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Research Article

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

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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/m^2) 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

Table 1: Distribution of age at first delivery by baseline characteristics.

	Age at first delivery		
	<25	≥25	*P* value
	Row %		
Age group			<0.001
30–49	43.6	56.4	
50–69	58.1	41.9	
70+	50.4	49.6	
Education			<0.001
Basic level	64.9	35.1	
Middle level	51.9	48.1	
High level	27.8	72.2	
Marital status			<0.001
Married	48.9	51.1	
Living with partner	49.4	50.6	
Divorced or living apart	55.9	44.1	
Widowed	55.0	45.0	
Single	35.8	64.2	
Oral contraceptive pill use ever			0.340
No	51.6	48.4	
Yes	49.7	50.3	
Hormone replacement therapy use ever			0.040
No	48.2	51.8	
Yes	53.6	46.4	
Toxemia in any pregnancy			0.049
No	93.9	6.1	
Yes	95.5	4.5	
Smoking			<0.001
Nonsmoking	47.1	52.9	
Stopped	49.6	50.4	
Occasionally	36.1	63.9	
Daily	61.7	38.3	
Physical activity			0.895
Ideal	46.6	53.4	
Sufficient	49.7	50.3	
Uncertain	49.8	50.2	
Insufficient	48.8	51.2	
	Mean		
Height (cm)	161.10	162.10	<0.001
Weight (kg)	70.80	69.20	<0.001
BMI (kg/m^2)	27.40	26.40	<0.001
Waist/hip ratio	0.87	0.86	<0.001
Glucose (mmol/L)	5.51	5.46	0.291
Cholesterol total (mmol/L)	6.02	5.83	<0.001
Cholesterol LDL (mmol/L)	3.71	3.56	<0.001
Systolic blood pressure (mm Hg)	136.80	132.01	<0.001
Diastolic blood pressure (mm Hg)	80.53	79.06	<0.001

Table 2: Association between age at first delivery (continuous) and cardiovascular diseases.

	n	Mean	SD	Age-adjusted			Adjusted*		
				OR	95% CI		OR	95% CI	
Hypertension									
No	2164	25.5	4.9	**1.05**	1.03	1.06	**1.03**	1.01	1.05
Yes	1025	24.5	4.4						
Arrhythmia									
No	2650	25.3	4.8	**1.03**	1.01	1.05	**1.03**	1.01	1.06
Yes	534	24.7	4.4						
Angina pectoris									
No	2963	25.3	4.8	**1.06**	1.02	1.10	**1.08**	1.02	1.14
Yes	225	24.6	4.6						
Myocardial infarction									
No	3090	25.3	4.8	**1.12**	1.06	1.18	**1.12**	1.05	1.20
Yes	100	24	3.9						
Heart failure									
No	2983	25.2	4.7	**1.05**	1.01	1.10	**1.06**	1.01	1.11
Yes	204	24.8	4.5						
Stroke									
No	3094	25.2	4.7	1.02	0.98	1.07	1.00	0.94	1.07
Yes	96	25.1	4.8						

*Adjusted for age, total number of pregnancy, education, smoking, BMI, waist/hip ratio, physical activity, systolic and diastolic blood pressure, fasting blood glucose, total and low-density lipoprotein cholesterol; bold OR: statistically significant.

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, preterm deliveries, and stillbirth), 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: 1.03–1.07), 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). 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 low-density lipoprotein cholesterol, systolic, and diastolic hypertension) 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, education, 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.

	Age at first delivery (years)																	
	≤25 versus 26–30						≤25 versus 31–35						≤25 versus >35					
	Age-adjusted			Adjusted*			Age-adjusted			Adjusted*			Age-adjusted			Adjusted*		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Hypertension																		
No																		
Yes	**1.28**	1.06	1.55	1.12	0.91	1.37	**1.50**	1.12	2.00	1.38	0.99	1.91	**2.73**	1.51	4.93	**2.15**	1.10	4.22
Arrhythmia																		
No																		
Yes	1.18	0.93	1.49	1.16	0.88	1.52	**1.69**	1.10	2.58	**1.82**	1.13	2.92	1.82	0.96	3.46	1.85	0.84	4.08
Angina pectoris																		
No																		
Yes	**1.70**	1.18	2.47	**1.95**	1.20	3.17	**1.98**	1.07	3.67	2.24	0.98	5.09	1.60	0.63	4.09	1.29	0.35	4.74
Myocardial infarction																		
No																		
Yes	1.52	0.90	2.57	1.17	0.59	2.34	2.73	0.99	7.49	**4.82**	1.39	16.75	NC			NC		
Heart failure																		
No																		
Yes	1.28	0.84	1.95	1.24	0.70	2.19	1.69	0.92	3.10	2.08	0.94	4.60	1.21	0.49	3.02	1.32	0.35	4.92
Stroke																		
No																		
Yes	1.09	0.67	1.77	0.84	0.42	1.67	2.05	0.81	5.18	2.35	0.62	8.86	1.28	0.41	4.05	1.07	0.20	5.78

*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 childbearing 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 childbearing 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

[1] M. J. J. De Kleijn, Y. T. Van der Schouw, and Y. Van der Graaf, "Reproductive history and cardiovascular disease risk in postmenopausal women. A review of the literature," *Maturitas*, vol. 33, no. 1, pp. 7–36, 1999.

[2] O. Joakimsen, K. H. Bønaa, E. Stensland-Bugge, and B. K. Jacobsen, "Population-based study of age at menopause and ultrasound assessed carotid atherosclerosis—the Tromso Study," *Journal of Clinical Epidemiology*, vol. 53, no. 5, pp. 525–530, 2000.

[3] G. A. Colditz, W. C. Willett, M. J. Stampfer, B. Rosner, F. E. Speizer, and C. H. Hennekens, "A prospective study of age at menarche, parity, age at first birth, and coronary heart disease in women," *American Journal of Epidemiology*, vol. 126, no. 5, pp. 861–870, 1987.

[4] A. Green, V. Beral, and K. Moser, "Mortality in women in relation to their childbearing history," *British Medical Journal*, vol. 297, no. 6645, pp. 391–395, 1988.

[5] D. A. Lawlor, J. R. Emberson, S. Ebrahim et al., "Is the association between parity and coronary heart disease due to biological effects of pregnancy or adverse lifestyle risk factors associated with child-rearing? Findings from the British women's heart and health study and the British regional heart study," *Circulation*, vol. 107, no. 9, pp. 1260–1264, 2003.

[6] R. B. Ness, T. Harris, J. Cobb et al., "Number of pregnancies and the subsequent risk of cardiovascular disease," *New England Journal of Medicine*, vol. 328, no. 21, pp. 1528–1533, 1993.

[7] A. I. Qureshi, W. H. Giles, J. B. Croft, and B. J. Stern, "Number of pregnancies and risk for stroke and stroke subtypes," *Archives of Neurology*, vol. 54, no. 2, pp. 203–206, 1997.

[8] K. Steenland, C. Lally, and M. Thun, "Parity and coronary heart disease among women in the american cancer society CPS II population," *Epidemiology*, vol. 7, no. 6, pp. 641–643, 1996.

[9] C. M. Beard, V. Fuster, and J. F. Annegers, "Reproductive history in women with coronary heart disease. A case-control study," *American Journal of Epidemiology*, vol. 120, no. 1, pp. 108–114, 1984.

[10] C. La Vecchia, A. Decarli, S. Franceschi, A. Gentile, E. Negri, and F. Parazzini, "Menstrual and reproductive factors and the risk of myocardial infarction in women under fifty-five years of age," *American Journal of Obstetrics and Gynecology*, vol. 157, no. 5, pp. 1108–1112, 1987.

[11] J. R. Palmer, L. Rosenberg, and S. Shapiro, "Reproductive factors and risk of myocardial infarction," *American Journal of Epidemiology*, vol. 136, no. 4, pp. 408–416, 1992.

[12] W. Guo, J. Y. Li, H. King, and F. B. Locke, "Diet and blood nutrient correlations with ischemic heart, hypertensive heart, and stroke mortality in China," *Asia-Pacific Journal of Public Health*, vol. 6, no. 4, pp. 200–209, 1992.

[13] E. Kharazmi, R. Kaaja, M. Fallah, and R. Luoto, "Pregnancy-related factors and the risk of isolated systolic hypertension," *Blood Pressure*, vol. 16, no. 1, pp. 50–55, 2007.

[14] A. Aromaa and S. Koskinen, *Health and Functional Capacity in Finland: Baseline Results of the Health 2000 Health Examination Survey*, series B, Publications of National Public Health Institute, Helsinki, Finland.

[15] A. Reunanen, A. Kattainen, and Working Group for Cardiovascular Diseases, "Cardiovascular diseases and diabetes," in *Health and Functional Capacity in Finland: Baseline Results of the Health 2000 Health Examination Survey*, A. Aromaa and S. Koskinen, Eds., pp. 47–51, National Public Health Institute, Helsinki, Finland, 2004.

[16] R. B. Ness, H. M. Schotland, K. M. Flegal, and F. S. Shofer, "Reproductive history and coronary heart disease risk in women," *Epidemiologic Reviews*, vol. 16, no. 2, pp. 298–314, 1994.

[17] S. A. Kaye, A. R. Folsom, R. J. Prineas, J. D. Potter, and S. M. Gapstur, "The association of body fat distribution with lifestyle and reproductive factors in a population study of postmenopausal women," *International Journal of Obesity*, vol. 14, no. 7, pp. 583–591, 1990.

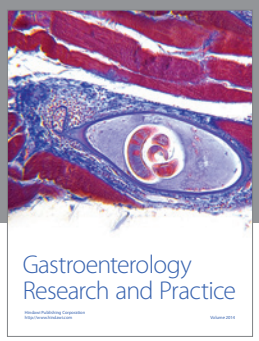
[18] S. E. Hankinson, G. A. Colditz, D. J. Hunter et al., "Reproductive factors and family history of breast cancer in relation to plasma estrogen and prolactin levels in postmenopausal women in the Nurses' Health Study (United States)," *Cancer Causes and Control*, vol. 6, no. 3, pp. 217–224, 1995.

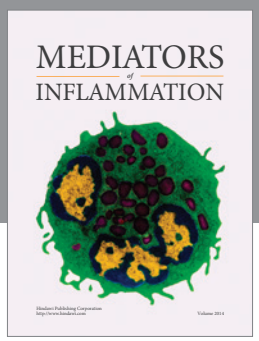
[19] T. O. Scholl, M. L. Hediger, and D. H. Belsky, "Prenatal care and maternal health during adolescent pregnancy: a review and meta-analysis," *Journal of Adolescent Health*, vol. 15, no. 6, pp. 444–456, 1994.

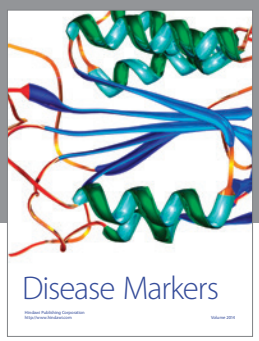
[20] G. A. Arnadottir, R. T. Geirsson, R. Arngrimsson, L. S. Jonsdottir, and O. Olafsson, "Cardiovascular death in women who had hypertension in pregnancy: a case-control study," *British Journal of Obstetrics and Gynaecology*, vol. 112, no. 3, pp. 286–292, 2005.

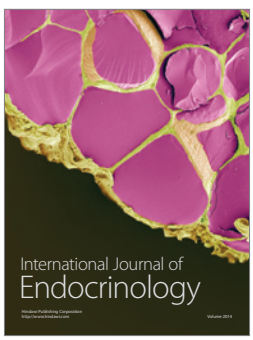
[21] P. Hannaford, S. Ferry, and S. Hirsch, "Cardiovascular sequelae of toxaemia of pregnancy," *Heart*, vol. 77, no. 2, pp. 154–158, 1997.

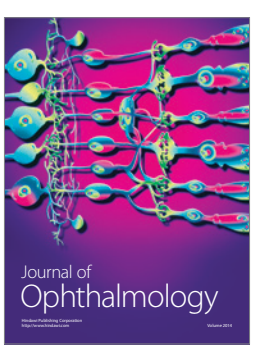
[22] B. J. Wilson, M. S. Watson, G. J. Prescott et al., "Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study," *British Medical Journal*, vol. 326, no. 7394, pp. 845–849, 2003.

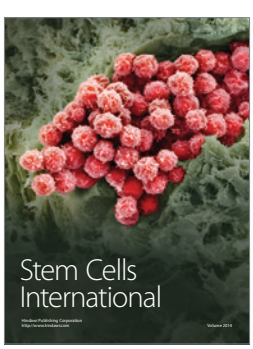


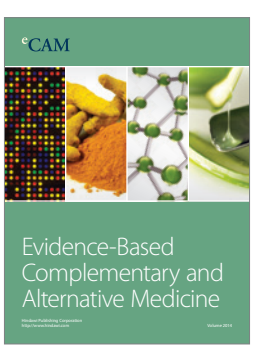


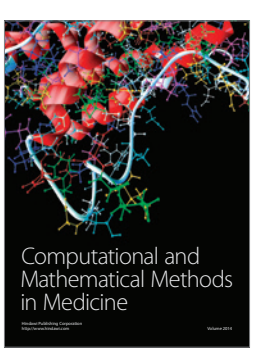


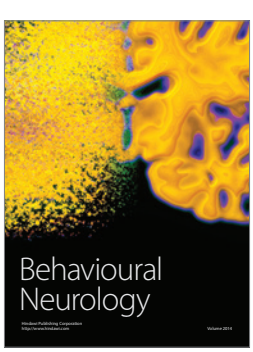


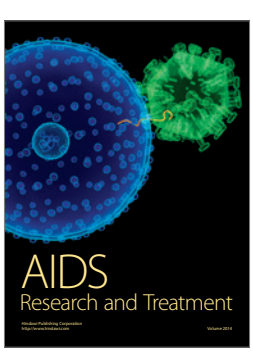


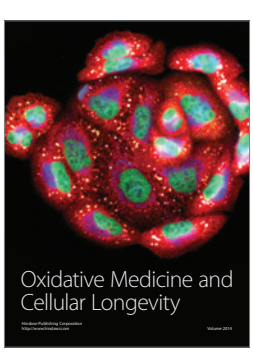












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