Check for updates

STUDY PROTOCOL

Lifestyle and reproductive health: the aetiology of ovarian cancer in Pakistan [version 1; peer review: 2 approved]

Qurratulann Alvi[1], Gul Muhammad Baloch[2], Karuthan Chinna[2], Ali Dabbagh[2]

[1]School of Biosciences, Faculty of Health and Medical Sciences, Taylor's University, Kualalampur, Selangor, 47500, Malaysia
[2]School Of Medicine,Faculty of Health and Medical Sciences, Taylor's University, Kualalampur, Selangor, 47500, Malaysia

v1 **First published:** 04 Aug 2020, **9**:901
https://doi.org/10.12688/f1000research.24866.1
Latest published: 04 Aug 2020, **9**:901
https://doi.org/10.12688/f1000research.24866.1

Abstract

Ovarian cancer is a fatal gynaecological cancer and eighth most common cancer in women globally. Lifestyle, reproductive and sociodemographic factors are among the influential parameters that may significantly affect the risk of ovarian cancer and its mortality rate. However, the epidemiological investigations have shown that the risk of ovarian cancers associated with these factors is different in varied geographical distributions. Lifestyle and reproductive factors have not been investigated thoroughly across a wide cultural diversity. The objective of this study is to investigate the association of these factors with ovarian cancer in Pakistan. This investigation will focus on the lifestyle effects of fat intake, intake of tea, habitual exercise, use of talc, personal hygiene, habit of holding urine for long time, obesity on ovarian cancer among Pakistani women. Reproductive variables will include age at menarche, natural menopausal age, parity, nulliparity (miscarriages, abortion, stillbirths), infertility, fertility treatment, tubal ligation, oral contraceptive use, and family history of breast or ovarian cancer. Sociodemographic variables will include effect of age, income, education, and geographical location. A case-control study will be conducted in the major cancer hospitals of Pakistan and the patients will also be interviewed. The controls will be recruited outside the hospital. For controls the same age limit and residency requirements will be applied. The information gained from this research will be an important contribution to develop programs for health promotion, with a focus on ovarian cancer prevention and women's health. The findings could be used for health policies and planning to prevent ovarian cancer. The research will pave the way for a public policy and interventions to reduce the burden of ovarian cancer in Pakistan.

Keywords

Ovarian Cancer, Reproductive Health, Lifestyle, Miscarriage, Pakistan

Open Peer Review

Reviewer Status ✓ ✓

	Invited Reviewers	
	1	**2**
version 1 04 Aug 2020	✓ report	✓ report

1. **Ramesh Kumar**, Ministry of National Health Services Regulation & Coordination, Government of Pakistan, Islamabad, Pakistan

2. **Sadiq Bhanbhro**, Sheffield Hallam University, Sheffield, UK

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Gul Muhammad Baloch (gulmuhammad.baloch@taylors.edu.my)

Author roles: Alvi Q: Conceptualization, Investigation, Writing – Original Draft Preparation; **Baloch GM**: Project Administration, Supervision, Writing – Review & Editing; **Chinna K**: Methodology, Software, Writing – Review & Editing; **Dabbagh A**: Formal Analysis, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2020 Alvi Q *et al*. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Alvi Q, Baloch GM, Chinna K and Dabbagh A. **Lifestyle and reproductive health: the aetiology of ovarian cancer in Pakistan [version 1; peer review: 2 approved]** F1000Research 2020, **9**:901 https://doi.org/10.12688/f1000research.24866.1

First published: 04 Aug 2020, **9**:901 https://doi.org/10.12688/f1000research.24866.1

Introduction

Ovarian cancer is one of the most frequently fatal gynaecologic cancers (Jayson *et al.*, 2014; Tworoger & Huang, 2016). According to the American Institute for Cancer Research report, in 2018 ovarian cancer globally accounted for 3.6% of all forms of cancers and the eighth leading cause of death among women globally (Merritt *et al.*, 2018). Only 46% of ovarian cancer patients survive beyond 5 years (Kathawala *et al.*, 2018). The high mortality associated with ovarian cancer is due to late diagnosis and resistance to treatment, (Carollo *et al.*, 2019; Nunes *et al.*, 2019).

According to a 2018 report by World Cancer Research Fund, the diagnosed cases of ovarian cancer are 295,414. The estimated age-standardized incidence and mortality rates of ovarian cancer in 2018 were 6.6 and 3.9, respectively (Bray *et al.*, 2018) and this number is expected to reach at 434,184 by 2040.

The incidence, prevalence, and mortality of ovarian cancer varies across geographical locations and countries (Coburn *et al.*, 2017). Globally, the highest incidence and mortality for ovarian cancer was reported in Serbia (16.6 and 6.8, respectively) and lowest in Gambia (0.6 and 0.43, respectively); in Europe itself, figures were highest in Serbia and lowest in Ireland (11.4 and 6.4, respectively); in Asia, rates are highest in Brunei (16 and 6.2, respectively) and lowest in Yemen (2.6 & 2.1, respectively) (https://gco.iarc.fr/today/online-analysis-table).

The epidemiological diversity could be linked to different risk factors for ovarian cancer (Hunn & Rodriguez, 2012). Poole *et al.* (2013) called for identifying modifiable risk factors. Jammal *et al.* (2017) believe that ovarian cancer prevention can be accomplished with clinical approaches.

The aetiology of ovarian cancer cannot be defined by single mechanism (Terry & Missmer, 2017). Hence understanding of risk factors is important (Webb & Jordan, 2017). Clinical evidence shows that by eliminating and decreasing the risk factors, the ovarian cancer cases can be prevented (Bray *et al.*, 2018). Lifestyle modifications can minimize cancer burden (Song & Giovannucci, 2016).

Ali (2018) noted that knowledge on ovarian cancer might increase survival rate. This can help women at risk of ovarian cancer to take special precautions (Li *et al.*, 2015; Torre *et al.*, 2018); thus, help reduce ovarian cancer risk (Momenimovahed *et al.*, 2019).

Schildkraut *et al.* (2019) reported obesity and family history of breast cancer to be major risk factors for ovarian cancer and Abbott *et al.* (2016) reported inadequacy of physical activity to be a risk factor. Gabriel *et al.* (2019) found the use of talc in genital areas to be a risk factor for ovarian cancer in England. In a Canadian study, Koushik *et al.* (2017) showed strong inverse association between parity and ovarian cancer. Harris *et al.* (2017) reported oral contraceptive and family history as the main risk factors in an American population. Lee *et al.* (2013) showed that consumption of green tea increases ovarian cancer risk in a Chinese population. Other risk factors include infertility (Rasmussen *et al.*, 2017), miscarriages (Moorman *et al.*, 2016) and age at menopause.

Doherty *et al.* (2017) suggests role of ethnically differing populations. Endpoints must represent the disease agent involved and rely on the quality of life (Wilson *et al.*, 2017). Responsive and timely health care facilities that use relational communication, could enhance women's health experience with ovarian cancer (Jelicic *et al.*, 2019).

Study objective

This study explores lifestyle (use of talc, obesity, pattern of weight change), reproductive health (miscarriages, age at menarche, menopausal age, parity, nulliparity) and socio-demographic factors (age, income, and geographical location) associated with ovarian cancer in Pakistan.

Methods

The research is now at an advanced stage after a development of a literature review, methodology and preparation of a validated questionnaire. The study will be conducted from July 2020 to December 2020. Data collection will start in July 2020.

Study design

This will be a case-control study. The cases will be ovarian cancer patients registered at cancer hospitals in Pakistan. Hospitals are selected based on receiving approval from the hospital administrations. The controls will be recruited from the general population, using random digit dialling of individuals in the vicinity of the selected hospitals, since this was what the participating hospitals wanted. Cases and controls will not be matched. In the analysis, the outcome variables will be corrected for all the variables. We do not have the ability to mitigate many sources of bias as we must comply with the hospital's' requirements.

Instrument

A validated questionnaire (validated by a panel of experts, each with doctorates and many years' experience in biostatistics, public health and biomedicine) will be used to elicit information on following parameters.

1. Socio demographic characteristics

2. Patient clinical data

3. Diagnostic data

4. Lifestyle factors

5. Reproductive health

Data collection

Patients' clinical and diagnostic data will be obtained from the respective hospital registries. Written informed consent will be obtained from all participants with the voluntary decision to participate in the study. Interviews will be conducted with questions relevant to the parameters mentioned above.

Sample size

Power and Sample Size software was used to calculate sample size. The level of significance and power were set as 0.05 and 80%, respectively. Based on results, the minimum required sample size is 387 for cases and 387 for controls. The figures are rounded up to 400 per group.

Inclusion criteria for cases

• Age 30 to 65

• Confirmed diagnosis of ovarian cancer by hospital or health care facility.

Exclusion criteria for cases

• Cognitively impaired

• Diagnosed with any other form of cancer

The inclusion criteria for control will be, age 30 to 65, healthy and cognitively not impaired; and exclusion criteria will be comorbidities, such as diabetes or cardiovascular disease.

Data analysis

Data will be analysed using SPSS version 25. Qualitative variables will be described as frequencies and percentages, while quantitative variables will be described as means and standard deviations if the variable is normally distributed and as median and interquartile ranges, otherwise. Univariate and multivariate binary logistic regression analyses will be used in testing association between the predictor variables and ovarian cancer. In the univariate analysis, the predictor variables will be tested on at time. The variables that are significant at 0.25 level will be included in the multivariate analysis. Finally, stepwise analysis will be used to determine the significant predictors of ovarian cancer.

Ethical consideration

Ethical approval for this study will be obtained from the participating hospitals/authorities in Pakistan. Respondents will be briefed, consent obtained and the confidentiality and participants' right to stop at any point of the study will be assured.

Data availability

No data are associated with this article.

References

Abbott SE, Bandera EV, Qin B, *et al.*: **Recreational physical activity and ovarian cancer risk in African American women.** *Cancer Med.* 2016; **5**(6): 1319–1327.
PubMed Abstract | Publisher Full Text | Free Full Text

Ali AT: **Towards Prevention of Ovarian Cancer.** *Curr Cancer Drug Targets.* Bentham Science Publishers. 2018; **18**(6): 522–537.
PubMed Abstract | Publisher Full Text

Bray F, Ferlay J, Soerjomataram I, *et al.*: **Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.** *CA Cancer J Clin.* 2018; **68**(6): 394–424.
PubMed Abstract | Publisher Full Text

Carollo E, Paris B, Samuel P, *et al.*: **Detecting ovarian cancer using extracellular vesicles: progress and possibilities.** *Biochem Soc Trans.* 2019; **47**(1): 295–304.
PubMed Abstract | Publisher Full Text

Coburn SB, Bray F, Sherman ME, *et al.*: **International patterns and trends in ovarian cancer incidence, overall and by histologic subtype.** *Int J Cancer.* Wiley Online Library, 2017; **140**(11): 2451– 2460.
PubMed Abstract | Publisher Full Text | Free Full Text

Epidemiology Working Group Steering Committee, Ovarian Cancer Association Consortium Members of the EWG SC, Doherty JA, *et al.*: **Current Gaps in Ovarian Cancer Epidemiology: The Need for New Population-Based Research.** *J Natl Cancer Inst.* Oxford University Press, 2017; **109**(10): djx144.
PubMed Abstract | Publisher Full Text | Free Full Text

Gabriel IM, Vitonis AF, Welch WR, *et al.*: **Douching, Talc Use, and Risk for Ovarian Cancer and Conditions Related to Genital Tract Inflammation.** *Cancer Epidemiol Biomarkers Prev.* 2019; **28**(11): 1835–1844.
PubMed Abstract | Publisher Full Text | Free Full Text

Harris HR, Titus LJ, Cramer DW, *et al.*: **Long and irregular menstrual cycles, polycystic ovary syndrome, and ovarian cancer risk in a population-based case-control study.** *Int J Cancer.* 2017; **140**(2): 285–291.
PubMed Abstract | Publisher Full Text | Free Full Text

Hunn J, Rodriguez GC: **Ovarian cancer: etiology, risk factors, and epidemiology.** *Clin Obstet Gyneco.* LWW 2012; **55**(1): 3–23.
PubMed Abstract | Publisher Full Text

Jammal MP, de Lima CA, Nomelini RS, *et al.*: **Is Ovarian Cancer Prevention Currently Still a recommendation of Our Grandparents?** *Rev Bras Ginecol Obstet.* ThiemeRevinterPublicaç\~oesLtda. 2017; **39**(12): 676–685.
PubMed Abstract | Publisher Full Text

Jayson GC, Kohn EC, Kitchener HC, *et al.*: **Ovarian cancer.** *Lancet.* 2014; **384**(9951): 1376–1388.
PubMed Abstract | Publisher Full Text

Jelicic L, Brooker J, Shand L, *et al.*: **Experiences and health care preferences of women with ovarian cancer during the diagnosis phase.** *Psychooncology.* Wiley Online Library, 2019; **28**(2): 379–385.
PubMed Abstract | Publisher Full Text

Kathawala RJ, Kudelka A, Rigas B: **The Chemoprevention of Ovarian Cancer: the Need and the Options.** *Curr Pharmacol Rep.* Springer, 2018; **4**(3): 250–260.
PubMed Abstract | Publisher Full Text | Free Full Text

Koushik A, Grundy A, Abrahamowicz M, *et al.*: **Hormonal and reproductive factors and the risk of ovarian cancer**. *Cancer Causes Control.* 2017; **28**(5): 393–403.
PubMed Abstract | Publisher Full Text

Lee AH, Su D, Pasalich M, *et al.*: **Tea consumption reduces ovarian cancer risk.** *Cancer Epidemiol.* 2013; **37**(1): 54–59.
PubMed Abstract | Publisher Full Text

Li K, Hüsing A, Fortner RT, *et al.*: **An epidemiologic risk prediction model for ovarian cancer in Europe: the EPIC study.** *Br J Cancer.* Nature Publishing Group, 2015; **112**(7): 1257–65.
PubMed Abstract | Publisher Full Text | Free Full Text

Merritt MA, Rice MS, Barnard ME, *et al.*: **Pre-diagnosis and post-diagnosis use of common analgesics and ovarian cancer prognosis (NHS/NHSII): a cohort study.** *Lancet Oncol.* Elsevier, 2018; **19**(8): 1107–1116.
PubMed Abstract | Publisher Full Text | Free Full Text

Momenimovahed Z, Tiznobaik A, Taheri S, *et al.*: **Ovarian cancer in the world: epidemiology and risk factors.** *Int J Womens Health.* Dove Press, 2019; **11**: 287–299.
PubMed Abstract | Publisher Full Text | Free Full Text

Moorman PG, Alberg AJ, Bandera EV, *et al.*: **Reproductive factors and ovarian cancer risk in African-American women.** *Ann Epidemiol.* 2016; **26**(9): 654–662.
PubMed Abstract | Publisher Full Text | Free Full Text

Nunes AS da A de, and others: **Cysteine, a facilitator of hypoxia adaptation and a promoter of drug-resistance: a new route to better diagnose and treat ovarian cancer patients**. 2019.
Reference Source

Poole EM, Merritt MA, Jordan J, *et al.*: **Hormonal and reproductive risk factors for epithelial ovarian cancer by tumor aggressiveness.** *Cancer Epidemiol Biomarkers Prev.* AACR, 2013; **22**(3): 429–437.
PubMed Abstract | Publisher Full Text | Free Full Text

Rasmussen ELK, Hannibal CG, Dehlendorff C, *et al.*: **Parity, infertility, oral contraceptives, and hormone replacement therapy and the risk of ovarian serous borderline tumors: A nationwide case-control study.** *Gynecol Oncol.*

2017; **144**(3): 571–576.
PubMed Abstract | Publisher Full Text

Schildkraut JM, Peres LC, Bethea TN, *et al.*: **Ovarian Cancer in Women of African Ancestry (OCWAA) consortium: a resource of harmonized data from eight epidemiologic studies of African American and white women.** *Cancer Causes Control.* 2019; **30**(9): 967–978.
PubMed Abstract | Publisher Full Text | Free Full Text

Song M, Giovannucci E: **Preventable Incidence and Mortality of Carcinoma Associated With Lifestyle Factors Among White Adults in the United States.** *JAMA Oncol.* American Medical Association, 2016; **2**(9): 1154–1161.
PubMed Abstract | Publisher Full Text | Free Full Text

Terry KL, Missmer SA: **Epidemiology of ovarian and endometrial cancers**. In: *Pathology and Epidemiology of Cancer.* Springer, 2017; 233–246.
Publisher Full Text

Torre LA, Trabert B, DeSantis CE, *et al.*: **Ovarian cancer statistics, 2018.** *CA Cancer J Clin.* Wiley Online Library, 2018; **68**(4): 284–296.
PubMed Abstract | Publisher Full Text | Free Full Text

Tworoger SS, Huang T: **Obesity and ovarian cancer**. In: *Obesity and Cancersity and Cancer.* Springer, Cham. 2016; 155–176.
PubMed Abstract | Publisher Full Text

Webb PM, Jordan SJ: **Epidemiology of epithelial ovarian cancer.** *Best Pract Res Clin Obstet Gynaecol.* Elsevier, 2017; **41**: 3–14.
PubMed Abstract | Publisher Full Text

Wilson MK, Pujade-Lauraine E, Aoki D, *et al.*: **Fifth Ovarian Cancer Consensus Conference of the Gynecologic Cancer InterGroup: recurrent disease.** *Ann Oncol.* Oxford University Press, 2017; **28**(4): 727–732.
PubMed Abstract | Publisher Full Text | Free Full Text

Open Peer Review

Current Peer Review Status: ✔ ✔

Version 1

Reviewer Report 10 August 2020

https://doi.org/10.5256/f1000research.27437.r68704

© **2020 Bhanbhro S.** This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

✔ **Sadiq Bhanbhro**
College of Health and Wellbeing and Life Sciences, Sheffield Hallam University, Sheffield, UK

This is a well-designed study protocol aimed to investigate the relationships between lifestyle factors, reproductive health, and risk of ovarian cancer in Pakistan. The aims, objectives and study design including sample size and data collection methods are appropriate and sufficiently described. The authors have cited the current and relevant literature. However, considering the sensitive nature of the topic under study, I would suggest the investigators need to provide more details on the recruitment of the potential study participants and the ethical considerations. For instance, the authors' need to identify and name the relevant academic ethics review committee that will approve the project.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public health, social sciences, research methods.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 07 August 2020

https://doi.org/10.5256/f1000research.27437.r68702

© 2020 Kumar R. This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Ramesh Kumar
Health Services Academy, Ministry of National Health Services Regulation & Coordination, Government of Pakistan, Islamabad, Pakistan

This will be an important study proposal and will be helpful for future research evidence. Ovarian cancer is a big problem in Pakistan and researchers are strongly needed to work in this area. Moreover, the author has proposed a case-control study that would explore multiple factors responsible to develop this problem in Pakistan.

This is a study protocol developed by the author and the author will collect the data and publish it later on

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research