Research Article
Maternal Age at First Delivery and Risk of Cardiovascular Disease Later in Life

Elham Kharazmi,1 Mahdi Fallah,1 and Riitta Luoto2,3

1 School of Health Sciences, University of Tampere, 33014 Tampere, Finland
2 UKK Institute for Health Promotion, 33501 Tampere, Finland
3 Department of Children and Families, National Health and Welfare Institute, 00271 Helsinki, Finland

Correspondence should be addressed to Elham Kharazmi; elhamkharazmi@gmail.com

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Background. To elucidate the association between maternal age at first delivery and cardiovascular health in women. Material and Method. A nationally representative survey, comprising 3,937 Finnish women aged 30–99 years with information on most of the potential cardiovascular disease (CVD) risk factors. Weighting survey analyses and logistic regression were performed. Results. Women who had their first delivery at age 25 or less had about five times higher odds ratio for myocardial infarction (fully adjusted OR: 4.82; 95% CI: 1.39–16.75) and about 2-fold higher odds ratio of arrhythmia (fully adjusted OR: 1.82; 95% CI: 1.13–2.92) compared to those who were 31–35 years at their first delivery. Each one year younger maternal age at first delivery predicted a higher risk of myocardial infarction (age-adjusted OR = 1.12; 95% CI: 1.06–1.18), hypertension (age-adjusted OR = 1.05; 95% CI: 1.03–1.07), arrhythmia (age-adjusted OR = 1.03; 95% CI: 1.01–1.05), angina pectoris (age-adjusted OR = 1.06; 95% CI: 1.02–1.10), and heart failure (age-adjusted OR = 1.05; 95% CI: 1.01–1.10). Conclusion. Maternal earlier age at first delivery is related to subsequent development of CVD, especially myocardial infarction. Our findings suggest a need for additional care and monitoring for CVD and its risk factors in women who had their first delivery at young ages.

1. Introduction

The association between reproductive history and risk of cardiovascular disease (CVD) is biologically plausible. Many studies have investigated the connection between the reproductive history of women and morbidity and mortality from cardiovascular diseases and have reported some controversial results [1, 2]. Earlier studies have suggested a small but adverse effect of parity and gravidity on subsequent CVD [3–8] that may not become apparent until older ages. There are few studies on the maternal age at first delivery and subsequent risk of CVD. A large retrospective cohort study found no significant association between age at first delivery and coronary heart disease (CHD) [3]. Three case-control studies found that the women who had their first delivery before the age of 25 appeared to be at higher risk of CHD [9–11] and ischemic heart disease [12]. Younger age at first delivery showed the higher risk of isolated systolic hypertension even after adjustment for age, height, weight, diastolic blood pressure, fasting blood glucose, low-density lipoprotein and total cholesterol, education, smoking, and physical activity [13]. However, the evidence of an association is far from conclusive. Due to long lag time between first delivery and appearance of cardiovascular disease in women, investigating this issue is quite hard, but on the other hand there is plenty of time for preventable and interventional actions. To further elucidate the association between maternal age at first delivery and cardiovascular health in women, we investigated this issue in a valid nationally representative sample.

2. Materials and Methods

2.1. Subjects. In a nationally representative sample involving 8,028 Finns aged 30 years or over, 88% were interviewed and 80% attended a comprehensive health examination in
the Health 2000 Survey carried out in 2000-2001. The implementation of the survey is described in detail elsewhere [14]. The most essential information on health and functioning capacity, such as state of health and illnesses, family medical history, health services, living habits, physical activity, mental health status, and working ability, was obtained from more than 93% of subjects. A large national network coordinated by the Finnish National Public Health Institute (KTL) was responsible for the planning and execution of the study. From this database, all the women (3,937) were included in our study (age range from 30 to 99). Ethical permission for the Health 2000 Study was received from the Uusimaa Hospital District.

2.2. Variables Used. Information on age at first and last delivery and also cardiovascular disease were obtained from the Health 2000 Survey, an extensive primary home interviewer-administered questionnaire. The diagnosis of angina pectoris and myocardial infarction in Health 2000 subjects was also available based on combined data from questionnaire and physician’s report.

The information on CVD was based on responses to the interview questions: “Have you ever been diagnosed with hypertension/myocardial infarction/angina pectoris/heart failure/arrhythmia/stroke?”

Blood pressure (BP) was measured by a nurse with a conventional and calibrated mercury sphygmomanometer from the sitting individuals’ right arm after a 10 min rest. BP was measured using a cuff size 15 × 43 cm; a larger cuff was used when necessary. Diastolic pressure was recorded at the fifth phase of the Korotkoff sounds [15]. The means of two measurements performed at a 2 min interval were used in this study. Weight was measured as part of the bioimpedance examination with a spring scale (Biospace, Inbody 3.0). The machine automatically calculated the body mass index (BMI; kg/m²) after measured height was entered. In subjects examined at home, BMI was calculated on the basis of measured height and the weight measured on a portable spring scale [15]. Serum total cholesterol was determined by commercial automated enzymatic methods (Olympus System Reagent, Germany). Direct enzymatic methods were used for low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol determinations (Roche Diagnostics, Mannheim, Germany). The analyses were performed on an Olympus AU400 (Germany) clinical chemistry autoanalyzer [15].

Systolic and diastolic blood pressure, fasting blood glucose, cholesterol, and age as a strong confounder as well as BMI and waist/hip ratio were used as continuous variables in the analyses. We also used education in three levels (basic, middle, and high), smoking (never smoker, past smoker, occasional smoker, and daily smoker) and physical activity (ideal, sufficient, uncertain, and insufficient) as categorical variables.

2.3. Statistical Analyses. Weighting (survey analysis) was used to make the results from our sample more generalizable to the source population. This applies to all the results presented in this paper, either descriptive or regression analyses. Survey logistic regression analysis was used for binary outcome variables (yes/no), hypertension, angina pectoris, myocardial infarction, heart failure, arrhythmia, and stroke to
identify any association between maternal age at first delivery and risk of cardiovascular disease. We considered twelve covariates in our analyses: age, gravidity (total number of pregnancy including miscarriage, abortion, and delayed delivery), systolic and diastolic blood pressure, fasting blood glucose, total and LDL cholesterol, smoking, BMI, waist/hip ratio, physical activity, and education (as a proxy for socioeconomic status). All analyses were done using STATA statistical software the 8th version.

3. Results

Age at first delivery was significantly associated with age at study time, height, weight, BMI, waist/hip ratio, education, marital status, use at any time of hormone replacement therapy, smoking, toxemia in any pregnancy, total and LDL cholesterol, and systolic and diastolic blood pressure (Table 1).

Out of 3,920 women, 3.2% responded affirmatively to the question regarding myocardial infarction (MI); 7.1% had experience of angina pectoris, 6.7% stated that they had had heart failure/cardiac insufficiency, 16.3% had had arrhythmia, 31.4% had had hypertension, and 3% had suffered a stroke.

Each one year younger maternal age at first delivery predicted a higher risk of myocardial infarction (age-adjusted OR = 1.12; 95% CI: 1.06–1.18; Table 2), hypertension (age-adjusted OR = 1.05; 95% CI: 1.01–1.10), angina pectoris (age-adjusted OR = 1.06; 95% CI: 1.02–1.10), and heart failure (age-adjusted OR = 1.05; 95% CI: 1.01–1.10). Women who had their first delivery at age 25 or less had about five times higher odds ratio of myocardial infarction (fully adjusted OR: 4.82; 95% CI: 1.39–16.75) and about 2-fold higher odds ratio of arrhythmia (fully adjusted OR: 1.82; 95% CI: 1.13–2.92) compared to those who were 31–35 years at their first delivery (Table 3). When 12 available confounders (age, total number of pregnancy, education, smoking, BMI, waist/hip ratio, physical activity, fasting blood glucose, total and LDL cholesterol) were included in the logistic regression model, the odds ratios did not change substantially.

4. Discussion

Younger maternal age at first delivery predicted a higher risk of cardiovascular disease especially myocardial infarction in mothers even after adjustment for almost all known risk factors of cardiovascular disease (age, gravidity, smoking, BMI, waist/hip ratio, physical activity, fasting blood glucose, and total and LDL cholesterol). Our results from a nationally representative sample were in line with three case-control studies examining the association of having first delivery before the age of 20 with the risk of heart disease, all of them reporting a significant association [9–11]. The results of a study by Palmer et al. suggest that parity and young age at first delivery are independent risk factors for coronary heart disease and that women with both of these reproductive characteristics have over twice the risk of...
Table 3: Association between categorized age at first delivery and cardiovascular diseases.

<table>
<thead>
<tr>
<th>Age at first delivery (years)</th>
<th>≤25 versus 26–30</th>
<th>≤25 versus 31–35</th>
<th>≤25 versus &gt;35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Age-adjusted OR</td>
<td>Adjusted* OR</td>
<td>Age-adjusted OR</td>
</tr>
<tr>
<td>Yes</td>
<td>1.28 (1.06, 1.55)</td>
<td>1.50 (1.12, 2.00)</td>
<td>2.73 (1.51, 4.93)</td>
</tr>
<tr>
<td>No</td>
<td>1.18 (0.93, 1.49)</td>
<td>1.69 (1.10, 2.58)</td>
<td>1.82 (1.13, 2.92)</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Age-adjusted OR</td>
<td>Adjusted* OR</td>
<td>Age-adjusted OR</td>
</tr>
<tr>
<td>Yes</td>
<td>1.70 (1.18, 2.47)</td>
<td>1.95 (1.20, 3.17)</td>
<td>1.98 (1.07, 3.67)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Age-adjusted OR</td>
<td>Adjusted* OR</td>
<td>Age-adjusted OR</td>
</tr>
<tr>
<td>Yes</td>
<td>1.52 (0.90, 2.57)</td>
<td>2.72 (1.95, 3.17)</td>
<td>4.60 (1.21, 3.02)</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Age-adjusted OR</td>
<td>Adjusted* OR</td>
<td>Age-adjusted OR</td>
</tr>
<tr>
<td>Yes</td>
<td>1.28 (0.84, 1.95)</td>
<td>2.19 (1.24, 2.19)</td>
<td>2.86 (1.28, 4.05)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Age-adjusted OR</td>
<td>Adjusted* OR</td>
<td>Age-adjusted OR</td>
</tr>
<tr>
<td>Yes</td>
<td>1.09 (0.67, 1.77)</td>
<td>1.67 (0.84, 1.67)</td>
<td>2.05 (0.81, 5.18)</td>
</tr>
</tbody>
</table>

* Adjusted for age, total number of pregnancy, education, smoking, BMI, waist/hip ratio, physical activity, systolic and diastolic blood pressure, fasting blood glucose, and total and low-density lipoprotein cholesterol; bold OR: statistically significant; NC: Not calculable.
myocardial infarction compared with women having neither of these characteristics. We found higher risk of myocardial infarction in women who delivered their first child in younger age, independent of parity, miscarriage, abortion, preterm delivery, stillbirth, and known conventional cardiovascular risk factors.

It is biologically plausible that reproductive history is associated with CVD risk. Levels of estrogens, progesterone, cortisol, and other steroid hormones during pregnancy increase to several hundred times their usual level, which may elevate LDL, decrease HDL, and produce insulin resistance, although the changes are reversible. As suggested by Ness et al. [16], the long-term hormonal fluctuations associated with multiparity may have latent effects by producing long-term alterations in CVD risk factors. The observed association for most of CVD (arrhythmia, angina pectoris, myocardial infarction, and heart failure) may reflect the direct biological effects of pregnancy and/or indirect effects through other metabolic and physiological changes (e.g., weight cycling) that increase the risk of CVD. Ness et al. [16] have proposed alternative explanation for the association of parity with CVD including the possibility that pregnancy or childbirth could cause increased stress or changes in other lifestyle factors (e.g., diet, exercise), which are in turn associated with increased risk of CVD. However, in our study, the association between maternal age at first delivery and hypertension remained significant even after considering most of these known risk factors. It is also possible that some or all of the observed associations are due to confounding by unmeasured variables or residual confounding from poorly controlled factors, such as change in lifestyle during the long lag time between childbirth and occurrence of CVD, which can be obtained by longitudinal studies which have not so far been conducted on this issue.

Changes in blood pressure may occur during pregnancy. It is also possible that the relation of number of pregnancies to blood pressure and hypertension may be different for women of younger ages. The results of studies on older women suggest that reproductive history exerts at most only a slight, long-term effect on blood pressure or risk of hypertension. Women with less education are known to be younger at first delivery and also have higher parity, which may be one factor related to other health behaviors and reproductive profiles. One reason for an increased risk of heart disease associated with early age at first delivery may be the small sustained drop in HDL cholesterol found after pregnancy, along with a positive association between parity and adiposity, particularly abdominal fat [17]. Hankinson et al. measured plasma estrogen levels in a sample of 216 subjects and found that plasma estrogen levels were lower among women with high parity and those with young age at first delivery after controlling for BMI, alcohol consumption, and age. The lower endogenous estrogen level is consistent with a lower HDL cholesterol level and with heart disease [18]. Hypertensive disorders of pregnancy have been reported to be more common in younger mothers [19] who have a known risk of long-term CVD [20–22]. Further studies are needed to explain the mechanisms behind the increasing risk of CVD with earlier age at first delivery.

The random sample with high response rate in the Health 2000 Survey and using weighting in the analysis can be considered an indicator of the high external validity of our results. The fact that this was a representative sample of Finnish women and the access to all the important confounders was the strength of this study. Indeed, the participation was markedly higher than in any other recent Finnish survey. High participation rate is crucially important in that it reduces the major biases otherwise caused by nonresponders. However, the cross-sectional design of our study caused some limitations, especially in the case of longer-lasting diseases, such as CVD, when any risk factor that results in death will be underrepresented among those with the disease. The survey was carried out at one time point and provides no indication of the sequence of events, whether exposure occurred before, after, or during the onset of the disease outcome, although the occurrence of CVD is low in child-bearing ages. This being so, it is generally impossible to infer causality from the results of cross-sectional studies.

Our findings suggest the need for additional care and consideration in monitoring older women who had their first delivery at younger age for heart diseases and its risk factors. Further studies are needed to find out the underlying reason for the association between young age at first delivery and higher risk of cardiovascular disease.

References


