some existing longitudinal studies. A 12-year follow-up study showed that women who had undergone hysterectomy with or without oophorectomy had a higher risk of experiencing depressive symptoms (RR = 1.20; 95 % CI = 1.06–1.36 and RR = 1.44; 95 % CI = 1.22–1.68, respectively) after more than five years after hysterectomy than those who did not undergo hysterectomy [17]. A 5-year follow-up study that included women who had undergone hysterectomy with ovarian conservation reported that women who had undergone hysterectomy were at a greater risk of depression compared with women who had not undergone hysterectomy (HR = 1.78; 95 % CI = 1.46–2.18) [15]. Furthermore, among younger women between the ages of 18 to 35 years, the risk of depression at 15 years after surgery was higher among those who had undergone hysterectomy compared with those who had undergone hysterectomy with ovarian conservation [16].

Some studies strongly supported that hysterectomy increased the risk of earlier ovarian failure, due to low estrogen levels after surgery [27]. In a study, 60 of 406 (14.8 %) premenopausal women experienced ovarian failure in a four-year follow-up after hysterectomy without bilateral oophorectomy, while only 37 of 465 (8.0 %) women who did not undergo hysterectomy had an ovarian failure [28]. In a 5-year follow-up study, among the 257 women who had undergone hysterectomy, 53 (20.6 %) reached menopause (defined by as a single Follicle Stimulating Hormone (FSH) measurement of at least 40 IU/L) compared to 19 (7.3 %) of 259 women who did not undergo hysterectomy [29]. Thus, the low estrogen concentrations may have driven the onset of menopause. Furthermore, previous studies suggested estrogen deficiency may play an important role in the onset of climacteric depression [30,31]. To prevent post-hysterectomy depression, regular

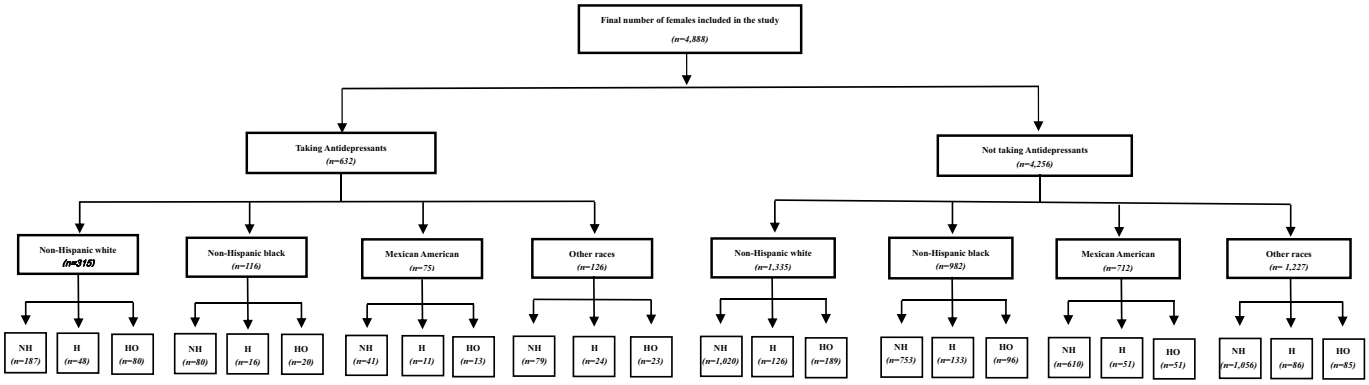

Fig. 1. Flow chart of history of hysterectomy after ethnic stratification.
NH: never had hysterectomy; H: undergone hysterectomy without oophorectomy; HO: undergone hysterectomy with oophorectomy.

Table 1
Characteristics of study sample in NHANES 2015–2018, stratified by use of antidepressants.

Variable	Taking antidepressants n (%) or mean ± SD	Not Taking antidepressants n (%) or mean ± SD	p-Value
Total number of participants	632	4256	
Age, years	54.03 ± 15.65	49.46 ± 17.64	<0.001*
Race			<0.001*
Non-Hispanic white	315 (49.84)	1335 (31.37)	
Non-Hispanic black	116 (18.35)	982 (23.07)	
Mexican American	75 (11.87)	712 (16.73)	
Other races[a]	126 (19.94)	1227 (28.83)	
Education			0.059
<High school	145 (22.98)	801 (18.83)	
High school	123 (19.49)	945 (22.22)	
>High school	363 (57.53)	2507 (58.95)	
Missing	1 (0.16)	3 (0.07)	
Marital status			<0.001*
Married/living with partner	119 (18.83)	760 (17.86)	
Never married	231 (36.55)	1991 (46.78)	
Widowed/divorced/ separated	282 (44.62)	1503 (35.31)	
Missing	0 (0.00)	2 (0.05)	
Occupation			<0.001*
Employed	219 (34.65)	2381 (55.94)	
Unemployed	412 (65.19)	1870 (43.94)	
Missing	1 (0.16)	5 (0.12)	
Percentage of federal poverty level			<0.001*
<1.0	159 (25.16)	796 (18.70)	
1.0–2.0	164 (25.95)	1020 (23.97)	
>2.0	237 (37.50)	1960 (46.05)	
Missing	72 (11.39)	480 (11.28)	
Smoking status			<0.001*
Current smoker	139 (21.99)	456 (10.71)	
Former smoker	29 (4.59)	119 (2.80)	
Non-smoker	156 (24.68)	693 (16.28)	
Missing	308 (48.73)	2988 (70.21)	
Alcohol use			<0.001*
≥4 drinks every day	98 (15.51)	246 (5.78)	
<4 drinks every day	452 (71.52)	3162 (74.30)	
Missing	82 (12.97)	848 (19.92)	
History of hysterectomy			<0.001*
Never had hysterectomy	397 (62.82)	3439 (80.80)	
Undergone hysterectomy without oophorectomy	99 (15.66)	396 (9.30)	
Undergone hysterectomy with oophorectomy	136 (21.52)	421 (9.89)	
Use of female hormones ever			<0.001*
Yes	155 (24.53)	623 (14.66)	
No	475 (75.16)	3613 (85.03)	
Missing	2 (0.32)	13 (0.31)	
Regular periods in the past year[b]			<0.001*
Regular periods	193 (30.54)	2021 (47.49)	
Undergone hysterectomy	235 (37.18)	817 (19.20)	
Natural menopause	204 (32.28)	1418 (33.32)	
BMI			<0.001*
<18.5	6 (0.95)	72 (1.69)	
18.5–25.0	111 (17.56)	1123 (26.39)	
25.0–30.0	141 (22.31)	1197 (28.12)	
30.0–35.0	162 (25.63)	883 (20.75)	
≥35.0	206 (32.59)	947 (22.25)	
Missing	6 (0.95)	34 (0.80)	
Sleeping problems			<0.001*
Yes	437 (69.15)	1098 (25.80)	
No	193 (30.54)	3157 (74.18)	
Missing	2 (0.32)	1 (0.02)	
Hours of sleep[b]	8.20 ± 1.78	7.70 ± 1.53	<0.001*
Current depression score[b]	7.97 ± 5.92	3.05 ± 3.90	<0.001*

BMI: body mass index; SD: standard deviation.
* Chi-square test. Significance at $p < 0.05$.
[a] Other races included Hispanic, Asian, and multi-racial.
[b] These variables do not have any missing values.

Table 2
The associations between hysterectomy (without or with oophorectomy) and use of antidepressants.

Exposure	Model 1 OR (95 % CI)	p-Value	Model 2[a] OR (95 % CI)	p-Value
Never had H	Reference		Reference	
Undergone H without O	2.17 (1.70, 2.76)	<0.000*	2.13 (1.43, 3.17)	0.000*
Undergone H with O	2.80 (2.25, 3.49)	<0.000*	2.04 (1.35, 3.06)	0.001*
Non-Hispanic white				
Never had H	Reference		Reference	
Undergone H without O	2.08 (1.44, 3.00)	0.000*	1.89 (1.04, 3.44)	0.038*
Undergone H with O	2.31 (1.70, 3.13)	<0.000*	1.78 (1.00, 3.24)	0.050
Non-Hispanic black				
Never had H	Reference		Reference	
Undergone H without O	1.13 (0.64, 2.00)	0.668	1.90 (0.75, 4.82)	0.174
Undergone H with O	1.96 (1.15, 3.35)	0.014*	3.09 (1.15, 8.27)	0.024*
Mexican American				
Never had H	Reference		Reference	
Undergone H without O	2.58 (1.27, 5.26)	0.009*	1.75 (0.53, 5.76)	0.360
Undergone H with O	3.05 (1.56, 5.97)	0.001*	2.28 (0.65, 7.94)	0.196
Other races[b]				
Never had H	Reference		Reference	
Undergone H without O	3.73 (2.25, 6.19)	<0.000*	3.14 (1.30, 7.56)	0.010*
Undergone H with O	3.62 (2.16, 6.05)	<0.000*	1.93 (0.81, 4.56)	0.136

H, hysterectomy; O, oophorectomy; OR, odds ratio; CI, confidence interval.
* Chi-square test. Significance at $p < 0.05$.
[a] Age, other races, educational level, marital status, occupation, ratio of family income to poverty, smoking status, alcohol use, use of female hormones ever, regular periods in the past year, body mass index, sleeping trouble, sleep hours, depression were adjusted in Model 2.
[b] Other races included Hispanic, Asian, and multi-racial.

endocrinological monitoring has been recommended to surveil ovarian failure after hysterectomy [32].

Due to the high prevalence of depressive symptoms after hysterectomy, patients who experience depressive symptoms should be referred to psychiatric care. Failure to discover and treat depression may result in worse health outcomes and heavier financial burden, and patients experiencing depressive symptoms may be prone to comorbid drug use and may even attempt to commit suicide [33]. However, at present, there is a lack of information about specific treatments for depressive symptoms experienced after hysterectomy. In this study, we found a significant association between antidepressants use and the hysterectomy among middle-aged women in America, which indicated that further research regarding the specific treatments for depressive symptoms experienced after hysterectomy is necessary.

A large number of studies elucidated numerous and varied depressive symptoms among women during perimenopause. Depressive symptoms, except for depressive mood, were also related with common somatic symptoms found among middle-aged women, including sleep problems, dizziness, headaches, asthenia, muscle pain, and urinary incontinence [34–37]. It was difficult to identify whether the cause of these symptoms was a result of depression or physical decline [38]. Some studies suggested that menopausal women who experienced major depression (excluding bipolar disorder) and required psychiatric

treatment (such as psychological interventions and antidepressant therapy), and displayed moderate or above depressive symptoms should be treated with antidepressants [39]. Furthermore, there has been a focus on the therapeutic effects of antidepressants on depressive symptoms in middle-aged women. Two randomized, double-blind, placebo-controlled trials reported that desvenlafaxine, when compared with placebo, significantly improved the depressive symptoms of major depressive disorder in perimenopausal and postmenopausal women [40,41]. In some small open-label studies, some selective serotonin reuptake inhibitors (including citalopram, escitalopram and vortioxetine), serotonin-norepinephrine reuptake inhibitors (including venlafaxine and duloxetine) and mirtazapine had shown favorable effects on mood and somatic symptoms (such as vasomotor symptoms, insomnia, and pain) [42–45].

Due to estrogen withdrawal, women during the menopause transition are vulnerable to depressed mood [46]. Some studies have reported that menopausal hormone therapy (MHT) may accelerate the response of selective serotonin reuptake inhibitors, and improve the rates of partial remission [47,48]. However, MHT is not approved for the treatment of depression in either Europe or USA due to insufficient evidence. In the current study, “use of female hormones, ever” were used more among women who also use antidepressants than those who do not use antidepressant. Thus, we adjusted the variable of “use of female hormones, ever” in Model 2, and did not find this variable to modify the relationship between hysterectomy status and the use of antidepressants.

In addition, studies have shown that some women may feel a sense of loss, as the removal of the uterus can also be seen as a loss of femininity [49]. Some thought that the surgery may have affected the individual's identity as a female as they can no longer child bear after hysterectomy [13]. These psychological factors may also contribute to post-hysterectomy depression. A study had shown that education and cognitive interventions were effective in reducing postoperative anxiety in Chinese women who have undergone hysterectomy [50].

Additionally, our study found different associations between antidepressants use and hysterectomy among women from different races. Compared with non-Hispanic white women, fewer Mexican American women who had undergone hysterectomy with or without oophorectomy received antidepressant treatment. The racial/ethnic disparities in depression symptoms among women who have undergone hysterectomy were seldomly reported, and there are knowledge gaps in understanding mental health conditions among different races [51]. Financial difficulties were related to mental health status - older African-American adults were less likely than their white counterparts to receive antidepressants [52,53]. Another study reported that half of the non-English-speaking women were less likely to receive adequate antidepressants due to the poor communication and language barrier [54]. However, it should be noted that after ethnic stratification, the risk of antidepressant use was increased in all groups after hysterectomy, and there was an overlap of 95 % confidence intervals between groups. In addition, because the number of women who had undergone hysterectomy and were taking antidepressants in each race group was small after ethnic stratification, the upper limit of the confidence interval may be rather large. Further studies focusing on effect of antidepressant treatment among different races with appropriate sample sizes are required.

Some authors reported that hysterectomy after the age of 45 years was related with weight gain and sleeping problems after the surgery [55], therefore, we stratified by the age at hysterectomy in our analysis. However, we did not find a statistically significant difference between the age groups, which may be a result of our small sample size of women who had undergone hysterectomy. This topic should be further explored in future research. In this study, we had conducted analyses using current depression as the outcome variable, but we did not find an association between hysterectomy and depression. There are two possible reasons for this finding. First, the antidepressants may have been alleviating symptoms among these patients and therefore they were not reporting severe symptoms in the PHQ-9. Second, current depression is measured by PHQ-9 in NHANES, which is a self-administered questionnaire and may not accurately diagnose depression [56]. A patient with depression diagnosed by a psychiatrist may have a very low PHQ-9 score.

Several strengths exist in this study. First, this study was the first to evaluate the association between antidepressants use and hysterectomy using the US national sample. Second, the participants who had undergone hysterectomy in this study were divided into those with or without oophorectomy; thus, eliminating the bias caused by the different underlying characteristic of the enrolled patients. In addition, this was the first study to analyze the use of antidepressants among women of different races who had undergone hysterectomy with or without oophorectomy. There are also several limitations in this study. First, this is a cross-sectional study, so the result could only reflect an association between dependent and independent variables. It is unable to observe a patient both prior to and after their hysterectomy as this is not a longitudinal cohort study. Second, estrogen level is an important influencing factor in depressive symptoms in women. However, due to a lack of information on the participants' estrogen levels, we were unable to include estrogen level information into the model. Third, the types and duration of hormone therapy were not included in the analysis due to the large amount of missing data in these variables. Fourth, the data on using antidepressants and the information on hysterectomy and oophorectomy were both obtained via self-report, which may be prone to recall bias. Fifth, the NHANES database did not provide any data on vasomotor symptoms and the indication for the surgery. This is important to note as they may play a differential role in antidepressant use. Finally, each type of antidepressant works differently and some may be better in improving certain symptoms than others; however, there was no information on specific antidepressants in NHANES, therefore, subgroup analyses for different antidepressants cannot be performed.

5. Conclusion

In summary, this study found that hysterectomy was positively and significantly associated with antidepressant use in the US. This was the first study to provide information on antidepressant treatment after hysterectomy, although there was no information on the use of specific antidepressants. These results may differ by race. Future studies should focus on psychosocial and medical interventions for women post-hysterectomy.

Contributors

L. J. Li contributed to conceptualization and performing formal analysis, and was responsible for writing the original draft.

Q. Chen contributed to conceptualization.

N. Zhang contributed to conceptualization and methodology.

X. Yao contributed to conceptualization, methodology, and interpretation of data.

C. X. Wang contributed to conceptualization, interpretation of data, and supervision.

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There are no linked research data sets in this paper. The data are available from NHANES.

Declaration of competing interest

The authors report no competing interest for this work.

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