Research paper

Association between menopause and suicidal ideation in mothers of adolescents: A longitudinal study using data from a population-based cohort

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ABSTRACT

Background: Midlife suicide among women has attracted increasing research attention. This study aimed to investigate the longitudinal association between menopause and suicidal ideation among middle-aged women.
Methods: Our data were derived from the Tokyo Teen Cohort, a population-based survey of early adolescents (N = 3171) and their primary caregivers (typically, mothers) in Japan. A total of 2944 mothers (baseline mean age = 44.0 years) were included in the analysis. The baseline assessment in this study was performed at second-wave survey from July 2014 to January 2017. A follow-up assessment was conducted at fourth-wave survey from February 2019 to September 2021. Suicidal ideation at baseline and follow-up was assessed using the Suicidal Ideation subscale of the 28-item General Health Questionnaire. Menopausal stage was classified based on self-report at fourth-wave survey.
Results: Participants who started the perimenopausal stage after baseline were significantly more likely to have suicidal ideation at follow-up than those who did not have experienced menopausal transition yet. Participants with greater social support were less likely to report suicidal ideation at follow-up, even after adjusting for baseline suicidal ideation.
Limitations: This study was based on self-report regarding menopausal stage and only included mothers of adolescents from Japan. An exact length of time from the onset to the presence of suicidal ideation was unavailable.
Conclusions: Women who have experienced the onset of menopausal transition presented an increased risk of suicidal ideation. Psychosocial interventions to increase social support may be beneficial in preventing mental health inequalities during menopausal transitions.

1. Introduction

Suicide risks among middle-aged women is a growing public health concern. Those aged 45–54 years have the highest suicide rate among women in the United Kingdom (Office for National Statistics, 2019). Moreover, around one in ten women in the United Kingdom have been reported to experience suicidal thoughts owing to perimenopause, when the body starts transitioning to menopause (Independent, 2021). Women in this age group have been considered to have an additional risk of mood changes resulting from menopausal transition and hormonal changes (El Khoudary et al., 2019). However, prior evidence has not been conclusively supportive of an association between menopause

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and increased risk of depression, owing to the use of a cross-sectional design and a single retrospective assessment of a history of lifetime depression (Rössler et al., 2016). Furthermore, little is known about suicide risks in women who have experienced menopausal transition. Suicidal ideation was more likely to be observed in women at perimenopause than at the premenopausal stage in six European countries (Usall et al., 2009) and South Korea (An et al., 2022). These findings were based on cross-sectional studies, which could not control for prior suicide risks. Therefore, there is a need for analyses that can determine the longitudinal direction of the association between menopausal transition and suicide risks to inform mental health promotion in middle-aged women experiencing this important milestone in the aging process.

This study aimed to examine the longitudinal association between menopausal stage and suicidal ideation among middle-aged women, using data from a population-based cohort. We hypothesised that women who have experienced menopausal transition would be more likely to have suicidal ideation after adjusting for pre-existing suicidal ideation.

2. Methods

2.1. Study design

This study used data from the Tokyo Teen Cohort Study (TTC), a population-based prospective cohort study (Ando et al., 2019). The TTC is a survey of adolescents and their primary caregivers (98.5 % mothers in the first-wave survey), and contains questions about menopause and suicidal ideation as well as a variety of other covariates. We defined the TTC second-wave survey when the child was 12 years old as the baseline, and the fourth-wave survey when the child was 16 years old as the follow-up. We chose the second-wave survey as the baseline because information on suicidal ideation among mothers was not collected at the first-wave survey.

2.2. Participants and setting

A sample of 3171 households with children aged 10 years who were born between September 2002 and August 2004 was randomly chosen from the residential registries of three municipalities of the Tokyo Greater Metropolitan Area. The first-wave survey was conducted between October 2012 and January 2015. When these children were 12 years old, 3007 household participated in the second wave of data collection. Of the 3007 primary caregivers, 2944 were included in the analysis who were mothers of children. In the first-wave survey, among the 2944 participants, there was a higher proportion of individuals with a partner than the 227 excluded participants (Supplement Table S2).

The TTC second-wave survey was conducted when the children were 12 years old from July 2014 to January 2017. The third-wave survey, when the children were 14 years old, was conducted between March 2017 and March 2019. The fourth-wave survey, when the children were 16 years old, was conducted between February 2019 and September 2021.

2.3. Procedures

In each wave, the survey was completed during two home visits. During the first visit, written informed consent from the primary caregiver (generally the mother) was obtained, and Part I self-report questionnaires were distributed. Participants were asked to complete the questionnaires at home before the second visit. During the second visit, both adolescents and primary caregivers were asked to complete Part II of the self-report questionnaire. The questionnaires were enclosed in envelopes immediately after their completion. In addition, primary caregivers participated in semi-structured interviews. All data were anonymised after collection.

2.4. Measurements

The outcome measure was suicidal ideation (SI). At both baseline and follow-up, the presence of suicidal ideation within the last month was measured using the Japanese version of the four-item subscale of the 28-item General Health Questionnaire (GHQ) (Goldberg and Hillier, 1979; Nakagawa and Daibo, 1982; Watson et al., 2001). Suicidal ideation in this study was defined as a positive response to any of the four subscale items.

The primary independent variable for suicidal ideation was menopausal stage. Participants were asked the question in fourth-wave survey, 'Do you think you have experienced menopausal transition?' Responses were categorised into 'not yet', 'yes, currently', or 'yes, finished'. When participants responded 'currently' or 'finished', they were also asked to report at what age the menopausal transition had started. Finally, participants who had finished menopausal transition were asked to report at what age the transition ended. Based on the responses and age at the second- and fourth-wave surveys, participants were classified into five groups: premenopause, perimenopause after baseline, perimenopause before baseline, postmenopause after baseline, and postmenopause before baseline (Fig. 1).

Having a history of depression was assessed using a single question on whether the respondent had been diagnosed with depression. We also measured covariates previously linked to menopausal symptoms, including physical factors, health-related behaviours, and social class (Kim et al., 2021). Physical factors included age and body mass index (BMI). Health-related behaviours included current smoking, habitual drinking, and physical activity. Social class included educational attainment and annual household income. Additionally, we assessed psychosocial factors that could attenuate psychological distress, including social support, neighbourhood social cohesion, having a partner, and engaging in paid work. Social support was measured using the Social Support Questionnaire (SSQ6) (Sarason et al., 1983; Sarason et al., 1987; Furukawa et al., 1999). The SSQ6 assesses the number of people that an individual feels they can turn to in times of need. A summary score for the six items was obtained and used for the analysis. Neighbourhood social cohesion was assessed using a five-item instrument (Sampson et al., 1997; Takakura et al., 2017). Respondents were asked to rate each item on a five-point Likert scale ranging from 'strongly agree' to 'strongly disagree'. The total score ranges from 5 to 25, with a higher total score indicating greater neighbourhood cohesion.

We also included adolescent characteristics such as age, sex, number of siblings, depressive symptoms, and suicidal ideation in covariates of this study. Data on covariates were collected in the second-wave survey, except for having a history of depression, which was collected in the third-wave survey, and educational attainment and number of siblings, which were only collected in the first-wave survey (see online Supplementary Table S1).

Since follow-up data collection in the fourth-wave survey included both periods of prior (February 2019 to March 2020) and during the COVID-19 pandemic (April 2020 to September 2021), we examined the difference in suicidal ideation between prior and during the pandemic in the sensitivity analysis.

2.5. Statistical analysis

The prevalence of suicidal ideation and 95 % CIs were estimated according to menopausal stage.

Binomial logistic regression analysis was conducted to examine the association between menopausal stage and suicidal ideation at follow-up. In this model, we used menopausal stage as the independent variable, and suicidal ideation as the dependent variable. Covariates included the menopausal stage at follow-up and baseline characteristics.

In addition, survival analysis was performed to consider the time from baseline (second-wave survey) to the presence of suicidal ideation at follow-up (fourth-wave survey). The Kaplan–Meier survival curve was
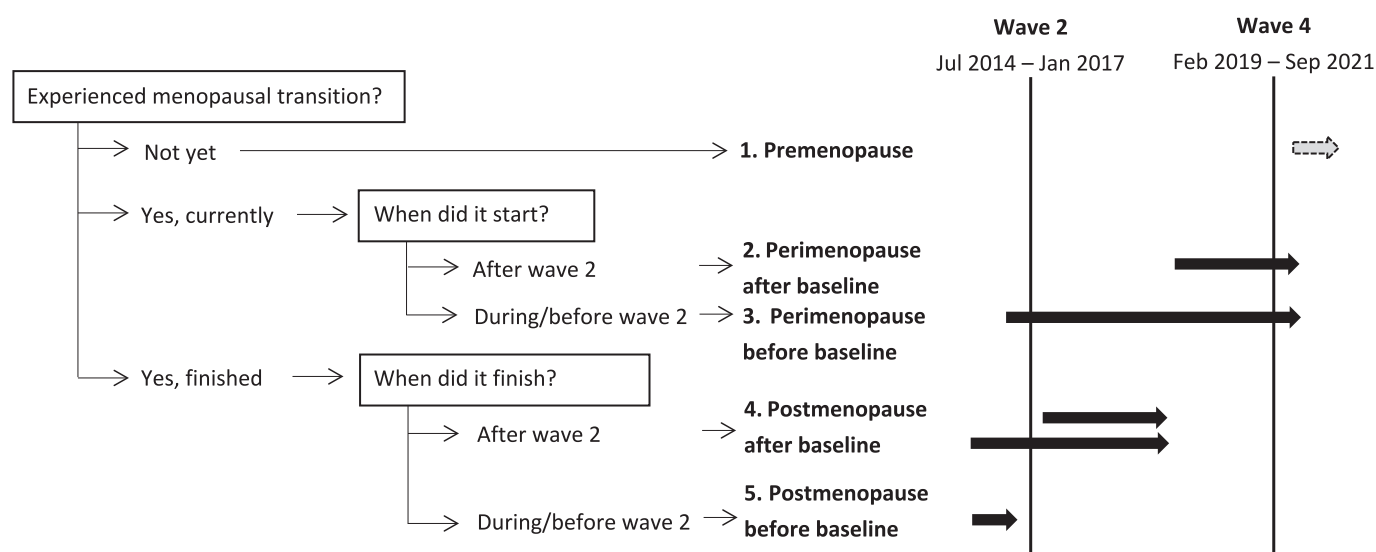
Fig. 1. Flowchart of sample stratification by self-reported menopausal stage

Mothers of adolescents participated in second-wave study (baseline) when the children were 12 years old, from July 2014 to January 2017. A follow-up assessment was conducted in fourth-wave survey (follow-up) when the children were 16 years old, from February 2019 to September 2021. In fourth-wave survey, participants were asked the question, 'Do you think you have experienced menopausal transition?' Responses were categorised into 'not yet', 'yes, currently', or 'yes, finished'. When participants responded 'currently' or 'finished', they were also asked to report at what age year the menopausal transition had started or ended. Based on the responses and age at second- and fourth-wave surveys, participants were classified into five groups: premenopause (participants had not experienced menopausal transition yet); perimenopause after baseline (participants had experienced the onset of after second-wave survey); perimenopause before menopause (participants had experienced menopausal transition that started before second-wave survey); postmenopause after baseline (participants had finished menopausal transition before fourth-wave survey); postmenopause before baseline (participants had finished menopausal transition before second-wave survey). As the assessment of menopausal transition was retrospective, we did not ask participants to provide the calendar year and month. Therefore, the exact length of menopausal transition was unavailable.

estimated by menopausal stage with the log-rank test. A Cox proportional hazards survival regression analysis was employed to estimate hazard ratios and 95 % confidence intervals of the menopausal stage and baseline characteristics. Finally, another Cox regression analysis was performed to model menopausal stage as a time-varying variable at the second-, third- and fourth-wave surveys. Menopausal stage in this model was classified into the following three categories: premenopause, menopause, and postmenopause. Maternal age at each wave was used as a survival time, and presence of suicidal ideation as a failure event. For this modelling purpose, information on maternal age and suicidal ideation was retrieved from the TTC third-wave survey.

In the multivariate logistic analyses, full information maximum likelihood was used to handle missing data (Cham et al., 2017). A sensitivity analysis was conducted for logistic regression models of suicidal ideation that excluded individuals with missing data. Another sensitivity analysis was also performed to control for the fourth-wave survey period (prior to vs. during the COVID-19 pandemic since April 2020). Data management and survival analyses were conducted using Stata 18.0 (StataCorp, College Station, Texas, USA). Logistic analyses were conducted using Mplus for Windows, version 8.9 (Muthén & Muthén, Los Angeles, California, USA). Statistical significance was set at $p < 0.05$.

2.6. Ethical considerations

The TTC study protocol was approved by the Institutional Review Boards of the Tokyo Metropolitan Institute of Medical Science, SOKENDAI (Graduate University for Advanced Studies), and the University of Tokyo. The study was conducted in accordance with the Helsinki Declaration as revised in 1989.

3. Results

3.1. Participant characteristics

Supplementary Table S3 presents the participants' characteristics. Participants' baseline mean age was 44.0 years (standard deviation = 4.2); 5.0 % were single mothers, 35.9 % had an annual household income of 10 million yen or more (highest category), and 39.2 % had graduated from university or graduate school. Of the participants, 3.2 % reported a history of depression. Half of the participants (58.7 %) did not report that they had experienced a menopausal transition at the time of data collection. One-fifth of the participants reported that they were at the perimenopausal stage, which had started after the second-wave survey.

3.2. Suicidal ideation

Suicidal ideation was observed in 7.8 % of the participants at baseline and in 9.7 % at the follow-up. Supplementary Fig. S1 illustrates the prevalence and 95 % CIs of suicidal ideation at the four-year follow-up according to menopausal stage. Follow-up suicidal ideation ranged between 7.9 and 12.9 % (95 % CI, 6.2–19.5 %).

3.3. Menopausal stage and suicidal ideation at follow-up

Table 1 displays the results of the logistic regression analysis for suicidal ideation at follow-up. After adjusting for baseline suicidal ideation, history of depression, physical factors, health-related behaviours, social class, and psychosocial factors, perimenopause after baseline was significantly associated with a greater likelihood of suicidal ideation at the follow-up. The presence of a four-year follow-up suicidal ideation was also significantly associated with maternal baseline suicidal ideation, a history of depression, low educational attainment, poor social support, and adolescent mental and behavioural problems and

Table 1
Results of binomial logistic regression analysis of suicidal ideation at follow-up.

	Odds ratio (95 % CI)	P-value
Menopausal stage, reference = premenopause		
Perimenopause after baseline	1.92 (1.25, 2.96)	0.003
Perimenopause before baseline	1.06 (0.51, 2.22)	0.880
Postmenopause after baseline	1.54 (0.77, 3.10)	0.223
Postmenopause before baseline	1.97 (0.83, 4.69)	0.125
Variable at baseline		
Suicidal ideation	7.74 (5.25, 11.41)	<0.001
Having a history of depression	2.11 (1.09, 4.11)	0.028
Physical factor		
Age, years	0.97 (0.92, 1.02)	0.176
Body mass index	1.00 (0.95, 1.06)	0.957
Health-related behaviours		
Current smoking	0.75 (0.41, 1.38)	0.355
Habitual drinking	0.98 (0.71, 1.35)	0.887
Physical activity	1.06 (0.75, 1.51)	0.735
Social class		
Educational attainment, reference = university or graduate school		
Junior high or high school	2.05 (1.29, 3.25)	0.002
Vocational school or college	1.09 (0.76, 1.56)	0.634
Annual household income, reference = 1000 million yen or more		
399 million yen or less	0.87 (0.46, 1.64)	0.661
400–699 million yen	0.78 (0.50, 1.20)	0.252
700–999 million yen	0.89 (0.60, 1.33)	0.577
Psychosocial factor		
Social support[a]	0.85 (0.76, 0.96)	0.009
Neighbourhood social cohesion[b]	1.01 (0.96, 1.07)	0.617
Having a partner	0.73 (0.35, 1.49)	0.381
Engaging in paid work, reference = not engaging		
4+ days per week	0.99 (0.68, 1.45)	0.969
1–3 days per week	1.05 (0.70, 1.59)	0.810
Adolescent characteristics		
Age, month	0.98 (0.93, 1.02)	0.268
Sex, male	1.04 (0.76, 1.42)	0.818
Number of siblings	0.98 (0.81, 1.19)	0.841
Mental and behavioural problems[c]	1.04 (1.01, 1.07)	0.019
Depressive symptoms[d]	1.00 (0.96, 1.04)	0.948
Suicidal ideation[e]	1.59 (1.06, 2.38)	0.025

$N = 2944$, full information maximum likelihood method was used.
CI, confidence interval.
A baseline assessment was conducted at second-wave survey. A follow-up assessment was conducted at fourth-wave survey.
Suicidal ideation within the last month was measured using the Suicidal Ideation subscale of the 28-item General Health Questionnaire.

[a] Social support was measured using the Social Support Questionnaire, with scores ranging from 0 to 6.
[b] Neighbourhood social cohesion was measured using five items of the neighbourhood collective efficacy scale, ranging from 5 to 25.
[c] Mental and behavioural problems were measured using four subscales of difficulties in the Strength and Difficulties Questionnaire, ranging from 0 to 40.
[d] Depressive symptoms were measured using the Short Mood and Feelings Questionnaire, ranging from 0 to 26.
[e] Suicidal ideation was assessed using the question, 'Have you ever had thoughts that your life is no longer worth living?' The four possible responses were 'no', 'probably no', 'probably yes', and 'yes'. Responses of 'yes' or 'probably yes' were regarded as indicating the presence of current suicidal ideation.

suicidal ideation.

In the sensitivity analysis that excluded individuals with missing data, the associations between menopausal stage and suicidal ideation did not significantly change (online Supplementary Table S4). Another sensitivity analysis that added the fourth-wave survey period (prior to vs. during the COVID-19 pandemic) did not alter the results meaningfully (online Supplementary Table S5). Participants who underwent follow-up assessment during the pandemic did not differ in the presence of suicidal ideation from those before the pandemic.

Supplementary Fig. S2 presents the Kaplan–Meier survival curve of suicidal ideation by menopausal stage. The log-rank test shows a significant difference in the presence of suicidal ideation by menopausal stage ($\chi^2(4) = 12.44$, $P = 0.014$).

Supplementary Table S6 indicates the results of the Cox proportional hazards survival regression analysis for suicidal ideation. Perimenopause after baseline was significantly associated with a greater hazard ratio of suicidal ideation at the follow-up. The presence of four-year follow-up suicidal ideation was also significantly associated with maternal baseline suicidal ideation and adolescent older age. Supplementary Table S7 presents the results of another Cox regression analysis using menopausal stage as a time-varying variable. Postmenopause was significantly associated with a lower hazard ratio of suicidal ideation at each wave survey. The presence of suicidal ideation at each wave was also significantly associated with a maternal history of depression, lower household income, poor social support and neighbourhood social cohesion, engaging in paid work for four or more days per week, adolescent larger number of siblings, greater mental and behavioural problems, and adolescent suicidal ideation.

4. Discussion

This population-based study of middle-aged women demonstrated that perimenopausal stage was associated with a greater risk of suicidal ideation at follow-up, after adjusting for baseline suicidal ideation, having a history of depression, and other covariates. Mothers with greater social support at baseline were less likely to have suicidal ideation at the follow-up. Moreover, adolescent mental and behavioural problems, and suicidal ideation were associated with greater risk of maternal suicidal ideation. The association between perimenopausal stage and suicidal ideation remained in the survival analysis considering the time between baseline and the four-year follow-up. However, the association between ongoing menopause and suicidal ideation was not found in another survival analysis using menopausal stage as a time-varying variable.

Perimenopausal stage, meaning the onset of menopausal transition after baseline, was associated with the manifestation of suicidal ideation at follow-up even after controlling for prior suicidal ideation. The results confirmed the association suggested by cross-sectional studies on menopausal symptoms and suicide risks (Usall et al., 2009; An et al., 2022). As menopausal women may experience feelings of social degradation (Delanoë et al., 2012), such feelings might lead to suicidal ideation. Both prior and concurrent mental health problems should be integrated into holistic treatment for somatic menopausal symptoms. A

further implication of this study is that mothers with greater social support reported fewer suicidal ideation, supporting prior literature suggesting that psychosocial factors may attenuate the impact of preexisting mental health problems, including suicidal ideation, on menopausal symptoms (Szeliga et al., 2021). Non-pharmacological interventions for menopause have shown promise in self-management and self-care (Vélez Toral et al., 2014). Our findings imply that the integration of increasing social support with self-management and self-care into holistic psychosocial interventions may help middle-aged women cope with menopausal transitions.

A history of depression was also associated with a greater risk of suicidal ideation at follow-up. Since nonadherence to medication treatment is often observed among patients with affective disorders (Pompili et al., 2013), some participants with a history of depression might have had undertreated depressive symptoms that could affect the risk of suicidal ideation. Furthermore, our results showed that preceding adolescent mental and behavioural problems and suicidal ideation were related to maternal suicidal ideation at follow-up. Mothers of adolescents with these challenges may face specific difficulties that increase the burden of parenting and worsen their mental health condition. Psychosocial interventions for middle-aged women may be required within support systems for adolescents with mental health problems.

4.1. Strengths and limitations

The strength of our study lies in the use of longitudinal and population-based data. Using these data enabled us to control for prior suicidal ideation in the analyses. The nonclinical sample provided information on mental health problems, which were often undiagnosed. However, this study has some limitations. Menopausal stage was based on self-report, which were not validated by hormone levels. Self-report might have led underreported perimenopausal stages. As the assessment of menopausal transition was retrospective, we did not ask participants to provide the calendar year and month. Therefore, we could not calculate the exact length of menopausal transition. The survival analysis based on the time from the onset of the menopausal transition would improve understanding of the association between menopause and the risk of suicidal ideation. Furthermore, the results were based on data obtained from Japanese individuals. Our participants were specifically limited to mothers of adolescents in the cohort. Our participants may have had a wider age range than the middle-aged adults who were the original participants in the population-based cohorts. Therefore, the generalisability of our findings should be cautiously considered. A variation in maternal age at baseline also limits the interpretation of the results from the survival analysis; we did not have any information on maternal suicidal ideation prior to the second-wave survey. Presence of suicidal ideation in this study did not necessarily mean the onset of symptoms at middle age.

4.2. Conclusions

Our population-based longitudinal study of middle-aged women revealed that women who experienced the onset of menopausal transition were at increased risk of suicidal ideation. Increasing social support is needed to attenuate mental health inequalities during menopausal transition. Future research should develop social support services to help women cope with menopausal transitions.

CRediT authorship contribution statement

Drs Hiraiwa-Hasegawa, Kasai, and Nishida designed the study and wrote the protocol. All authors contributed to the acquisition of data. All authors contributed to the analysis and interpretation of data. Drs. Nakanishi and Yamasaki drafted the manuscript. Drs. Endo, Stanyon, Sullivan, Yamaguchi, Ando, Hiraiwa-Hasegawa, Kasai, and Nishida provided critical review of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.08.055.

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