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ORIGINAL ARTICLE

Association of menstruation cycle with completed suicide: a hospital-based case-control study

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Abstract

The purpose of the study was to determine the phases of the menstrual cycle in the reproductive age group of females who committed suicide as compared with a control group of females who died from causes other than suicide. The study included 86 cases in the suicidal group and 80 cases in the non-suicidal group. The menstrual phase was decided by the gross and histological examination of the uterus and ovary at autopsy. Deaths were more common during the secretory phase (56.9%) in the suicidal group, while in the non-suicidal group, death occurred more commonly in the proliferative phase (66.3%). In reference to proliferative phase, deaths were more in the secretory phase and menstrual phase in the suicidal group, adjusted odd's ratio (OR) being 3.7 ($p = 0.042$) and 4.7 ($p = 0.032$), respectively. Corpus luteum was present in the right ovary of 43 and 14 victims of suicidal and non-suicidal deaths, respectively, while it was in the left ovary of 3 and 11 victims of suicidal and non-suicidal death, respectively. Odd's ratio was 10.3 for corpus luteum to be in the right ovary in comparison with the left ovary for the suicidal group ($p = 0.001$). This study revealed that suicidal chances in a woman are significantly more in the menstrual phase and the secretory phase of the menstrual cycle. The presence of corpus luteum in the right ovary is associated with an increased risk of suicide, but the reason is not known.

Keywords Completed suicide · Corpus luteum · Histopathology · Menstrual cycle phase · Psychosocial status

Introduction

Suicidal behavior may be influenced by the menstrual cycle, and there are many studies on the relationship between suicide and menstruation cycle phases based on cases of suicide attempts and suicidal deaths. These studies have shown mixed results. Some of them concluded that there was no relationship between phases of the menstrual cycle and

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suicidal behavior. Holding and Minkoff (1973) conducted a prospective study on 74 cases of non-suicidal self-injury who were admitted and treated at Regional Poisoning Treatment Centre. They had divided the menstrual cycle in the preovulatory and postovulatory phase for the study. In their study, they failed to associate non-suicidal self-injury cases with a particular phase of the menstrual cycle. Birtchnell and Floyd (1974) conducted a prospective study on 76 attempted suicide patient by self-poisoning or self-injury who were brought to them for psychiatric analysis. They did not find any relation between the menstrual cycle phase and attempted suicide cases. Luggin et al. (1984) conducted a prospective study on the relationship between the menstrual cycle phases and 121 psychiatric admission with premenstrual syndrome, suicidal attempts, and other psychotic and non-psychotic symptoms. For the study, they divided menstrual cycle into four equal duration phases. They found that psychiatric admissions are more during the menstrual period in comparison with the intermenstrual period. However, they did not find any characteristic difference between the attempted suicide group and other groups. Ekeberg et al. (1986) conducted a prospective study on suicidal and non-suicidal attempts with various toxic agents among 156 women on the day of admission with regular menstruation to know the association with the menstrual cycle. Suicidal attempts were classified when the patient had taken the drug with full intention to die, and otherwise, intake was classified as non-suicidal attempts. They did not find any statistically significant relationship between suicidal attempt and the menstrual cycle.

Contrary to the abovementioned studies, there are other studies which have found a relationship of suicidal attempt or completed suicide with menstrual cycle phase. Frequent suicide attempts before and after menses (fourth and first week) and during the premenstrual phase have been reported by Dalton (1959) in her analysis of admission records of 36 cases from two large mental hospitals. They had divided the menstrual cycle into seven 4-day phases. Mandell and Mandell (1967) studied the relationship between the incidence of 87 suicide calls, after excluding cases such as pregnancy, no menarche and perimenopausal women, and the phase of the menstrual cycle of the callers. They found that the highest calls were received with the callers in their menstrual phase, followed by the callers in the premenstrual phase. Tonks et al. (1968) conducted a study on 95 general hospital admission with self-injury and divided the menstrual cycle into menstruation (1–5 days), premenstrual (22–28 days), and ovulation (11–16 days) phases. They found that more than one-third cases were in premenstrual phase. Glass et al. (1971) studied 13 emergency psychiatric admissions and divided the menstrual cycle into menstruation phase (first week), midcycle phase (second-third week), and premenstrual phase (fourth week). They found that over 75% of the cases who had made a suicide attempt were in the premenstrual phase. Wetzel et al. (1971a, b) conducted a similar study on calls, as Mandell and Mandell, to Suicide Prevention Inc. in St Louis from patients with attempted suicide and suicidal thoughts. They studied 56 cases and found that these cases were more common during the menstrual and luteal phases in comparison with the follicular phase. Baca-Garcia et al. (2000, 2003) conducted two prospective studies on the patients admitted to a general hospital in Madrid with 80 cases in the year 2000 and 120 cases in the year 2003, all more than 18 years in age. They divided the menstrual cycle into three phases, i.e., follicular phase, midcycle phase, and the luteal phase. They further divided the follicular phase into the menstruation phase and non-menstrual follicular phase. In both studies, they found that the incidence of suicide attempts was significantly higher in the menstruation phase of the menstrual cycle.

In all the abovementioned studies, the phase of the menstrual cycle was determined by the history given by the patient. No confirmatory test was done, and the state of the uterus was not examined directly. Contrary to these studies, other studies have examined the uterus grossly and/or microscopically to confirm the phases of the menstrual cycle. Some of these studies failed to come up with any association between suicide and menstrual cycle phase while others were able to show the association.

McKinnon et al. (1959) studied 102 consecutive deaths of women aged 18–46 years at coroner's autopsy. The endometrial histology was done to know the phase of the menstrual cycle and divided them as the follicular phase and the early (2 days), middle (7 days), and late stages of the luteal phase (5 days). They concluded that the frequency of death, suicidal as well as non-suicidal, was found to have been significantly higher during the middle stage of the luteal phase than other phases. However, they did not compare between suicidal and non-suicidal groups. Venezis (1990) examined 257 consecutive endometrial samples from females that were autopsied between 1982 and 1989. Out of 257 endometrial samples, 171 were histologically examined. They divided the menstrual cycle into menstrual phase (days 1–5), proliferative phase (days 6–15), early secretory phase (days 16–19), and mid/late secretory phase (days 20–28). There were 46 deaths from natural causes, 44 accidental deaths, 50 suicides, and 31 homicides. The results from all combined categories of death, and within their four subgroups, did not show any significant bias to any particular phase or phases of the cycle. In fact, the deaths were distributed evenly.

Dogra et al. (2007) conducted a naked eye examination of the uterus of 217 cases of suicide victim at autopsy to ascertain the phase of the menstrual cycle, by noting whether the uterus was menstruating. The menstruating uterus was found significantly more in suicide victim than the control group in their study. In a histopathological study of the uterus, Leenaars et al. (2009) confirmed the findings of the study of Dogra et al. (2007). They reported a case control histopathological

study of the uterus at autopsy to ascertain the relationship between menstruation and suicide. Approximately 25% of the 56 people who died by suicide were menstruating, whereas only 4.5% of control cases were menstruating. They concluded that the menses in the people who died by suicide was well beyond expectation and well beyond their control group.

Based on this short literature survey, it can be said that there is not a unanimous opinion on whether any relationship between the menstrual cycle phases and suicide exists or not. The present study was undertaken on the suicidal death cases to have the answer.

Methods

The study was conducted in the Department of Forensic Medicine of All India Institute of Medical Sciences, New Delhi, in collaboration with departments of Pathology and Psychiatry. All consecutive autopsies of females in the reproductive age group were studied during the 2-year study period. The study excluded females, who did not attain menarche or were using any contraceptives, or were pregnant or have attained menopause. Unknown cases and cases with decomposition changes were also excluded from the study.

To study menstrual phase cycle, this study has used the endometrial histopathology method as it provides more accurate results and cost-effective too, in comparison with other methods such as biochemical, immunohistochemical, and electron microscopy (Filho et al. 1998). Endometrial histopathology not only provides the normal menstrual cycle changes, but also indicates any dysfunctional bleeding (Kaur et al. 2014). A detailed autopsy was performed, including gross and histopathological examination of the uterus as well as both the ovaries. These were examined macroscopically for menstrual cycle phases viz. menstrual phase, follicular/proliferative phase, and the luteal/secretory phase. For histopathology, uterine sections were taken from the anterior and posterior wall of the uterus at the right angle to the uterine cavity and ovarian sections were taken to include the cortex and medulla of both the ovaries. The tissue sections were processed, and the slides were stained with hematoxylin and eosin for microscopic examination. The phases of the menstrual cycle were tentatively decided on the basis of gross examination of the endometrium and ovaries (Fig. 1) and later were confirmed on the basis histological appearance of uterine endometrium and ovarian stroma.

Microscopically menstrual shading was demonstrated by ulcerated endometrium with hemorrhage. The proliferative endometrium of follicular phase showed regularly arranged tubular glands lined by columnar epithelial cells with elongated hyperchromatic nuclei and prominent nuclear stratification. The stroma exhibited compact spindle cells with scant eosinophilic cytoplasm. Early luteal endometrium showed columnar epithelium lining the glands and presence of subnuclear vacuoles. Stroma was less compact as compared with the proliferative endometrium and showed mild edematous changes. Late luteal endometrium revealed tortuous glands lined by low columnar to cuboidal epithelium with oval to round vesicular nuclei and a moderate amount of pale eosinophilic cytoplasm. Stroma showed decidual changes (Fig. 2a–d).

Fig. 1 Gross examination showing thickened endometrium and presence of hemorrhagic corpus luteum in ovary suggesting secretory phage

Cause of death, the manner of death, and the method of suicide were determined on the basis of inquest papers including crime scene reports, autopsy findings, suicide notes and, interview with the relatives. Relatives were interviewed to know about the age of menarche, menstrual cycle characteristics, use of any hormonal contraceptives, and obstetric and gynecological history. Overall mood, drug abuse, socioeconomic status, and a previous suicide attempt by the victim were also assessed during the interview. The information was collected in the predesigned proforma.

Statistical analysis was done in following three steps: (1) association of menstruation and other factors with suicidal and non-suicidal cases was done using chi-squared test; (2) unadjusted odds ratio (95% CI) was computed for various factors, and confounders were identified; and (3) multivariate logistic regression analysis was used to compute the odds ratio (95% CI) between menstrual cycle phases and suicidal and non-suicidal cases adjusting the confounding variables. Age, marital status, mood, socioeconomic status, and weight of the uterus were considered as confounding factors. STATA 12.0 statistical software was used for the analysis. In this study, p value less than 0.05 was considered as statistically significant and less than 0.001 was considered highly significant.

Ethical clearance

Ethical clearance was obtained from the institutional ethical committee (Ref. No. IEC/NP-427/2013RP-05/2013, dated 17 October 2013) before the commencement of the study.

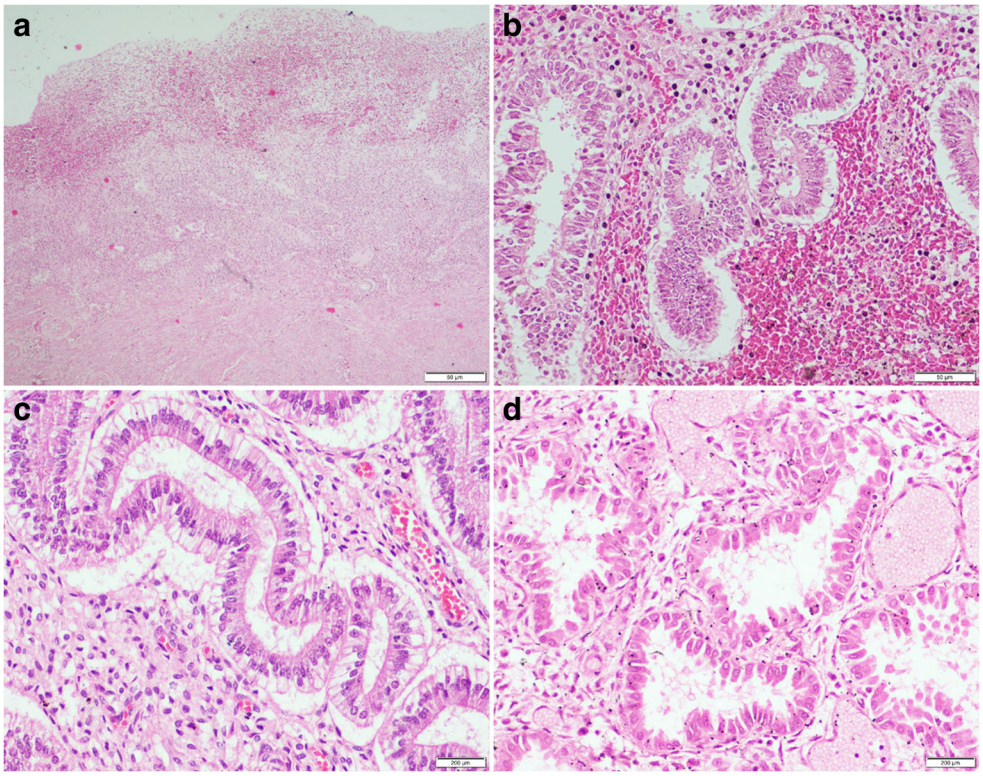

Fig. 2 **a** Hematoxylin and eosin (H&E)-stained section showing menstrual endometrium with superficial ulceration (H&E, ×100). **b** Section showing proliferative endometrium with stratified columnar epithelial lining tubular glands and compact spindle cell stroma (H&E, ×200). **c** Sections showing early secretory endometrium with the presence of subnuclear vacuoles in the glands and mild edematous stroma (H&E, ×200). **d** Section showing dilated tortuous glands with low columnar to cuboidal epithelial lining of late secretory endometrium. Stroma showing decidualized changes (H&E, ×200)

Results

There were a total of 547 autopsies conducted on girls and women in the reproductive age group, out of which 282 cases were of suicidal deaths and 265 cases were of non-suicidal deaths. After considering exclusion criteria, we have studied a total of 166 cases, out of which 86 cases were in suicidal group and 80 cases were in the non-suicidal group (control). The age range in the suicidal group was 12–48 years with a mean age of 23.7 years while the age range in the non-suicidal group was 15–55 years with mean age of 32.1 years ($p < 0.001$). Most of the women in both the groups were either homemakers (43% in the suicidal group and 58% in non-suicidal group) or students (43% in the suicidal group and 13% in non-suicidal group). About 47% of women in the suicidal group were married while the same was 75% in the non-suicidal group.

Most of the suicide deaths were due to hanging (78 cases, 91%); others were due to poisoning (7 cases, 8%) and jumping from heights (1 case, 1%). No association could be ascertained between the method of suicide and phases of the menstrual cycle. This finding is non-specific as most of the cases of female suicide are hanging at our center. Cause of death in the non-suicidal group was mostly natural causes (55%) and road traffic accidents (39%); the rest of them were homicide (Table 1). The reasons behind suicide were family problems (25 cases, 29%), academic failure (20 cases, 23%), various physical illnesses (18 cases, 21%), love affairs (4 cases, 5%), and economic and financial reasons (3 cases, 3%). In 16 cases (19%), the reason behind suicide was not known to the interviewee. Among suicide victims, 11 cases (13%) were of depressed mood and in the non-suicidal group; three cases (4%) were of depressed mood. However, the mood of the suicide documented here was a perception by the relatives who have participated in the interview and was not a medical diagnosis as none of the suicide victims were under treatment for any psychiatric/psychological illness. Likewise, no interviewee could point out any specific change in the mood of the suicide victim during menstruation.

The weight of the uterus in the suicidal group was ranging from 70.5 to 138.0 g with a mean of 104.9 g, while in non-suicidal group, range of the weight of the uterus was 55.0 to 160.0 g with a mean weight of 110.7 g ($p = 0.356$). In suicidal cases, 48% of the victims were married, whereas in non-suicidal case, 75% of victims were married ($p < 0.001$). Most of the suicide victims were homemakers and students (43% each) while in non-suicidal groups, homemakers (62.5%) were most common followed by the students (12.5%). The difference between the two groups for homemakers ($p = 0.012$) and students ($p < 0.001$) were statistically significant. As per socioeconomic status (Kuppuswamy scale), victims of suicidal and non-suicidal group were more commonly seen in upper middle (43% and 48%, respectively, $p = 0.754$) and in lower socioeconomic status (33% and 30%, respectively, $p = 0.792$), followed by lower middle class (15% and 20%, respectively, $p = 0.534$).

Table 1 Demographic characteristics of the suicidal and non-suicidal cases

Suicidal group (86 cases)		Non-suicidal group (80 cases)	
Age group (years)	Cases	Age group (years)	Cases
12–15	8	15–20	13
16–20	30	21–25	11
21–25	22	26–30	10
26–30	13	31–35	18
31–35	6	36–40	14
36–40	3	41–45	3
41–45	2	46–50	6
46–50	2	51–55	5
Occupation			
Housewife	37	Housewife	50
Student	37	Student	10
Working	10	Working	16
Not employed	2	Not employed	4
Marital status			
Divorcee	1	Divorcee	0
Married	40	Married	60
Unmarried	45	Unmarried	20
Cause of death			
Fall from height	1	Accidents	31
Hanging	78	Natural	44
Poisoning	7	Homicide	5

Deaths were more common during the secretory/luteal phase (56.9%) in the suicidal group while in non-suicidal group death occurred more commonly in the proliferative/follicular phase (66.3%). In the suicidal group, deaths were more in the secretory phase and menstrual phase in suicidal group, in reference to proliferative/follicular phase, adjusted odd's ratio being 3.7 ($p = 0.042$) and 4.7 ($p = 0.032$), respectively, when adjusted for age, marital status, mood, socioeconomic status, and weight of the uterus (Table 2).

One incidental finding was the presence of corpus luteum in right and left ovary in the victims. In the right ovary, corpus luteum was present in 43 and 14 victims of suicidal and non-suicidal deaths, respectively, while in the left ovary, corpus luteum was present in 3 and 11 victims of suicidal and non-suicidal death, respectively. When we compared the presence of corpus luteum in right and left ovary for suicide group, the odds ratio was 10.3 with corpus luteum in right ovary ($p = 0.001$).

Discussion

The present study mainly reports the histopathological examination of the uterus and ovary of reproductive age group female to study the menstrual phase and comparison of the menstrual phase of suicidal victims (who committed suicide) with non-suicidal victims (who died due to non-suicidal causes).

This study shows that suicidal death is more common during the menstrual phase and secretory/luteal phase as compared with the proliferative/follicular phase when all other factors (age, marital status, mood, socioeconomic status, and weight of the uterus) are statistically adjusted between suicidal and non-suicidal victims. This finding is in accordance with the study done by Wetzel et al. (1971a, b) on attempted suicide cases and cases with suicidal thoughts. Studies by Dogra et al. (2007) on gross appearance and Leenaars et al. (2009) on histopathology also confirmed this finding. McKinnon et al. (1959) also have found the luteal phase to be more commonly associated with luteal phase, but they had not differentiated between suicidal and non-suicidal cases. However, the studies on attempted suicide cases showed conflict findings. Some of them could not establish any relationship between menstrual cycle phase and attempted suicide (Ekeberg et al. 1986; Holding and Minkoff 1973; Buckle et al. 1965; Birtchnell and Floyd 1974) while some of them found attempted suicide cases more frequently during menstruation (Baca-Garcia et al. 1998; Forestié et al. 1986; Trautman 1961; Thin 1968; Seeman 1997). However, most of the studies did not define what they considered as "attempted suicide cases," and phases of the menstrual cycle were determined based on the history of the patient. This may be the drawback of the studies on attempted suicide causing the conflicting relationship between menstrual cycle phases and attempted suicide. In the present study, menstrual cycle phase was determined through histopathology and we included cases of complete suicide. Based on the present study, it can be concluded that at least complete suicide cases have a relationship with the menstrual cycle phases of the deceased.

This relationship can be explained by the hypothesis of hormonal effect. A study says that the hypoestrogenic phases of the cycle (luteal and menstrual phase) are associated with suicide attempts (Forestié et al. 1986). The finding of the present study concurs with Forestié et al. (1986) that suicidal death occurs when estrogen-level dips and progesterone comes into play, i.e., during menstruation and the secretory/luteal phase. Lester (1990) hypothesized that the effect of estrogen over dopamine can influence mood in women and therefore influence suicidal behavior. Estrogen increased dopaminergic activity in the brain in the form of increased dopamine receptors in rats (Fink et al. 1996) and also in human (Jacobs and D'Esposito 2011). According to Pitchot et al. (2001), decreased level of dopamine has been found to be associated with suicide attempts in various studies. Role of serotonin has also been hypothesized to be associated with suicidal risk, especially in those with risk factors. Mann (1998) found that low serotonergic functions increase suicidal risk. A pilot study on gene-hormone interaction on female suicide attempters showed that polymorphism of the serotonin transporter promoter area may be protective (Baca-Garcia et al. 2003).

Table 2 Statistics table for all the associated factors of the study with their unadjusted and adjusted odds ratio and *p* value

Factors		Non-suicidal ($n = 80$)	Suicidal ($n = 86$)	Unadjusted odds ratio (95% CI)	*p* value	Adjusted odds ratio (95% CI)	*p* value
Uterus	Proliferative/follicular	53 (66.3%)	26 (30.2%)	Ref.	–	Ref.	–
	Secretory/luteal	23 (28.8%)	49 (56.9%)	4.3 (2.2 to 8.6)	< 0.001	3.7 (1.0 to 12.9)	0.042
	Menstruating	4 (5.0%)	11 (12.8%)	5.6 (1.6 to 19.3)	0.006	4.7 (1.1 to 19.1)	0.032
Right ovary	Cyst	66 (82.5%)	43 (50%)	Ref.	–	Ref.	–
	Corpus luteum	14 (17.5%)	43 (50%)	4.7 (2.3 to 9.6)	< 0.001	2.0 (0.6 to 7.3)	0.269
Left ovary	Cyst	69 (86.3%)	83 (96.5%)	Ref.	–	Ref.	–
	Corpus luteum	11 (13.8%)	3 (3.5%)	0.2 (0.1 to 0.8)	0.027	0.2 (0.0 to 0.9)	0.037
Corpus luteum	Left ovary	10 (41.7%)	3 (6.5%)	Ref.	–	–	–
	Right ovary	14 (58.3%)	43 (93.5%)	10.2 (2.5 to 42.5)	0.001	–	–

Adjusted for age, marital status, mood, socioeconomic status, and weight of the uterus

Studies on female rats suggested that estrogen may increase serotonin concentration (Fludder and Tonge 1975), serotonin-receptor concentration (Vitali et al. 1984), and serotonin binding (Uphouse et al. 1986). Hypoestrogenic state causes a reciprocal decrease in serotonin activity (Sumner and Fink 1995). Psychosocial gender factors, premenstrual syndrome, and emotional instability linked with the fear of unexpected pregnancy after a delay of menstruation can trigger acute psychiatric problems leading to suicidal ideation and attempts (Birtchnell and Floyd 1974; Dalton 1959; Bebbington 1998; Canetto and Sakinofsky 1998). Most of the above psychological phenomena are linked with decreased estrogen level (Fink et al. 1996).

One incidental finding in this study is the presence of corpus luteum in the right ovary and its association with complete suicide. It is found that the presence of corpus luteum in the right ovary, compared with the presence of corpus luteum in left ovary, is associated with ten times more chances of suicide when compared with non-suicides. In general, ovulation from each of the two ovaries occurs approximately the same number of times, and different studies have supported this (Balasch et al. 1994; Fukuda et al. 1996). However, few studies have shown that the right ovary tends to undertake more ovulation than the left ovary (Potashnik et al. 1987; Check et al. 1991). In a study by Fukuda et al. (2000), ovulation from the right ovary occurred more often than from the left ovary (55% versus 45%; $p < 0.001$) in fertile and infertile women. These facts suggest that this ovarian finding of our study is not unusual; however, the association of this aspect of the menstrual cycle with suicide needs to be further explored.

In suicidal cases, about half of the victims were married, whereas in non-suicidal case, three-forth victims were married and the difference was statistically significant. It shows that married women are less prone to suicide than unmarried women; however, literature is of conflicting views on this matter (Vijayakumar 2015).

Limitation of the study

The main limitation of the study was the psychological analysis of the suicide victim. We did not use any scale for detailed analysis. The relatives were interviewed at the time when they were still mourning about the loss, and their answer regarding the mood of the deceased was according to their own perceptions, and there was no clinical diagnosis. Another limitation of the study was single hospital study catering a specific region, and as such, generalization should be done with caution.

Conclusion

Our study indicates that the menstrual phase and secretory/luteal phase of the menstrual cycle in a woman are associated with more chances of suicide in comparison with the proliferative/follicular phase. The odd's ratio for menstrual phase was 4.7, and for secretory/luteal phase, it was 3.7 in comparison with proliferative/follicular phase. This finding is supported by various studies worldwide. The finding can be explained on the basis of the effect of decreased estrogen level in menstrual and secretory/luteal phase causing decreased dopamine and serotonin activity leading to suicidal behavior. However, the study lacks behind in the psychiatric evaluation of the deceased and is region-specific which may not represent the whole population. Exploration on the preventive aspect of suicide, based on the findings of the present study, should take these factors into account.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants and/or animals Requisite ethical clearance was taken from the Institutional Ethical Committee.

Informed consent Consent taken from each participants as per ethical guidelines.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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