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Associations between Psychiatric Disorders and Menstrual Cycle

Characteristics

Mary Lee Barron, PhD, APRN, BC, FNP,

Saint Louis University School of Nursing, 3525 Caroline Mall, St Louis, MO 63104, (314) 977-8978 barronml@slu.edu

Louise H. Flick, DrPH,

Southern Illinois University-Edwardsville, School of Nursing, Edwardsville, IL 62026-1066, (618) 650-3283 Iflick@siue.edu

Cynthia A. Cook, PhD, RN,

Associate Chief Nurse for Research (118), Richard L. Roudebush VA Medical Center, 1481 West 10th Street, Indianapolis, Indiana 46202, 317-554-0000 cynthia.cook@va.gov

Sharon M. Homan, PhD, and

Saint Louis University School of Public Health, Salus Center, Rm 471, St. Louis, MO 63104-1314, (314)977-8103 homansm@slu.edu

Claudia Campbell, PhD

Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, Suite 1900, New Orleans, La 70112, (504)988-7700 ccampbel@tulane.edu

Abstract

An understanding of the relationship between psychiatric disorders and menstrual characteristics is important to the assessment and care of women. Menstrual cycle regularity and length have significant associations with specific current and lifetime psychiatric disorders. The purpose of this study was to investigate whether psychiatric disorders are associated with menstrual cycle length or regularity. The sample included 628 pregnant Medicaid-eligible women from Women, Infants and Children Supplemental Nutrition Program sites in 5 counties in rural Missouri and the city of St. Louis. Women were assessed for current (12-month) and lifetime psychiatric disorders with the Diagnostic Interview Schedule IV. Menstrual length and regularity were assessed by self-report. Analyses consisted of logistic regression while controlling for race.

Independent of the effects of race: 1) women who reported irregular cycles were less than half as likely to have a current anxiety disorder as those that reported regular cycles; and 2) women with shorter cycles (\leq 28 days) have one and one-half times to two times greater risk of current affective disorder, lifetime affective disorder, lifetime anxiety disorder, lifetime substance use or dependence disorder and lifetime drug abuse or dependence. A significant interaction effect for race and cycle length indicated that cycle length predicted likelihood of having any lifetime psychiatric disorder for Caucasians only and there was no association between cycle length and lifetime psychiatric diagnosis for African-American women.

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Societal assumptions about mental health and menstrual cycles have been largely negative over the past century. Premenstrual syndrome has been the target of numerous jokes, and Dalton's substantial work on premenstrual syndrome has even been used as a criminal defense in the United Kingdom during the early 1980s (Lewis, 1990). Despite this, a better understanding of the observed link between mental health and menstrual cycles is critical to the provision of quality nursing care for women, because there is little evidence to guide the assessment and proper treatment of women in this area. The physiologic basis for women's mental health has begun to be explored, particularly since the success of selective serotonin reuptake inhibitors for depression has highlighted the importance of the biologic origins of mental illness. Likewise, the course of psychiatric illness may be biologically influenced by the menstrual cycle. It is also possible that menstrual length and irregularity could, in turn, be influenced by mental health. When more is known about the relationships between these two important areas, then patient education, clinical screening, and treatment modalities can be more knowledgeably implemented. The purpose of this research is to examine the relationship of menstrual cycle length and regularity to the presence of current and lifetime psychiatric disorders in a large community sample.

Literature Review

Menstrual cycle patterns can have a direct influence on physical well-being, including ovarian function, pregnancy maintenance, cardiovascular disease, migraine headaches, diabetes mellitus, and breast cancer (Solomon et al., 2002; Solomon et al, 2001; Terry, Willett, Rich-Edwards, Hunter & Michels, 2005). For example, disruption of the hypothalamic-pituitarygonadal (HPG) axis, which can result in irregular cycles or amenorrhea, is associated with polycystic ovarian syndrome (McIntyre, Mancini, McCann, Srinivasan & Kennedy, 2003; Rasgon, et al., 2005). Research on neurotransmitters and their effects on the female hormones point to the connection between menstrual cycle physiology and risk of cardiovascular disease (ACOG, 2000; Genazzani, et al., 2000). Monoamines and serotonin are known to cause altered physiologic and behavioral states. Serotonin mediates mood and behavioral disorders in which depression and irritability are prominent; monoamines are implicated in anxiety disorders. Estrogen and progesterone are known to modulate levels of both serotonin and monoamines. The complexity and relevance of hormones in human behavior is not well understood. It is not simply a matter of an excess or a deficiency of hormones, since studies on premenstrual syndrome (PMS) demonstrate that women with severe PMS respond differently to normal hormone levels. (Parry, et al., 1997; Schmidt, Nieman, & Danaceau, Adams & Rubinow, 1998)

Although anecdotal evidence links mental health and menstrual cycles, little research has focused on specific psychiatric disorders and comorbid menstrual symptoms, despite its importance in guiding the assessment and treatment of women. In an observational study of women treated for bipolar disorder (BPD), Rasgon and colleagues (2005) noted menstrual abnormalities such as menorrhagia, polymenorrhea, oligomenorrhea, and amenorrhea in 65% of women (N=80). Similarly, Joffe and others (2006) found that early-onset (within 5 years of menarche) menstrual dysfunction prior the onset of psychiatric illness is reported more commonly by women with BPD than by women with unipolar depression and healthy controls, possibly reflecting abnormalities in the HPG axis associated with BPD.

The prevalence of one of the most common mood states, depression, increases with reproductive developmental events: puberty, pregnancy, postpartum and perimenopause (Harlow, Wise, Otto, Soares & Cohen, 2003; Kessler et al., 2005; Stein & Nair, 2000; Steiner, Dunn, & Born, 2003). This suggests that reproductive hormones play a role in depression (Robertson, Grace, Wallington & Stuart, 2004). Bisaga and colleagues (2002) examined the association between menstrual functioning and psychopathology in high school girls. Irregular

cycles, late menarche, and being in the first gynecologic year post menarche were each differentially associated with depressive disorder, obsessive-compulsive disorder, and eating disorder. Harlow and colleagues (2003) explored the relationship between depression and the onset of perimenopause. Compared with nondepressed women, depressed women had twice the risk of an earlier perimenopausal transition. Lower estrogen levels have been found in women who are depressed (Harlow et al., 2003; Young, Midgley, Carlson, & Brown, 2000). Additionally, Harlow hypothesizes that depression may permanently alter the HPG regulation of one's reaction to stressful events (Harlow et al, 2003). Rasgon and colleagues (2002) reported the case of a woman whose treatment-resistant depressive symptoms resolved only after her polycystic ovarian syndrome was treated and regular menstrual cycles were restored.

In sum, a better understanding of the observed link between psychiatric illness and menstrual cycle characteristics is critical to the provision of quality nursing care for women, since there is little evidence to guide the assessment and proper treatment of women in this area. Little empirical evidence documents this important link. Thus, the purpose of this study is to investigate the association between current and lifetime psychiatric disorders with menstrual cycle length and regularity.

MATERIALS AND METHODS

Sample

Data from a prospective cohort study of prenatal mental health and its impact on birth outcomes, health care utilization, and costs were used to investigate the relationship between psychiatric disorder and menstrual cycle regularity and length. The study was approved by the Institutional Review Board at Saint Louis University. The original data were collected between February 2000 and August 2001.

Subjects for the study were Medicaid-eligible pregnant women who participated in the Women, Infants, and Children's Supplemental Nutrition Program (WIC) in both St. Louis City and in five rural southeastern Missouri counties. The sample was stratified by place of residence (urban/rural) and representative by race (African-American and Caucasian) in each of the county WIC programs sampled. Subjects were 13 years or older and spoke English. The final sample was 744 (85% response rate). The participants underwent a 2–3 hour in-person interview with a trained research assistant using the Diagnostic Interview Schedule, IV (DIS-IV) and a pregnancy questionnaire once during her pregnancy either at the WIC site or in her home. Electronic files containing WIC intake, pregnancy information, and birth certificate data were obtained for each subject from the Missouri Department of Health and Senior Services.

The sample, after exclusions described below, included 363 African-Americans (57.8%) and 265 Caucasians (42.2%). Approximately 60% (n=374) resided in rural Southeast Missouri, and 39.1% (n=254) lived in St. Louis city. One in five was currently married. Mean age was 22.2 years (SD=5.1); with a range of 13–43 years.

Of the 628 women in the sample, 477 (76.0%) reported regular cycles, 139 (22.1%) reported irregular cycles, 3 (0.5%) did not know their cycle regularity, and 9 (1.4%) had missing data. The mean cycle length was 28.5 (SD=5.7) days. Women reporting cycle lengths of 28 days or less comprised just over one-half of the sample (n=327, 52.1%). Another 39.8% (n=250) reported 29 days or more, and the remaining 8.1% (n=51) gave no cycle length information. Thus, a total of 577 subjects had complete data for the cycle length variable.

Instruments

Sociodemographics characteristics were drawn from the Diagnostic Interview Schedule Version IV (Robins, Cotler, Bucholz, et al, 2003), and from the WIC certificate data recorded

by WIC staff upon enrollment [maternal age, race, residence, height, and prepregnancy weight].

The Diagnostic Interview Schedule IV (DIS-IV) was used to measure 12-month and lifetime psychiatric disorders. This instrument is a lay-administered structured diagnostic interview based on the Diagnostic Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). The interview assessed symptom counts, onset, recency, and duration of symptoms; periods of remission: disruption in social and work relationships; and receipt of treatment. Good to excellent reliability with the DIS for most diagnoses (kappa .60 to .81) has been demonstrated (Horton, Compton, & Cottler, 1998). Validity has been demonstrated in comparing the DIS to other diagnostic structured interview assessments (Dascalu, Compton, Horton, & Cottler, 2003), in comparing lay administered to psychiatrist administered versions of clinical populations (Levitan, Blouin, Navarro, & Hill, 1991), and the general population (Robins, Helzer, Ratcliff, & Seyfried, 1982)

⁶Current' psychiatric disorder was defined as meeting full diagnostic criteria for any of the 22 diagnoses based on symptoms within the 12 months prior to the pregnancy interview. ⁶Lifetime' psychiatric disorder was defined as having met criteria at any point in the woman's life. The woman may or may not have active symptoms at the time of interview, although for most current diagnoses more than 90% of subjects had active symptoms when interviewed. ⁶Any current psychiatric disorder' was defined as meeting DSM-IV criteria for at least one diagnosis, based on symptoms in the previous 12 months. Grouped diagnoses (affective disorders, anxiety disorders, substance use or dependence disorders) was based on the categories within the DSM-IV and were assigned when subjects met criteria for one of the individual diagnoses within the respective diagnostic category.

Procedure

For the current study, subjects using hormonal contraceptives were excluded. Each subject was asked what type/s of contraception she used, if any, at conception and in the 3 months before conception. Because long-acting hormonal contraceptives (Depo-Provera, Norplant) are known to cause profound menstrual irregularity, subjects using them were excluded from the sample (n=14). Additionally, women using oral contraceptives (n=92) were excluded from the final sample, because oral contraceptives regulate cycles and establish cycles of timed frequency. Cases where women who had no knowledge of when their last menstrual period occurred were recorded as missing (n=10). These exclusions reduced the total sample for these analyses consisted of 628 women.

Studies have documented that women accurately recall menstrual cycle characteristics (Creinin, Keverline & Meyn, 2004; Must et al., 2002). Women were questioned about menstrual characteristics with the following questions "How many days are there from the <u>beginning</u> of one monthly menstrual period to the next period?" and "In the year before this pregnancy, were your periods usually regular or irregular? That is, is the length of time between your periods about the same each cycle?" The answer was coded as regular, irregular, or "don't know". Raw data were examined for interviewer notations about the women's answers. Subsequently, a new variable was developed that reflected interviewer comments. If the woman indicated she was regular but interviewer comments suggested irregularity such as, "I skip a month," then she was placed in the irregular category. Conversely, if a woman answered that her cycles were irregular but gave a range such as "24–27 days" she was assigned to the "regular" group.

Subjects were divided into three groups by age: adolescent (≤ 20 years), young adult (21–35 years) and perimenopausal women (≥ 36 years). Menstrual cycle irregularity has long been observed to be more frequent during adolescence and perimenopause compared to young

adulthood (Treolar, Boynton, Behn & Brown, 1967); therefore, confounding by age was controlled using this grouping. Additionally, cycle length has been shown to decrease with age (Liu, Gold, Lasley & Johnson, 2004), and prevalence of psychiatric disorder increases with age (Robins & Regier, 1991).

Smoking is associated with short cycles (Rowland et al, 2002). The DIS nicotine dependence module was used to assess onset, recency, quantity and frequency of tobacco product use as well as the criteria for dependence. A variable indicating any tobacco use in the last 12 months, a period that coincides with the period assessed for cycle regularity and length was created.

The influence of body mass index on menstrual function has been studied for decades. Symons, Sowers, and Harlow (1997) studied 436 women aged 24–35 who generated 4392 menstrual cycles. While controlling for age, BMI, body fat, and lean mass, women with lowest levels or highest levels of BMI both have longer than average cycle lengths (Symons, Sowers, & Harlow, 1997). At the initial WIC pregnancy visit in this study women were measured for height and they reported their prepregnancy weight. BMI was calculated from these WIC data. When height or prepregnancy weight was not available from WIC data (n=63), maternal prepregnancy height or weight was drawn from the birth certificate data. Data were available for 624 of the 628 cases. Subjects were classified into four BMI groups: underweight (< 19.8); normal weight (19.8–24.99); overweight (25–29); and obese (29.01 and higher) using the Institute of Medicine categories for pre-pregnancy weight (Institute of Medicine, 1990). These four categories were collapsed into two categories (underweight and average; overweight and obese) due to low numbers in the underweight and overweight group (see Table 1).

Researchers have consistently found that patients with diabetes are approximately twice as likely to experience depression as those without diabetes (Brown, 2004). Depression was almost 50% more prevalent in patients with diabetes (17.9% versus 11.2%, p < 0.001) in a large study of primary care patients (Nichols & Brown, 2003). Women were asked in the DIS-IV pregnancy interview for age of onset for diabetes as well as the date of last symptom. Diabetic status was evaluated by cross-checking diabetes onset on the DIS with birth certificate data (indicating diabetes during pregnancy) to differentiate those with pre-existing and gestational diabetes. If the woman had developed diabetes the same year she conceived or during the target pregnancy, the diabetes was considered gestational. If onset was prior to conception and duration was ongoing, diabetes was considered pre-existing. Women with pre-existing diabetes (n=15) and those who developed gestational diabetes were thus identified (n=11).

Statistical Methods

Data entry, cleaning, and management were conducted using SAS-PC (Versions 8.0 and 9.0). SPSS (Version 14.0) was used for recoding and statistical analyses. Univariate binary logistic regression analyses were conducted to examine the simple associations between menstrual cycle variables (cycle length and regularity) and each of the co-variates: age, race, place of residence, smoking, pre-existing diabetes and prepregnancy BMI.

Univariate logistic regression was then used to determine the relationship of the 13 diagnostic categories (lifetime and current) with menstrual cycle variables. Unadjusted odds ratios and 95% confidence intervals were produced to describe relationships. When statistically significant relationships with either of the menstrual cycle variables were found, individual diagnoses within that category with a prevalence of at least 1% (n=8) were examined using univariate logistic regression.

Because the purpose of the analyses was to produce the best estimate of the association between the menstrual cycle variables and likelihood of having a psychiatric disorder, multivariate

binary logistic regression was used to test study hypotheses while adjusting for effects of potentially confounding variables. Covariates were included in these models if they were significantly associated with the dependent variable in the earlier (univariate) analyses with the exception of race, which was included in all models because it was used in sample selection. All possible two variable interactions were examined as a batch and dropped if non-significant.

Results

The DIS-IV assessed women for 22 current and lifetime diagnoses. The prevalence of these disorders have been reported elsewhere (Cook et al., Unpublished manuscript, 2007). The sample analyzed here had very similar prevalence figures with nearly one-third (n=197, 31.4%) meeting criteria for a current psychiatric disorder. Almost one-half of the women (n=285, 45.4%) had one or more lifetime diagnosis of a psychiatric disorder. When comparing rates of psychiatric disorders between Caucasian and African-American subjects, Caucasians were significantly more likely to have a current disorder and a lifetime psychiatric disorder (prevalence of current disorder for Caucasians was 36.9% and African Americans 26.9%; p<. 01 and lifetime prevalence was 57.3% and 37.5%; p<.001 respectively) than African-Americans. There were no significant differences when comparing menstrual length and regularity by age, residence, marital status, BMI, smoking status, and pre-existing diabetes.

Table 2 reports the prevalence of each disorder by menstrual cycle regularity with odds ratios indicating whether irregular cycles were associated with an increased or decreased risk for each disorder. Women who reported irregular cycles were three times more likely to have current Attention Deficit Hyperactivity Disorder (ADHD; OR=3.05, 1.31–7.10) and less than one-half as likely to have a current anxiety disorder compared to those who reported regular cycles (OR 0.42, 0.19–0.95). Those with irregular cycles were twice as likely to have lifetime Bipolar I disorder. While none of the other individual diagnoses included in this analysis achieved statistical significance, all of those tested showed a lower prevalence of disorders among those with irregular cycles compared to those with regular cycles.

Table 3 reports the prevalence of each current and lifetime psychiatric disorder by menstrual cycle length with the unadjusted odds ratios indicating whether shorter or longer cycle lengths were associated with an increased or decreased risk for each disorder. Among women with shorter cycles, 25% had a lifetime substance abuse or dependence disorder. Among the lifetime substance abuse disorders, tobacco dependence was *not* significantly associated with shorter cycle length. However, both alcohol abuse or dependence (OR=2.12, 1.09–4.10) and drug abuse or dependence (OR=1.98, 1.01–3.85) were significantly associated with shorter cycle length.

Multiple logistic regression analyses were used to test for effects of menstrual cycle length and regularity on the likelihood of a psychiatric disorder diagnosis while adjusting for race. None of the other sociodemographic variables were included because they were not significantly associated with the menstrual cycle variables. Women with irregular cycles were less than one-half as likely to have a current anxiety disorder and almost three times more likely to have ADHD compared to women with regular cycles. Caucasian women were more than twice as likely as African-American women to have ADHD, independent of cycle regularity (see Table 4). Caucasian women, independent of the effects of cycle regularity, had a marginally higher risk (OR=1.58, 1.12–2.22) for a current psychiatric disorder compared to African-American women.

When menstrual cycle length was entered as a main effect variable (without inclusion of the interaction with race) to predict lifetime psychiatric disorders, results indicated women with shorter cycles have about a one and one-half times greater risk of having at least one lifetime

psychiatric disorder than women with longer cycles (OR=1.63, 1.14–2.33; see Table 5). However, the interaction between menstrual cycle length and race proved significant. The results indicated that the association between cycle length and having at least one lifetime psychiatric disorder was accounted for primarily by an association for Caucasian women. Among African-American women, there was no association between cycle length and having a psychiatric lifetime diagnosis; among Caucasian women, women with short cycles are 2.2 (1.3–3.8) times more likely to have a lifetime disorder.

Shorter menstrual cycles were associated with a one and one-half times greater risk of lifetime substance use or dependence disorder (OR=1.62, 1.05–2.51). Women with shorter cycles were twice as likely to report lifetime drug abuse or dependence. Independent of cycle length, Caucasian women were nearly five times as likely to report substance abuse and two-and-half times more likely to report drug abuse or dependence. The prevalence of current alcohol abuse/ dependence was too low to be tested for association with cycle regularity or length. This was not surprising because there is a social stigma about alcohol intake during pregnancy.

Discussion

The 31.4% rate of any current psychiatric disorder in this sample was similar to that found in other population studies for young women (Insel & Fenton, 2005). Neither cycle length nor regularity was associated with current or lifetime major depression. Other research studies have explored a relationship between depression and menstrual history (Cohen, Soares, Vitonis, Otto & Harlow; 2006; Harlow et al., 2003; Young, Midgley, Carlson, Brown, 2000) as well as bipolar disorder and menstrual abnormalities (Rasgon, Bauer, Glenn, Elman & Whybrow, 2003; Rasgon et al, 2005) Young and colleagues established that blood levels of reproductive hormones (luteinizing hormone, follicle-stimulating hormone, and progesterone) were generally normal in women with depression, but the blood level of estradiol was significantly lower. Harlow and colleagues found that women with a history of depression experienced perimenopause earlier, which is consistent with lower estrogen levels. The finding that shorter cycles are associated with current and lifetime affective disorders in this study may also be consistent with lower estrogen levels but this possible relationship requires further study.

That African-American women were less likely than Caucasian women to have an affective disorder is consistent with national findings on the mental health of minority women (USDHHS, 2003). However, these figures may represent under diagnosis. Lower rates may reflect African-American cultural values of resilience, adaptability, and strength (Andrews & Boyle, 2003) with psychiatric symptoms perceived as weakness and therefore less likely to be reported. While the DIS was developed with both Caucasian and African American respondents there may be cultural differences in the validity of the DIS. However, an ethnographic study comparing African American and Caucasian respondents who had participated in a large DIS-based prevalence study found differences in how anxiety symptoms were described by education but not by ethnicity (Heurtin-Roberts et al., 1997).

Our finding that women reporting irregular cycles had less than one-half the risk of a current anxiety disorder is new information since there is no known published data on anxiety and cycle regularity. Because depression and anxiety often occur together, one might expect they have similar patterns of cycle regularity. However, the dissimilarity found in this study may be explained by differing neuroendocrine pathways that vary in substantial, yet unknown ways. Another consideration is that earlier studies had few women of lower socioeconomic or multiethnic backgrounds in their samples (Breitkopf et al., 2006).

Reporting an irregular cycle was also associated with a higher prevalence of ADHD in the unadjusted analysis but adjustment for race reduced this to non-significance, suggesting the

apparent relationship between ADHD and cycle irregularity was confounded by race. Caucasian women were significantly (OR=6.87, 3.92–12.04) more likely to have ADHD than African-American women and since Caucasian women were also more likely to have irregular cycles this gave the appearance of an association between irregular cycles and the diagnosis of ADHD when there was none.

This investigation has several limitations. All women were pregnant when recruited thus eliminating any potential subjects with menstrual abnormalities severe enough to prevent conception. Subjects were minimally questioned about the character of their menses and providing a definition of regularity to subjects may have affected the results. Retrospective recall of menstrual cycle length could also have been influenced by women's construction of the expected length of their menstrual cycle. Common lay wisdom and numerous illustrations give 28 days as the normal length of menstrual cycle. The extent to which women in this cohort, if prospectively recorded, would vary from the expectation of a 28 cycle is not known. Women with psychiatric disorder also may be less able to accurately recall their last menstrual cycle prior to conception than women without a disorder.

Due to strong societal disapproval of substance and alcohol use during pregnancy, participants may have underestimated their current use. However, evaluating lifetime substance use is more likely to evoke an accurate response since this removes the stigma of pregnancy use.

Despite these limitations, strengths of this study include the large population based sample, representative of poor women enrolled in WIC, which is inclusive of rural African American subjects. Twenty-three lifetime and current psychiatric disorders were assessed simultaneously based on self-reported symptoms so the diagnoses were not dependent on subjects having sought care or identifying their symptoms as indicating psychiatric disorder. This study affirms that shorter cycle lengths are associated with mood disorders and introduces new findings about anxiety disorder and menstrual cycle irregularity.

Implications for Practice

Advances in our understanding of women's health, including the recognition and treatment of psychiatric disorders, will increase the ability of nurses to comprehensively care for women. Our findings suggest the importance of assessing women presenting with psychiatric illness for menstrual cycle disturbances and for gynecologic problems often associated with menstrual irregularities. The first step is to make sure that the gynecologic history is on the assessment tool used to screen the patient. Gynecologic assessment of the woman should include:

- 1. A careful history using open-ended communication techniques. Women need to feel safe in what they are saying and the menstrual cycle may be inherently tied to sexuality even though this has not been openly stated.
- 2. Clarifying techniques. Some women have irregular cycles but think this is normal. Therefore the patient should be encouraged to describe her cycle in her own words. The nurse should seek consensual validation of information.
- **3.** State the implied. Some women have difficulty talking about the menstrual cycle. The woman should be given time to change her answer as she may initially give a socially acceptable answer. Some women want to feel normal in one aspect of their health, as they are already being seen for a psychiatric disorder.

Re-screening the woman for menstrual cycle characteristics should also be performed when other labs are ordered such as the CBC and Thyroid profile. Additionally, if the woman is taking psychotropic medications (e.g. valproic acid, aripiprazole) and then periodic screening is advised as there may be effects on the menstrual cycle. The nurse can refer the patient to or encourage her to follow up with a gynecology practice should abnormalities be suspected.

In conclusion, this study is a step toward understanding the relationship between menstrual cycle characteristics and specific psychiatric disorders. Common factors may underlie the pathophysiology of menstrual disturbances and psychiatric disorder such that successful treatment of psychiatric disorder may improve menstrual cycle disturbances and vice versa. A further understanding of the complexities of this relationship may help to guide the assessment and proper treatment of women in this area.

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 Table 1

 Sociodemographic and Menstrual Cycle Characteristics

Covariate	Irregular Cycles #	n=101 %	cO.R (95%CI)	Cycles ≤ 28 days n=327 # %	cO.R (95%CI)
Maternal Age					
<20 years	28	(27.2)	0.70(0.43 - 1.11)	105 (32.1)	0.86(0.63 - 1.26)
20–35 years	72	(6.69)	Reference	213 (65.1)	Reference
≥ 36 years	3	(2.9)	1.14(0.31 - 4.15)	9 (2.8)	1.67(0.51-5.56)
NACC	Ī				
African-American	51	(49.5)	Reference	193 (59.0)	Reference
Caucasian	52	(50.5)	1.49(0.98-2.28)	134 (41.0)	1.06(0.76 - 1.48)
Residence					
Rural	54	(52.4)	0.77 ($0.46 - 1.08$)	187 (57.2)	0.82 (0.58–1.15)
Urban	49	(47.6)	Reference	140 (42.8)	Reference
Marital Status					
Not married	78	(75.7)	0.77(0.47 - 1.27)	254 (77.4)	0.79 (0.52–1.19)
Married	25	(24.3)	Reference	73 (22.3)	Reference
BMI					
≤24.99	46	(45.5)	Reference	158 (48.5)	Reference
≥25.00	55	(54.5)	1.05(0.68 - 1.60)	168 (51.5)	0.83(0.60-1.16)
Pre-existing diabetes	2	(1.8)	0.85(0.19 - 3.84)	10 (3.1)	2.60(0.71 - 9.54)
Tobacco Use	64	(62.1)	1.14(0.74 - 1.90)	196 (59.9)	1.10(0.79 - 1.54)

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Psychiatric Disorder and Menstrual Cycle Regularity

Psychiatric Disorder	Regular Cycles n=525 #	%	[#	rregular Cycles N %	i=103 cO.R (95%CI)
	-		5	(1.00)	
Any	100	(0.16)	10	(1.0c)	(/7.1-20.0) (0.39-1.4/)
Attective	7/2	(13.7)	14	(13.6)	0.99(0.54–1.83)
Major Depressive	43	(8.2)	9	(5.8)	0.69(0.29 - 1.67)
Bipolar I	28	(5.3)	8	(7.8)	1.49 (0.66–3.38)
Anxiety	77	(14.7)	7	(6.8)	$0.42 (0.19 - 0.95)^{*}$
Generalized Anxiety	22	(4.2)	0		
Anv Phobia	27	(5.1)	ŝ	(2.9)	0.55(0.16 - 1.86)
PTŠD	44	(8.4)	9	(5.8)	0.68(0.28-1.63)
Substance	23	(4.4)	4	(3.9)	0.88(0.30-2.61)
Drug Abuse/Dependence	21	(4.0)	4	(3.9)	0.97 (0.33–2.61)
Alcohol Abuse/Dependence	9	(1.1)		(0)	
Tobacco dependence	68	(13.0)	16	(15.5)	1.24 (0.68–2.23)
ADHD	16	(3.0)	6	(8.7)	$3.05(1.31-7.10)^{**}$
Behavior disorder	29	(5.5)	5	(4.9)	0.87(0.33-2.31)
Lifetime Disorders					
Any	231	(44.0)	54	(52.4)	1.40(0.92 - 2.14)
Affective	125	(23.8)	26	(25.2)	1.08 (0.66–1.76)
Major Depressive	87	(16.6)	13	(12.6)	0.73 (0.39 - 1.36)
Bipolar I	35	(6.7)	13	(12.6)	$2.02(1.03 - 3.97)^{*}$
Anxiety Disorder	117	(22.3)	22	(21.4)	0.94(0.57 - 1.58)
Generalized Anxiety	34	(6.5)	1	(1.0)	0.14(0.19 - 1.05)
Obsessive-Compulsive	10	(1.9)	2	(1.9)	1.02 (0.22-4.72)
Any phobia	43	(8.2)	7	(6.8)	0.82(0.36 - 1.87)
PTSD	74	(14.1)	18	(17.5)	1.29 (0.73–2.27)
Substance	113	(21.5)	25	(24.3)	1.17 (0.71–1.92)
Drug Abuse/Dependence	42	(8.0)	6	(8.7)	1.10(0.52 - 2.39)
Alcohol Abuse/Dependence	45	(8.6)	10	(6.7)	1.15(0.56-2.36)
Tobacco Dependence	68	(13.0)	16	(15.5)	1.24 (0.68–2.23)
Psychotic	6	(1.1)	4	(3.9)	3.49 (0.97–12.61)
ADHD	16	(3.0)	9	(8.7)	$3.05 \left(1.31 - 7.10 \right)^{*}$
Behavior disorder	32	(6.1)	11	(10.7)	1.84(0.90-3.79)
*					

p<.05

** p<.01 Categories of grouped diagnoses: Affective, Anxiety, Psychotic, Behavior, Eating, ADHD, and Substance Use Disorders

Individual diagnoses of too low prevalence to analyze include: Dythymia, Bipolar II, Agoraphobia, Panic Disorder, Current Obsessive Compulsive Disorder, Schizoaffective Disorder, Schizophrenia, Schizophrenia, Oppositional Disorder, Conduct Disorder, Antisocial Personality Disorder, Anorexia and Bulimia.

Psychiatric Disorder and Menstrual Cycle Length

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Psychiatric Disorder	Cycles ≥ 29 days		Cycles ≤ 28 days		
	#	%	##	%	cO.R (95%CI)
Current Disorders					
Any	72	(28.8)	107	(32.7)	1.20(0.84 - 1.72)
Affective	24	(9.6)	55	(16.8)	1.90(1.14-3.18)
Major Depressive	15	(0.0)	32	(6.8)	1.70(0.90 - 3.21)
Bipolar I	6	(3.6)	22	(6.7)	1.93(0.87 - 4.27)
Anxiety	27	(10.8)	53	(16.2)	1.60(0.97 - 2.62)
Generalized Anxiety	vo :	(2.0)	16	(4.9)	2.52 (0.91–6.98)
Any Phobia	12	(4.8)	18	(5.5)	1.16(0.55-2.44)
PTSD	16	(6.4)	30	(9.2)	1.48 (0.79–2.76)
Substance	6	(3.6)	14	(4.3)	1.20(0.51 - 2.81)
Drug Abuse Dependence	6	(3.6)	12	(3.7)	1.02 (0.42 - 2.46)
Alcohol Abuse Dependence		0	S	(1.5)	
Tobacco dependence	30	(12.0)	47	(14.4)	1.23 (0.75–2.01)
ADHD	5	(2.0)	16	(4.9)	2.52(0.91 - 6.98)
Behavior disorder	10	(4.0)	20	(6.1)	1.56(0.72 - 3.40)
Lifetime Disorders					•
Any	66	(39.6)	159	(48.6)	1.44 (1.03–2.02)
Affective	48	(19.2)	90	(27.5)	$1.60(1.07-2.38)^{*}$
Major Depressive	33	(13.2)	61	(18.7)	1.51(0.95 - 2.39)
Bipolar I	15	(0.0)	27	(8.3)	1.41 (0.73–2.71) "
Anxiety Disorder	46	(18.4)	84	(25.7)	$1.53 (1.02 - 2.30)^{*}$
Generalized Anxiety	10	(4.0)	24	(7.3)	1.90(0.89 - 4.05)
Obsessive-Compulsive	-	(0.4)	8	(2.4)	6.24 (0.78–50.23)
Any phobia	17	(6.8)	31	(9.5)	1.44(0.78-2.66)
PTSD	34	(13.6)	53	(16.2)	1.23 (0.77–1.96) _
Substance use/ dependence	43	(17.2)	81	(24.8)	1.59 (1.05–2.40)
Drug Abuse/Dependence	13	(5.2)	32	(9.8)	$1.98\ (1.01-3.85)$
Alcohol Abuse/Dependence	13	(5.2)	34	(10.4)	2.12 (1.09–4.10) *
Tobacco Dependence	30	(12.0)	47	(14.4)	1.23 (0.75–2.01)
Psychotic	5	(2.0)	4	(1.2)	0.61 (0.16–2.28)
ADHD	S	(2.0)	16	(4.9)	2.52 (0.91–6.98)
Behavior disorder	13	(5.2)	25	(1.6)	1.51(0.76 - 3.01)

* p<.05

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			Table 4		
	Logistic Regression Analy	ses for Psychiatric Disord	er and Cycle Regularity		
Current	Any	Affective	MDD	Bipolar I	
Irregularity	OR(95%CI) 0.89(0.56-1.41)	OR (95% CI) 0.96(0.52–1.78)	OR(95%CI) 0.67(0.28–1.62)	OR(95%CI) 1.47(0.65–3.33)	
Caucasian Lifetime	$1.58(1.12-2.22)^{**}$	1.37 (0.87–2.16)	1.37(0.77–2.47)	1.21(0.62–2.39)	
Irregularity Caucasian	1.31(0.85-2.02) 2.23(1.62-3.00)*	1.02(0.62–1.67) 1 84(1 27–2 67)*	0.69(0.37 - 1.30) 1 63(1 06-2 52)*	1.89(0.66–5.36) 1.60/0.81–3.18)	
Current	Anxiety OR(95%CD	GAD OR(95% CI)	Any Phobia OR(95%CI)	OCD OR(95% CI)	PTSD OR(95%CI)
Irregularity	0.41(0.18-0.92)*	a	0.52(0.15-1.75)	a	0.64(0.26-1.55)
Caucasian Lifetime	1.42(0.89 - 2.26)	1.23(0.52 - 2.90)	1.90(0.91 - 4.00)		1.72(0.96 - 3.07)
Irregularity	0.92(0.55 - 1.54)	0.14(0.18 - 1.01)	0.51(0.12-2.24)	0.96(0.20 - 4.45)	1.25(0.71 - 2.20)
Caucasian	1.37(0.94-2.01)	1.40(0.70 - 2.78)	1.30(0.70 - 2.44)	1.94(0.61 - 6.22)	1.43(0.92 - 2.23)
Current	Substance Use or Dependence	Drug Abuse or Denendence	Tobacco Dependence	ADHD	Behavior Disorder
	OR(95%CI)	OR(95%CI)	OR(95% CI)	OR(95%CI)	OR(95% CI)
Irregularity	0.81(0.27 - 2.40)	0.89(0.29-2.65)	2.83(1.21-6.63) *	1.05(0.56 - 1.95)	0.90(0.39 - 2.39)
Caucasian Lifetime	2.45(1.10-5.45)*	2.45(1.10-5.86)*	2.36(1.02–5.47)*	6.87(3.92–12.04)*	0.74(0.36–1.52)
Irregularity	1.02(0.61 - 1.72)	1.02(0.48 - 2.17)	2.83 (1.21–6.63) *	1.05(0.56 - 1.95)	1.80(0.87 - 3.70)
Caucasian	4.34(2.88–6.53)***	2.27(1.26 - 4.09)*	2.36(1.02-5.47)*	6.87(3.92–12.04)***	1.28(0.69 - 2.4)
a too few cases					

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		Tabl	e 5		
	Logistic Regression Analyses f	or Psychiatric Disorder and	l Cycle Length		
Current	Any	Affective	MDD	Bipolar I	
	OR(95%CI)	OR(95% CI)	OR(95%CI)	OR(95%CI)	
≤28 days	1.20(0.84 - 1.72)	1.90(1.14 - 3.17)*	1.69(0.90 - 3.20)	1.93(0.87 - 4.26)	
Caucasian Lifetime	1.63(1.14–2.33)*	1.43(0.89 - 2.32)	1.45(0.80–2.65)	1.22(0.59–2.53)	
≤28 days	1.45(1.03-2.04)*	1.60(1.07-2.39)*	1.50(0.95 - 2.38)	1.40(0.73 - 2.70)	
Caucasian	$2.41(1.71-3.39)^{***b}$	$1.88(1.28-2.78)^{**}$	1.68(1.07 - 2.62)*	1.68(0.89 - 3.16)	
Current	Anxiety OR(95% CI)	GAD OR(95% CI)	Any Phobia OR(95%CI)	OCD OR(95%CI)	PTSD OR(95%CI)
≤28 days	1.59(0.98-2.62)	2.52(0.91 - 6.97)	1.14(0.54-2.43)	a	1.47(0.78-2.76)
Caucasian Lifetime	1.40(0.87 - 2.25)	1.10(0.45 - 2.66)	2.00(0.95-4.20)		1.67(0.91–3.07)
≤28 days	1.53(1.02-2.29)*	1.89(0.89 - 4.04)	1.43(0.77 - 2.65)	1.84(0.77 - 49.95)	1.22(0.77 - 1.95)
Caucasian	1.35(0.91 - 2.00)	1.33(0.66-2.66)	1.39(0.77 - 2.52)	1.83(0.49 - 6.95)	1.46(0.92 - 2.30)
Current	Substance Use or Dependence OR(95%CI)	Drug Abuse or Dependence OR(95%CI)	Tobacco Dependence OR(95%CI)	ADHD OR(95%CI)	Behavior Disorder OR(95%CI)
≤28 days	1.18(0.50-2.79)	1.00(0.41 - 2.43)	1.22(0.73 - 2.05)	2.50(0.90-6.96)	1.57(0.72 - 3.42)
Caucasian Lifetime	2.88(1.20-6.92)*	3.08(1.22–7.75)*	7.95(4.39-14.39)***	3.06(1.21–7.73)*	0.72(0.33 - 1.57)
<28 days	1.62(1.05-2.51)*	1.97(1.01-3.85)*	1.22(0.73 - 2.05)	2.50(0.90-6.96)	1.51(0.75 - 3.01)
Caucasian	$4.75(3.08-7.31)^{***}$	2.37(1.27-4.42)*	$7.95(4.39 - 14.36)^{***}$	3.06(1.21 - 7.73)*	1.2(0.62 - 2.34)
a too few cases					

 $b_{\rm interaction effect}$