RESEARCH ARTICLE

Association of education level with the risk of female breast cancer: a prospective cohort study

Runxue Jiang[1†], Xia Wang[2†], Zhiguo Sun[1], Shouling Wu[3], Shuohua Chen[3] and Haifeng Cai[1*]

Abstract

Background Breast cancer is a serious threat to female health, and its incidence varies with education level (EL). In the present study, the association between EL and the risk of developing female breast cancer was investigated.

Methods From May 2006 to December 2007, 20,400 observation subjects in Kailuan Cohort received questionnaires and were subjected to clinical examinations for data collection on baseline population characteristics, height, weight, lifestyle and past disease history. Then, these participants were followed up with from the date of recruitment to December 31, 2019. Cox proportional risk regression models were used to analyse the association between EL and the risk of developing female breast cancer.

Results The cumulative follow-up period of 20,129 observation subjects that meet the inclusion criteria of this study was 254,386.72 person-years, and the median follow-up time was 12.96 years. During the follow-up period, 279 cases of breast cancer were diagnosed. In comparison with the low EL group, the risk of developing breast cancer was significantly higher in the medium (hazard ratio [HR] (95% confidence interval [CI]) = 2.23 (1.12–4.64)] and high [HRs (95% CI) = 2.52 (1.12–5.70)] EL group.

Conclusion An increased risk of breast cancer was associated with a higher EL, and some certain factors, such as alcohol use and hormone therapy, may play a mediating role.

Keywords Education level, Breast cancer, Cohort study

Introduction

Breast cancer poses a serious threat to female health worldwide. Based on GLOBOCAN data, in 2020 alone, the number of new cases of breast cancer reached 2.26 million, and the incidence of breast cancer ranks first among female malignant tumours [1]. Although breast cancer is highly dangerous, its aetiology remains unclear, and its known risk factors include genetic factors [2], lack of physical activity, unhealthy weight, alcohol intake, and hormone replacement therapy [3].

Notably, the incidence of malignant tumours varies with the education level (EL). A negative correlation has been observed between EL and the risk of developing gastric, liver, lung, and oesophageal cancer in humans [4, 5], the association of EL with breast cancer remains controversial. EL is associated with an increased risk of breast cancer[5, 6], while other studies have yielded contradictory results [7]. The association between EL and breast cancer was determined by analysing the effect of

†Runxue Jiang and Xia Wang contributed equally to this work.

*Correspondence:
Haifeng Cai
tangshanchf@163.com
[1] Department of Oncology Surgery, Tangshan People's Hospital, Tangshan 063000, China
[2] Department of Gynaecology, Tangshan Hongci Hospital, Tangshan 063000, China
[3] Health Department of Kailuan(Group), Tangshan 063000, China

Jiang *et al. BMC Women's Health*   (2023) 23:91

Page 2 of 6

EL on breast cancer in the population from the Kailuan Study.

Materials and methods
Study cohort
The Kailuan Study, which began in 2006, is an ongoing observational cohort study of a functional community population. The EL information of the Kailuan Study subjects was obtained at baseline (from May 2006 to December 2007). Then, continuous follow-up data, including breast cancer data, were obtained from the establishment of the cohort to the present, allowing us to study the association between EL and breast cancer. More details about the Kailuan Study can be found in the literature [8, 9]. Subjects who met the following criteria were recruited: (1) participation in the baseline survey of the Kailuan Study; (2) complete data on EL; and (3) signed the informed consent form. Those with history of malignancy were excluded. The study was approved by the Ethics Committee of Kailuan General Hospital and was conducted in accordance with the Declaration of Helsinki.

Collection of exposure information
Face-to-face questionnaire interviews and health examinations were performed by well-trained physicians or nurses by using a standardized protocol to gather information at baseline. These baseline data included sociodemographic characteristics (e.g., age and EL), lifestyle characteristics (smoking, alcohol consumption, salt intake and physical activity), history of previous diseases (hypertension, diabetes mellitus and malignant tumour) and physical examination data (height and weight). Participants were asked to take off their hats and shoes and wear thin clothes during the measurement. Height and weight were measured, and body mass index (BMI) was calculated as weight (kg)/height^2 (m^2).

Definition of variables
EL was classified into three categories, namely, low EL (illiteracy and primary), medium EL (middle school) and high EL (college and above). Smoking was defined as smoking one or more cigarettes per week in a recent year, and participants were classified into never smokers, former smokers and current smokers. Alcohol drinking was defined as drinking one or more alcoholic drinks per month for no less than six consecutive months, and participants were classified into never drinkers, former drinkers and current drinkers. Physical activity was classified according to the frequency of physical activity (20 min = 1 instance of activity) performed during leisure time. The categories of physical activity include exercise occasionally (< four instances of activity per week) and frequent exercise (≥ four instances of activity per week).

Collection of endpoint event information
The follow-up period was considered from the establishment of Kailuan Cohort (May 2006 – December 2007) to December 31, 2019. The follow-up endpoint was newly diagnosed breast cancer or death in the observed subjects (whichever came first). First, information on the participant medical records was obtained through the Tangshan City health insurance system. Then, the medical histories of subjects were collected by professionally trained investigators. Pathology, imaging (including magnetic resonance imaging, computed tomography, and colour Doppler ultrasonography) and blood biochemical examination results were verified by clinicians to confirm the diagnosis of breast cancer. Tumour cases were coded according to the International Classification of Diseases-10 (ICD-10), and breast cancer was coded as C50. Information on fatal events was obtained from the Kailuan Group social insurance system.

Statistical methods
SAS 9.4 was used to perform statistical analysis of the data. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as the number of cases (percentage). Differences in baseline demographic characteristics among the low, medium and high EL groups were analysed using variance analysis and Chi square test. A multivariable Cox proportional hazards regression model was applied to analyse the associations between EL and the risk of developing breast cancer. Subgroup analysis was performed according to age, BMI, physical activity and hypertension history, and the associations between EL and the risk breast cancer were explored in different subgroups. Sensitivity analysis was conducted to evaluate the consistency of our findings after excluding participants new breast cancer within 2 years of the start of the follow-up period. All statistical tests were considered statistically significant at $P < 0.05$ (two-sided).

Results
Baseline characteristics
The number of female participants in the 2006 baseline survey was 20,400. A total of 116 individuals with a history of malignancy and 155 participants lacking baseline EL data were excluded, and 20,129 female participants were eventually included in the statistical analysis. The mean age of the observed subjects was 48.75 ± 11.50 years. The low, medium and high EL groups included 1,078, 16,833 and 2,218 subjects, respectively. In comparison to the medium- and high-EL groups, the

Jiang *et al. BMC Women's Health*   (2023) 23:91

Page 3 of 6

mean age, BMI and the proportions of subjects with current smoking, heavy salt intake, frequent physical activity, hypertension and diabetes were higher in the low EL group, whereas the proportions of current drinkers were lower (all *P* values < 0.0001; Table 1).

Association between EL and risk of breast cancer

The cumulative follow-up period in this study was 254,386.72 person-years, with a median follow-up time of 12.96 years. A cumulative total of 279 new breast cancer ($n = 8$ in the low EL group; $n = 244$ in the medium EL group; $n = 27$ in the high EL group) were detected during the follow-up period. Cox proportional risk regression analysis was carried out with the occurrence of breast cancer as the dependent variable and EL difference as the independent variable. In comparison with the low EL group, model 1 was adjusted for age, while model 2 was adjusted for smoking, alcohol consumption, BMI, physical activity, salt intake, hypertension and diabetes mellitus based on model 1. The hazard ratios (HRs) and 95% confidence intervals (95% CI) for breast cancer in the medium and high EL group were 2.23(1.12–4.64) and 2.52(1.12–5.70), respectively. In the sensitivity analysis, after excluding participants who developed breast cancer

within 2 years after the start of the follow-up period, the risk of breast cancer was significantly higher in the medium and high EL group (Table 2).

Subgroup analysis of EL and risk of breast cancer

Subgroup analysis was performed according to age, BMI, physical activity and hypertension history, and the associations between EL and the risk breast cancer was explored in different subgroups. In comparison with the low EL group, in participants aged 50 years and above and the exercise occasionally subgroups, an increased risk of breast cancer was observed in the patients in the medium and high EL group, while an increased risk of breast cancer was observed in high EL's subjects with BMI ≥ 28 and hypertension subgroup (Table 3).

Discussion

This prospective study based on the Kailuan cohort explored the association between EL and breast cancer risk. The results show that the risk of breast cancer is significantly increased in the medium and high EL groups compared with the low EL group. This study provides reference for the prevention and screening of breast cancer.

Table 1 Baseline characteristics of the participants

Characteristics	Total cohort (*n* = 20,129)	Low EL (*n* = 1,078)	Medium EL (*n* = 16,833)	High EL (*n* = 2,218)	*P*
Age(years, mean ± SD)	48.75 + 11.50	58.51 + 8.26	49.38 + 10.72	39.29 + 12.51	0.000
BMI(kg/m², mean ± SD)	24.66 + 3.79	26.33 + 3.88	24.78 + 3.75	22.95 + 3.45	0.000
Smoking status, n(%)					
Never	19,662(97.68)	961(89.15)	16,502(98.03)	2199(99.14)	0.000
Former	89(0.44)	31(2.88)	51(0.30)	7(0.32)	
Current	378(1.88)	86(7.98)	280(1.66)	12(0.54)	
Alcohol consumption, *n*(%)					
Never	18,744(93.12)	1018(94.43)	15,919(94.57)	1807(81.47)	0.000
Former	84(0.42)	5(0.46)	48(0.29)	31(1.40)	
Current	1301(6.46)	55(5.10)	866(5.14)	380(17.13)	
Salt intake, *n*(%)					
Light	1888(9.38)	164(15.21)	1408(8.36)	316(14.25)	0.000
General	16,882(83.87)	791(73.38)	14,406(85.58)	1685(75.97)	
Heavy	1359(6.75)	123(11.41)	1019(6.05)	217(9.78)	
Physical activities, *n*(%)					
Occasionally	17,445(86.67)	777(72.08)	14,697(87.31)	1971(88.86)	0.000
Frequently	2684(13.33)	301(27.92)	2136(12.69)	247(11.14)	
Hypertension, *n*(%)					
No	13,563(67.38)	466(43.23)	11,143(66.20)	1954(88.10)	0.000
Yes	6566(32.62)	612(56.77)	5690(33.80)	264(11.90)	
Diabetes mellitus, *n* (%)					
No	18,503(91.92)	899(83.40)	15,445(91.75)	2159(97.34)	0.000
Yes	1626(8.08)	179(16.60)	1388(8.25)	59(2.66)	

EL Education level

P < 0.001

Jiang *et al. BMC Women's Health*   (2023) 23:91

Page 4 of 6

Table 2 Associations between EL and breast cancer risk

EL	Total cases	Person years	Incident cases	HR(95%CI)	
				Model1	Model 2
Low	1078	13,467.46	8	Ref	Ref
Medium	16,833	213,025.99	244	2.37(1.17–4.81)	2.23(1.12–4.64)
High	2218	27,893.27	27	2.51(1.12–5.64)	2.52(1.12–5.70)
Excluding participants who developed breast cancer within the first 2 years of follow-up					
Low	1075	13,466.04	5	Ref	Ref
Medium	16,805	213,001.34	216	3.23(1.33–7.87)	3.13(1.28–7.67)
High	2214	27,889.00	23	3.19(1.19–8.54)	3.21(1.19–8.67)

EL Education level

Compared with the low El group respectively

Model1 was adjusted for age; model2 was further adjusted for smoking status, alcohol consumption, BMI, physical activity, salt intake, hypertension, and diabetes mellitus

Table 3 Subgroup analysis of the association between EL and breast cancer risk

Variable	EL	B	SE	WALD	*P*	HR(95%CI)
Age (years)						
< 50	medium	0.023	0.716	0.001	0.974	1.02(0.25–4.17)
	high	0.357	0.762	0.219	0.640	1.43(0.32–6.37)
≥ 50	medium	0.968	0.421	5.288	0.022	2.63(1.15–6.01)
	high	1.344	0.534	6.348	0.012	3.84(1.35–10.92)
BMI(kg/m^2)						
< 28	medium	0.736	0.421	3.057	0.080	2.08(0.92–4.76)
	high	0.716	0.478	2.248	0.134	2.05(0.80–5.22)
≥ 28	medium	1.037	0.725	2.045	0.153	2.82(0.68–11.69)
	high	1.808	0.848	4.549	0.033	6.10(1.16–32.11)
Physical activities						
Occasionally	medium	0.850	0.418	4.133	0.042	2.34(1.03–5.31)
	high	0.995	0.470	4.474	0.034	2.70(1.08–6.80)
Frequently	medium	0.800	0.740	1.169	0.280	2.23(0.52–9.49)
	high	0.571	1.019	0.314	0.575	1.77(0.24–13.04)
Hypertension						
No	medium	0.841	0.587	2.052	0.152	2.32(0.73–7.32)
	high	0.807	0.637	1.605	0.205	2.24(0.64–7.82)
Yes	medium	0.779	0.465	2.806	0.094	2.18(0.88–5.43)
	high	1.385	0.577	5.758	0.016	3.99(1.29–12.39)

EL Education level

Compared with the low El group respectively

Adjusted for age, smoking status, alcohol consumption, BMI, physical activity, salt intake, hypertension, and diabetes mellitus

The risk of breast cancer significantly increased among subjects with medium and high EL, and this result is consistent with previous research results [5]. In a meta-analysis [6] that includes 18 cohorts, compared with low EL participants, the breast cancer risk of subjects with high EL significantly increased [pooled RR(95%CI) = 1.22 (1.14–1.30)]. In another study, higher EL was associated with a lower risk of breast cancer after adjusting for several confounding factors [7]. These differences in findings may be related to differences in subject race and the length of the follow-up period.

Subgroup analysis results showed that the risk of developing breast cancer is increased in medium and high EL subjects aged ≥ 50 years and exercise occasionally and in high EL subjects with BMI ≥ 28 and hypertension. In a meta-analysis, although the effect was different for

Jiang *et al. BMC Women's Health*   (2023) 23:91

Page 5 of 6

pre- and post-menopausal women and for women of different geographic and ethnic groups, a statistically significant association was still observed between hypertension and increased breast cancer risk [10]. Therefore, prevention and screening should be prioritised in the older women. Enhancing physical exercise, controlling BMI level and keeping blood pressure normal are of essential for the prevention and control of breast cancer.

Although the association between EL and breast cancer risk has not been fully understood, several following aspects may tentatively explain the relationship between EL and breast cancer development. Firstly, women with more education are likely to have advanced age at first pregnancy, birth and fewer children, thus increasing their risk of developing breast cancer [11, 12]. Secondly, women with a higher EL are associated with a later menopause onset [13], which is also a breast cancer risk factor [14]. Moreover, more education was correlated with higher alcohol intake and higher prevalence of hormone therapy, and both factors may contribute to the development of breast cancer [6]. In addition, people with higher EL may have better screening compliance, and increased screening can reduce breast cancer mortality but increase incidence [15, 16].

This study has some limitations, such as the absence of some confounders (e.g., use of hormone therapy and age at menopause). The larger study cohort and longer follow-up time aims to minimise the effect of the above missing factors, and the abovementioned variables will be increased in subsequent studies. Secondly, only baseline data of EL were used for the analysis of the association between EL and breast cancer risk, and time-dependent exposures during follow-up were not considered. Some subjects may have received on-the-job education, so changes in EL may affect the risk of developing breast cancer, which should be explored in depth in subsequent studies.

Conclusion

An increased risk of breast cancer was associated with a higher EL. This condition was more prominent in the sensitivity analysis, and certain factors such as alcohol use and hormone therapy may play a mediating role. Breast cancer can be reduced by reducing alcohol intake, maintaining a normal BMI, controlling blood pressure, increasing physical activity and improving screening compliance.

Authors' contributions
RJ and XW: Conception, design, validation, formal analysis, investigation, and writing-original draft. RJ, XW, ZS, and SC: Acquisition, analysis and interpretation of data. SW and SC: Data curation, validation, investigation, resources. HC: Methodology, writing-review & editing, funding acquisition. All authors read and approved the fnal manuscript.

Availability of data and materials
The data that support the fndings of this study are available from the Kailuan Study but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Kailuan Study.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Kailuan General Hospital, Ethics number KS-2006–5. The participants provided their written informed consent to participate in this study.

Consent to publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

References
1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49. https://doi.org/10.3322/caac.21660.
2. Coignard J, Lush M, Beesley J, et al. A case-only study to identify genetic modifiers of breast cancer risk for BRCA1/BRCA2 mutation carriers. Nat Commun. 2021;12(1):1078. https://doi.org/10.1038/s41467-020-20496-3.
3. Al Ajmi K, Lophatananon A, Mekli K, Ollier W, Muir KR (2020) Association of Nongenetic Factors With Breast Cancer Risk in Genetically Predisposed Groups of Women in the UK Biobank Cohort. JAMA Netw Open. 3(4):e203760. doi: https://doi.org/10.1001/jamanetworkopen.2020.3760.
4. Rota M, Alicandro G, Pelucchi C, et al. Education and gastric cancer risk-An individual participant data meta-analysis in the StoP project consortium. Int J Cancer. 2020;146(3):671–81. https://doi.org/10.1002/ijc.32298.
5. Larsen IK, Myklebust TÅ, Babigumira R, Vinberg E, Møller B, Ursin G. Education, income and risk of cancer: results from a Norwegian registry-based study. Acta Oncol. 2020;59(11):1300–7. https://doi.org/10.1080/0284186X.2020.1817548.
6. Dong JY, Qin LQ. Education level and breast cancer incidence: a meta-analysis of cohort studies. Menopause. 2020;27(1):113–8. https://doi.org/10.1097/GME.0000000000001425.
7. Hajian-Tilaki K, Kaveh-Ahangar T, Hajian-Tilaki E. Is educational level associated with breast cancer risk in Iranian women? Breast Cancer. 2012;19(1):64–70. https://doi.org/10.1007/s12282-011-0273-6.
8. Lyu Z, Li N, Wang G, et al. Independent and joint associations of blood lipids and lipoproteins with lung cancer risk in Chinese males: A prospective cohort study. Int J Cancer. 2019;144(12):2972–84. https://doi.org/10.1002/ijc.32051.
9. Li X, Chen H, Wang G, et al. Metabolic Syndrome Components and the Risk of Colorectal Cancer: A Population-Based Prospective Study in Chinese Men. Front Oncol. 2019;9:1047. https://doi.org/10.3389/fonc.2019.01047.
10. Han H, Guo W, Shi W, Yu Y, Zhang Y, Ye X, He J. Hypertension and breast cancer risk: a systematic review and meta-analysis. Sci Rep.

Jiang *et al. BMC Women's Health*   (2023) 23:91

Page 6 of 6

2017;20(7):44877. https://doi.org/10.1038/srep44877.PMID:28317900; PMCID:PMC5357949.

11. Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. Breast Cancer Res Treat. 2014;144(1):1–10. https://doi.org/10.1007/s10549-014-2852-7.

12. Nelson HD, Zakher B, Cantor A, et al. Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. Ann Intern Med. 2012;156(9):635–48. https://doi.org/10.7326/0003-4819-156-9-201205010-00006.

13. Ceylan B, Özerdoğan N. Factors affecting age of onset of menopause and determination of quality of life in menopause. Turk J Obstet Gynecol. 2015;12(1):43–9. https://doi.org/10.4274/tjod.79836.

14. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. Lancet Oncol. 2012;13(11):1141–51. https://doi.org/10.1016/S1470-2045(12)70425-4.

15. Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. The benefits and harms of breast cancer screening: an independent review. Br J Cancer. 2013;108(11):2205–40. https://doi.org/10.1038/bjc.2013.177.

16. Myers ER, Moorman P, Gierisch JM, et al. Benefits and Harms of Breast Cancer Screening: A Systematic Review. JAMA. 2015;314(15):1615–34. https://doi.org/10.1001/jama.2015.13183.

Publisher's Note