Associations of Fertility History and Cognitive Decline, Depression, Chronic Disease Comorbidity in West China: Results from WCHAT Study

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Abstract

Objectives

The purpose of the study was to investigate the association between fertility history and cognition function, depression and chronic comorbidity in west China.

Methods

We included 4,276 women aged 50 or older in our study, and we analyzed associations between parity history and cognitive decline, depression, chronic disease comorbidity in west China using univariate and multivariate models. Multivariate models were adjusted for age, ethnic groups, occupation, marriage status, educational level, lifestyle factors, sleeping time and so on.

Results

Of 4,276 women in west China, 18.4% were either childless or had one child, 33.8% had two children, 23.7% had three children, and 24.1% had four or more children. Compared to low parity (0-1 children), having 4 or more children was significantly associated with depression (OR 1.379, 95%CI 1.046-1.819), chronic disease comorbidity (OR 1.714, 95%CI 1.252-2.346), mild cognitive decline (OR 2.179, 95%CI 1.503-3.159) and moderate/severe cognitive decline (OR 1.806, 95% CI 1.064-3.067).

Conclusions

This study indicated that high parity was significantly associated with poorer cognitive functioning, depression and chronic disease comorbidity. For a better mid-late life health, reproductive women should plan their number of desired children.

Introduction

Fertility plays an important role in the health of mid-aged and older women, but the conclusions remains conflicted. Some studies indicated that nulliparous women and women with five or more children had significantly higher mortality than other women in their later life[1,2]. While some studies did not find any relationship between birth numbers and women's later life health[3]. Besides, having children at a very young age is detrimental to women's later life health, as well as late childbearing[4,5]. Research showed that risk enhancement from delayed childbirth with regard to cardiovascular disease, especially diabetes, hypertension, and congestive heart failure[6]. Moreover, changes in childbearing pattern during recent decades, with fewer children and higher age at births, having a higher risk of breast cancer incidence[7]. However, studies investigate the relationship between fertility history and cognitive function were also conflicting. One previous study found that poorer cognition in childless people and better cognition among mothers experiencing child birth at higher ages, indicating that factors related to childbearing are beneficial for later cognitive functioning, and this was affected by socioeconomic position[8]. A study from China found that high parity was associated with a lower decline in cognitive function, as a result of the cognitively protective role of endogenous estrogen[9]. While a study in Untied States indicated that high parity showed a greater decline in cognitive functioning in older women[10]. And other studies have found no associations[11].

In this study, we got the cross-sectional data from the West-China Health and Aging Trend (WCHAT) study[12-14]. And we aimed to investigate the association between fertility history and cognitive function, as well as other geriatrics syndrome like depression, anxiety, and chronic disease.

Methods
This research is a cross-sectional study using baseline data of the WCHAT study, which was approved by the Ethical Review Committee (reference: 2017-445). Data were collected from 4 provinces in West China, including Yunnan, Guizhou, Sichuan, and Xinjiang.

**Study participants**

All participants aged 50 years old or older were enrolled. Participants were recruited by convenience and asked verbally by the researchers about their willingness to take part in the study. Before the investigation, informed consent was signed and obtained by each participant. In this study, the baseline survey of the WCHAT study included 7,536 participants aged 50 or older over from 18 ethnicity groups in four provinces (Sichuan, Yunnan, Guizhou, Xinjiang), and 2838 men were excluded at first. 337 participants without complete questionnaire information were excluded, too. Then we excluded mental illness (6), tumor (37) and participants without cognitive function or depression assessment (42). Finally, we included 4,276 women in the current analysis.

**Fertility history**

We collected fertility history variables from baseline data of WCHAT. Number of children was measured whether participants had 0, 1, 2, 3, or 4+ natural living children.

**Covariates**

The baseline demographic information included general personal data: age, gender, ethnic groups, marital status, educational level, occupation. Lifestyle characteristics included sleeping time, tea-drinking, alcohol drinking and smoking. Cognitive status was measured using a 10-item Short Portable Mental Status Questionnaire (SPMSQ). For SPMSQ scoring, 0~2 indicated complete cognitive function, 3~4 indicated mild cognitive functional impairment, 5~7 indicated moderate cognitive function impairment, and 8~10 indicated severe cognitive function impairment. This judgment was based on educational level[15]. Depressive symptoms were assessed using the 15-item Geriatric Depression Scale (GDS-15). The scale, which contains 15 items that require only a yes/no answer, is the most widely used scale for the detection of depression. Scores ≥5 are considered as depression[16]. A medical history of chronic disease was self-reported. These disease conditions included hypertension, coronary heart disease, chronic obstructive pulmonary disease, gastrointestinal disease, liver disease, kidney disease, stroke, osteoarticular disease and diabetes mellitus. Chronic diseases comorbidities were considered as having two or more chronic diseases.

**Statistical analysis**

The normality of variables was initially studied by using R version 3.6.1. We examined differences in baseline sample characteristics by fertility history using Chi-square tests for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. Associations with a p-value of 0.1 or less in the univariate analysis were selected for the multiple regression analysis. Covariates selected for the full model included age, ethnic groups, education level, marriage status, lifestyle factors. This analysis was conducted using logistic regression with dummy variables using low parity (0-1 child) as the reference group. A value of P<0.05 was considered to be statistically significant.

**Results**

The study included 4,276 women. Of these, 18.4% were either childless or had one child, 33.8% had two children, 23.7% had three children, and 24.1% had four or more children. Compared to low parity (0-1), the other three groups had lower educational level and cognitive decline (Table 1). Interestingly, Han group had low parity and other ethnic group including Zang, Qiang, Yi, and Uyghur had high pairty. Specifically, the groups of high parity (3 or more) had higher prevalence of depression and chronic disease comorbitidy compared to low parity (0-1) group (Table 1).
Table 2 shows the associations between fertility history and cognitive decline, depression, chronic disease comorbidity in a univariate model, respectively. It shows that high parity including 3 or more children was significantly associated with cognitive decline, depression, and chronic disease comorbidity, with a dosage effect.

Table 3 and figure 1 shows the association between fertility history and depression in a fully adjusted model, adjusting age, ethnic groups, marriage status, smoking, drinking, educational level, occupation, sleeping time. Compared to low parity (0-1 children), having 4 or more children was significantly associated with depression (OR 1.379, 95%CI 1.046-1.819), chronic disease comorbidity (OR 1.714, 95%CI 1.252-2.346), mild cognitive decline (OR 2.179, 95%CI 1.503-3.159) and moderate/severe cognitive decline (OR 1.806, 95% CI 1.064-3.067).

Discussion

China is now entered into an aging society and women had more health problem than men. The relationship between fertility history and later health conclusions are inconsistent in China. A study used data from the 2000 wave of the Chinese Longitudinal Healthy Longevity Survey (CLHLS) found that there was no statistical correlation between the self-rated health of older people and the number of their surviving children[17]. While other studies in England and Wales suggested that both nulliparous and high-parity women had higher risks of mortality and morbidity than those of two or three children[1]. And an very early study found that almost 50% of females who lived to 80 years and over were childless[18]. In our study, it showed that high parity (4 or more children) occupies 24.1% and we investigated the association between parity history and cognitive decline, depression and chronic disease comorbidities, respectively. This is a first study to investigate fertility history and these health problems together in a large sample of participants.

For the association between fertility history and depression, we found that high fertility (4 or more children) was significantly associated with depression. In previous studies, most researchers focused on postnatal depression (PND) and found that women experiencing PND at their first or second birth have lower completed fertility, with PND at the first birth leading to lowered fertility[19]. A recent study showed that associations between childhood disadvantage and later-life depression are partially mediated by fertility stressors[20]. Besides, infertile women who experience severe anxiety and stress could be more prone to depression[21]. High parity might increase economic strain, pressures to increase working hours and less wealth accumulation, and all of these factors had been associated with depression. As a matter of fact, first childbirth at a young age was often related to high parity, which gather further pressures on women's health and might be related with depression[22]. However, whether high parity leading to depression needs a longitudinal study.

While for the cognitive decline, previous studies had indicated that socioeconomic differences are an important driver of the association between high parity and poorer cognitive function[8]. And they also found that childlessness experienced faster cognitive decline even after adjustment for socioeconomic, health, and social engagement variables[8]. While in our study, we found that high parity was significantly associated with cognitive decline and had a dosage effect. The mechanism including many aspects. Firstly, high parity leading to high economic pressure and women might be more anxious than others, leading to cognitive decline. A recent research found that behavioral and social factors associated with rearing many children may have contributed to the development of frailty in both sexes[23]. Secondly, higher parity is associated with an increased prevalence of selected components of the metabolic syndrome, like cholesterol and fasting glucose[24]. And these adverse cardiovascular health outcomes might mediate the effect of high parity on the cognitive decline. Thirdly, a famous research found that pregnancy renders substantial changes in brain structure, primarily reductions in gray matter (GM) volume in regions subserving social cognition, endured for at least 2 years post-pregnancy[25].

Interestingly, we found the association of high parity with chronic disease comorbidity, also having a dosage effect even in a fully adjusted model. However, previous studies on this aspect was sparse. Most studies focused on the relationship between fertility history and mortality, showing a U-shaped pattern that childless or those with five or more children had the highest mortality[26]. Specifically, pregnant women were more easily to get some disease like hypertension, diabetes and heart disease, thus might affect their postnatal health. A study in China also found that women with four children or more
were more likely to suffer from activities of daily living (ADL) impairment and poorer self-related health than those with one to three children[27]. Consistently, a study in Australia indicated that those who experienced both a disrupted marital history and a high level of fertility were found to be in poorer health[28].

**Limitation**

Nonetheless, this study presents some limitations. It is derived from a cross-sectional study which was not possible to conclude the existence of a causal association between fertility history and cognitive decline, depression or chronic disease comorbidity in women. And although regression models were adjusted for many health-related variables like demographic factors, life style factors, sleeping time and educational level, other potential confounders like childbearing age and annual income are still needed to be adjusted. And we conducted a centralized investigation, not a household survey in which most of the participants are relatively healthy people.

**Conclusions And Implications**

Our study showed that high parity was associated with health problems (cognitive decline, depression, and chronic disease comorbidity) in women. For better mid-late life health, reproductive women should plan their number of desired children as well as the timing of births. Importantly, both families and public policy should pay more attention to the health of women.

**Declarations**

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**Consent for publication**

Not applicable.

**Conflict of Interest Statement**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Availability of Data and Materials**

The datasets generated and analyzed during the current study are not publicly available due to this is a newly database which has a lot of important information and we are applying some important projects based on this. But this dataset will be available two years later and is also available now from the corresponding author on a reasonable request.

**Statement of Ethics**

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Subjects (or their guardians) have given their written informed consent. The current research was approved by the Ethical Review
Committee of West China Hospital with the committee's reference number 2017(445) and the registration number is ChiCTR 1800018895.

Author Contributions

Xiaolei Liu and Xiaoyan Chen design and write the manuscript. Lisha Hou, Fengjuan Hu and Xin Xia helped analyze the data. Gongchang Zhang, Shuyue Luo and Xuchao Peng helped collect data. Jirong Yue and Birong Dong helped revise the manuscript.

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Tables

Table 1. Weighted means/percentages for covariates by childbearing characteristics (n=4276).
| Variables                  | Parity(0-1) n=787(18.4) | Parity (2) n=1447(33.8) | Parity (3) n=1014(23.7) | Parity(≥4) n=1028(24.1) | P-value |
|---------------------------|-------------------------|-------------------------|-------------------------|--------------------------|---------|
| age                       | 58.31±6.72              | 58.32±6.70              | 61.9±7.58               | 67.96±8.19               | 0.01    |
| Marriage status           |                         |                         |                         |                          | 0.01    |
| Unmarried                 | 21(2.67)                | 0*                      | 0*                      | 0*                       |         |
| Married                   | 640(81.32)              | 1236(85.42)             | 794(78.30)              | 689(67)                  |         |
| Divorced                  | 23(2.92)                | 24(1.66)                | 22(2.17)                | 15(1.5)                  |         |
| Widowed                   | 103(13.09)              | 187(12.92)              | 198(19.53)              | 324(31.5)                |         |
| Ethnic groups             |                         |                         |                         |                          |         |
| Han                       | 544(69.12)              | 551(37.08)*             | 311(30.67)*             | 229(22.28)*              | 0.01    |
| Zang                      | 104(13.21)              | 246(17.00)*             | 222(21.89)*             | 191(18.58)*              |         |
| Qiang                     | 48(6.10)                | 269(18.59)*             | 247(24.36)*             | 266(25.88)*              |         |
| Uyghur                    | 35(4.45)                | 74(5.11)                | 78(7.69)*               | 146(14.20)*              |         |
| Yi                        | 29(3.68)                | 162(11.20)*             | 76(7.50)*               | 117(11.38)*              |         |
| others                    | 27(3.44)                | 145(11.02)*             | 80(7.89)*               | 79(7.68)*                |         |
| Smoking history           |                         |                         |                         |                          | 0.771   |
| Yes                       | 17(2.16)                | 31(2.14)                | 24(2.37)                | 37(3.6)                  |         |
| No                        | 770(97.84)              | 1416(97.86)             | 990(97.63)              | 991(96.4)                |         |
| Drinking history          |                         |                         |                         |                          | 0.01    |
| Yes                       | 66(8.39)                | 160(11.06)*             | 139(13.71)*             | 129(12.55)*              |         |
| No                        | 721(91.61)              | 1287(88.94)             | 875(86.29)              | 899(87.45)               |         |
| Sleeping time             | 7.34±1.50               | 7.33±1.50               | 7.29±1.60               | 7.4±1.64                 | 0.462   |
| Cognitive function        |                         |                         |                         |                          | 0.01    |
| Complete                  | 715(90.85)              | 1239(85.63)*            | 809(79.78)*             | 697(67.8)*               |         |
| Mild decline              | 50(6.35)                | 148(10.22)              | 157(15.48)              | 211(20.53)               |         |
| Moderate/severe decline   | 22(2.8)                 | 60(4.15)                | 48(4.74)                | 120(11.67)               |         |
| Education level           |                         |                         |                         |                          | 0.01    |
| Primary school or below   | 349(44.35)              | 858(59.30)*             | 815(80.37)*             | 893(86.87)*              |         |
| Middle school             | 257(32.65)              | 353(24.39)              | 122(12.03)              | 75(7.29)                 |         |
| High school or above      | 181(23)                 | 236(16.31)              | 77(7.60)                | 60(5.84)                 |         |
| Occupation                |                         |                         |                         |                          | 0.01    |
| Physical work             | 635(80.69)              | 1213(83.83)             | 928(91.52)*             | 961(93.48)*              |         |
Table 2. The univariate regression analysis between fertility history and depression, cognitive function and chronic disease comorbidity.

| Variables               | Mild cognitive decline | Moderate/severe cognitive decline | Depression | Chronic disease comorbidity |
|-------------------------|------------------------|-----------------------------------|------------|-----------------------------|
| Number of Children      | p OR 95% CI            | p OR 95% CI                       | p OR 95% CI| p OR 95% CI                 |
| (ref. = 0-1 children)   |                        |                                   |            |                             |
| 2                       | 1.708 1.224-2.384      | 0.074 1.574 0.957-2.587           | 0.113 1.20 | 0.958-1.503 0.057 1.293 0.993-1.684 |
| 3                       | 2.775 1.988-3.875      | 0.012 1.928 1.153-3.226           | 0.01 1.381 | 1.090-1.749 0.01 1.473 1.117-1.941 |
| 4 or more               | 4.329 3.126-5.994      | 0.01 5.595 3.510-8.920            | 0.01 1.83 1.459-2.310 | 0.01 2.449 1.885-3.183 |

Table 3. Logistic regression for fertility history on depression/ chronic disease comorbidity/ cognitive function.
| Variables                                | p-value | OR   | 95% CI |
|------------------------------------------|---------|------|--------|
| Number of Children (ref. = 0-1 children) |         |      |        |
| Depression                               |         |      |        |
| 2                                        | 0.765   | 0.965| 0.762  | 1.221 |
| 3                                        | 0.747   | 1.043| 0.806  | 1.351 |
| 4 or more                                | 0.023   | 1.379| 1.046  | 1.819 |
| chronic disease comorbidity              |         |      |        |
| 2                                        | 0.023   | 1.379| 1.046  | 1.819 |
| 3                                        | 0.027   | 1.4   | 1.038  | 1.888 |
| 4 or more                                | 0.001   | 1.714| 1.252  | 2.346 |
| Mild cognitive decline                   |         |      |        |
| 2                                        | 0.113   | 1.322| 0.936  | 1.867 |
| 3                                        | 0.003   | 1.729| 1.212  | 2.467 |
| 4 or more                                | 0.01    | 2.179| 1.503  | 3.159 |
| Moderate/severe cognitive decline        |         |      |        |
| 2                                        | 0.967   | 1.011| 0.597  | 1.712 |
| 3                                        | 0.653   | 0.881| 0.508  | 1.529 |
| 4 or more                                | 0.029   | 1.806| 1.064  | 3.067 |

Note. The regression model was adjusted by age, ethnic groups, marriage status, smoking, drinking, educational level, occupation, sleeping time.