Demographic, Lifestyle And Reproductive Factors Associated With Ovarian Cancer Among Married Women In Pakistan

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ABSTRACT

Background and objectives Ovarian cancer is a fatal gynecological cancer and the eighth most common cancer in women, globally. Socio-demographic, lifestyle and reproductive factors are most often associated with ovarian cancer. However, epidemiological investigations have shown that the magnitude of these risk factors may differ by geographical locations. The objective of this study is to investigate the association of these factors with ovarian cancer among married women in Pakistan. Method A casecontrol study was conducted in two major cancer centers in Pakistan from 2019 to 2021. The controls were recruited within the same hospital, matched for age. Results In this study, there were 214 cases and 205 controls. The odds of ovarian cancer was higher among those in low socioeconomic group (OR= 26.98 (95%CI=9.74,74.75)). Use of talcum powder (OR=14.05 (95%CI=3.53, 55.97)), habit of holding (OR=21.74(95%CI=8.00,58.82)) urine and frequency of bathing (OR=0.43(95%CI =0.24,0.80)) were significantly associated with ovarian cancer. Nulliparity (OR=9.32(95%CI=2.32,37.39) and chronic disease (OR=14.02(95% CI=3.10, 63.39)) were also significant risk factors for ovarian cancer. Conclusion Women in Pakistan, especially those in the low socio-economic level, need to be education on ovarian cancer and the related risk factors.

Keywords Ovarian Cancer, Lifestyle, Reproductive factors.

INTRODUCTION

Ovarian cancer is a group of diseases that originate in the ovaries, or in the related areas of the fallopian tubes and the peritoneum (Centre for Disease Control and Prevention). According to the American Institute for Cancer Research report, globally, ovarian cancer accounted for 3.6% of all forms of cancers and is the eighth leading cause of death among women (Merritt et al., 2018). It is said that less than 50% of ovarian cancer patients survive more than 5 years (Kathawala et al., 2018) And the high mortality is due to late diagnosis and resistance to treatment (Carollo et al., 2019; Nunes et al., 2019). It has been reported that 4 out of 5 ovarian cancer patients are diagnosed at advanced disease stage (Howlader at al, 2019). Ovarian cancer is a silent killer and since there is no screening test for ovarian cancer, the cases are often diagnosed at late stage and the recurrence is high (Stewart et al, 2019).

As the aetiology of ovarian cancer cannot be defined by a single mechanism (Terry & Missmer, 2017), understanding the associated risk factors is important (Webb & Jordan, 2017). Better understanding of root cause or risk factors can help in taking precautionary measures to prevent the incidence of ovarian cancer (Webb and Jordan, 2017) among the women. Evidence shows that eliminating or decreasing the effect of the associated risk factors can prevent ovarian cancer (Bray et al., 2018). For example, researchers agree that lifestyle modifications can minimize ovarian cancer burden (Song & Giovannucci, 2016).

Classification of socioeconomic status (SES) is often based on an individual's income, education and occupation. Lower SES has been shown to be associated with an increased likelihood of cancer and

late-stage diagnosis in many studies (Karpinskyj et,al, 2020). However, there have been no consensus with regards to ovarian cancer. Obesity and family history of breast cancer have been identified as the major risk factors for ovarian cancer (Schildkraut et al., 2019) and inadequacy of physical activity seem to increase the chances of ovarian cancer (Abbott et al., 2016). A study in England identified the use of talcum powder in the genital areas as a risk factor for ovarian cancer (Gabriel et al., 2019). A similar finding was reported by Rosenblatt et al (2011) in a study in the state of Washington in the United States. In a Canadian study, increased parity seemed to reduce the changes of ovarian cancer (Koushik et al., 2017). A study in the American population associated the use of oral contraceptive and family history with ovarian cancer (Harris et al. 2017). In a study in China, Lee et al. (2013) showed that consumption of green tea as a risk factor for ovarian cancer. Other factors linked to ovarian cancer include infertility (Rasmussen et al., 2017), miscarriages (Moorman et al., 2016) and age at menopause (Schildkraut et al., 2001). Modifiable risk factors include health behaviours and lifestyle factors.

The occurrence, prevalence, and mortality of ovarian cancer vary across different parts of the world, probably due to differences in genetic profile and the environment. (Coburn et al., 2017). A better understanding of ovarian cancer, the associated risk factors, in a specific geographical location will improve the awareness among women in a geographical location. This will help to reduce incidence of ovarian cancer, increase survival rate, reduce death and improve quality of life, particularly among those who are at high risk (Ali, 2018)

The incidence of ovarian cancer is high in developing countries like Pakistan (Zahra et al.,2013). In Pakistan, the incidence and mortality rate of ovarian cancer is 5.9 and 4.6, respectively (World Health Organization, 2018).The objective of this study is to determine the sociodemographic, lifestyle and reproductive factors associated with ovarian cancer among married women in Pakistan.

MATERIALS And METHODS

Study Setting

A case-control study was conducted in the states of Punjab and Sindh in Pakistan. For this study one cancer hospital was selected in each state and ovarian cancer patients aged 18 to 65 who were registered in the selected cancer hospitals were considered as the cases. Those who have been diagnosed with other types of cancer and those who were cognitively impaired were excluded in this study. The controls were recruited from the outpatients visiting the cancer hospitals. Sample size calculation was based on the findings reported in previous studies in relation to ovarian cancer. In the calculation the G*Power software was used, setting the level of significance and power as 0.05 and 80%, respectively. The minimum required sample size was 387. The study was conducted from December 2019 to May 2021.

Study Instrument

In this study, a structured questionnaire was used. The questionnaire was designed to obtain information on socio demographic characteristics, lifestyle factors and reproductive health. This questionnaire was content validated by a panel of experts in this area. Prior to data collection, the questionnaire was pilot tested among 30 patients. The participants were briefed on the purpose of the study and written consents were obtained from all participants. Participants were told that they could choose not to continue with the study at any time point, without giving any reason. For the cases, selfreported anthropometric data were systematically cross-checked with corresponding entries in medical records and any discrepancy found was subsequently rectified.

Statistical Analysis

Data were analysed using IBM SPSS version 25 software. Qualitative variables were described as frequencies and percentages, while quantitative variables were described as medians, minimum and maximum. Chi-square and multivariate binary logistic regression analyses were used in testing the associations between the predictor variables and ovarian cancer. The variables that are significant at 0.25 level in the Chi-square tests were included in the multivariate analysis. Finally, the stepwise analysis was used to determine the significant predictors of ovarian cancer.

Ethical Consideration

The study protocol was approved by the Human Research Ethics Committee of relevant hospitals. Ethical approval was obtained from the Institute Of Nuclear Medicine & Oncology (INMOL) Lahore established by Pakistan Atomic Energy Commission (PAEC) and Chandka Medical College Hospital Larkana. Consent was obtained from the participants.

RESULTS

There were 419 respondents in this study, 214 cases and 205 controls. The demographic characteristics of the respondents by group are shown in Table 1. There was no significant difference in age of the women in the two groups. In terms of BMI, the cancer patients were heavier compared to those in the control group. Majority of the patients resided in rural areas (75.2%), did not have formal education(50.0%), were not employed(89.3%), were from low socioeconomic status(84.6%) and did not live near industries(96.3%). As shown in table 2, 78% of the women with ovarian cancer had the habit of holding urine, and at least 50% of them had only one bath a day or none at all. Consumption of green tea was low in both groups. More women with ovarian cancer had nulliparity compared to those in the control group (Table 3).

Table 1 Demographic characteristics of cases and controls

| Variable | Case | Control | p-value |
|-----------------------------|------------------|------------------|---------|
| | Frequency (%) | Frequency (%) | |
| Residence | | | |
| Urban | 53(24.8%) | 95(46.3%) | 0.000 |
| Rural | 161(75.2%) | 110(53.7%) | |
| Education | | | |
| None | 107(50.0%) | 77(37.6%) | 0.000 |
| Some school College | 58(27.1%) | 31(15.1%) | |
| | 49(22.9%) | 97(47.3%) | |
| Occupation – self | | | |
| None | 191(89.3%) | 134(65.4%) | 0.000 |
| Government | 10(4.7%) | 20(9.8%) | |
| Private | 13(6.1%) | 51(24.9%) | |
| Occupation – Head of family | | | |
| None | 33(15.4%) | 13(6.3%) | 0.006 |
| Government Private | 7(3.3%) | 13(6.3%) | |
| | 174(81.3%) | 179(87.3%) | |
| Socio-economic Status | | | |
| Low | 181(84.6%) | 21(10.2%) | 0.000 |
| Middle | 25(11.7%) | 180(87.8%) | |
| High | 8(3.7%) | 4(2.0%) | |
| Residence near Industries | | | |
| Yes | 8(3.7%) | 66(32.2%) | 0.000 |
| No | 206(96.3%) | 139(67.8%) | |
| Chronic Disease | | | |
| Yes | 24(13.8%) | 8(4.3%) | 0.002 |
| No | 150(86.2%) | 176(95.7%) | |
| Age | 36(20, 67)* | 36(19, 66)* | 0.631 |
| BMI | 27.0(17.1,49.8)* | 25.9(18.2,45.0)* | 0.014 |

*Median(min, max)

Table 2 Lifestyle characteristics of cases and controls

| Variable | Case | Control | p-value |
|----------|---------------|---------------|---------|
| | Frequency (%) | Frequency (%) | |

| Telcom power use | | | |
|-------------------------|------------|------------|--------|
| Yes | 22(12.6%) | 13(7.1%) | 0.046 |
| No | 152(87.4%) | 171(92.9%) | |
| Holding urine | | | |
| Yes | 136(78.2%) | 19(10.3%) | <0.001 |
| No | 38(21.8%) | 165(89.7 | |
| Tea Consumption | | | |
| Green Tea | 3(1.7%) | 23(12.7%) | <0.001 |
| Milk Tea | 160(92.0%) | 146(80.7%) | |
| No Теа | 11(6.3%) | 12(6.6%) | |
| Number of baths per day | 1(0,3)* | 2(0,3)* | <0.001 |

*Median(min, max)

Table 3 Reproductive characteristics of cases and controls

| Variable | Case | Control | p-value |
|---------------------|---------------|---------------|---------|
| | Frequency (%) | Frequency (%) | |
| Nulliparity | | | |
| Yes | 37(26.1%) | 10(5.5%) | <0.001 |
| No | 105(73.9%) | 173(94.5%) | |
| Fertility treatment | | | |
| Yes | 69(45.1%) | 46(29.6%) | 0.547 |
| No | 84(54.9%) | 125(73.1%) | |
| Parity | 3(0,10)* | 3(0,10)* | 0.201 |
| Age at menarche | 11(10,14)* | 11(9,14)* | 0.547 |
| Menstruation cycle | 7(3,8)* | 7(3,8)* | 0.964 |

*Median(min, max)

Results from logistic regression analyses

Among the demographic variables, all except age, were significant at 0.25 level. However, in multivariate logistic regression analysis only occupation, socio-economic status and chronic diseases were significant. Among the lifestyle factors, use of telcom powder, holding urine, number of times bathed per day and tea consumption were significant. Among the reproductive factors, parity and nulliparity were significantly associated with ovarian cancer. Occupation, socio-economic status, chronic disease, use of telcom powder, holding urine, number of times bathed per day, tea consumption, parity and nulliparity were then tested in multivariate analysis. The results are shown in table 4.

All the variables that were significant at 0.25 level in the univariate analyses were tested in multivariate logistics regression analysis. The results are shown in Table 4. Among the demographic variables, only occupation, socio-economic status, chronic diseases were significant. Among the lifestyle factors only use of telcom powder, holding urine, number of times bathed per day were significant and among the reproductive factors only nulliparity was significantly associated with ovarian cancer. In stepwise analysis, only socio-economic status, chronic disease, use of telcom powder, number of times bathed per day, holding urine and nulliparity were significantly associated with ovarian cancer (Table 4).

The odds of ovarian cancer in the low socio-economic group was higher compared to that of the middle/high class. The odds of ovarian cancer was higher among those with nulliparity, had chronic diseases, used talcum powder and had the habit of holding urine. The odds of ovarian cancer decreased with increasing frequency of baths per day.

| Variables | Multivariate | | Stepwise analysis | |
|----------------------------|----------------------|--------|---------------------|--------|
| | AOR (95% CI) | Р | AOR (95% CI) | Р |
| Occupation: self | | 0.014 | | |
| None | 2.86(0.57, 14.97) | 0.201 | | |
| Government | 0.32(0.04, 2.74) | 0.297 | | |
| Private | 1 | | | |
| Occupation: head of family | | 0.503 | | |
| None | 0.94(0.19, 4.69) | 0.938 | | |
| Government | 3.05(0.47, 19.72) | 0.242 | | |
| Private | 1 | | | |
| Socio-economic status | | | | |
| Low | 36.70(10.80, 124.71) | <0.001 | 26.98 (9.74, 74.75) | <0.001 |
| Middle/High | 1 | | | |
| Nulliparity | | | | |

Table 4 Results from multivariate and stepwiselogistic regression

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| Yes | 9.83(2.22, 62.40) | 0.004 | 9.32 (2.32, 37.39) | 0.002 |
|----------------------|-----------------------|--------|---------------------|--------|
| No | 1 | | 1 | |
| Tea Consumption | | 0.833 | | |
| Green Tea | 0.39(0.02, 8.81) | 0.550 | | |
| Milk Tea | 0.55 (0.05, 6.18) | 0.631 | | |
| No Tea | 1 | | | |
| Chronic Disease | | | | |
| Yes | 11.78(2.22, 62.40) | 0.004 | 14.02(3.10, 63.39) | 0.001 |
| No | 1 | | 1 | |
| Use of Talcum powder | | | | |
| Yes | 5.05(1.15, 22.11) | 0.032 | 14.05 (3.53, 55.97) | <0.001 |
| No | 1 | | 1 | |
| Holding Urine | | | | |
| Yes | 35.71 (11.63, 111.11) | <0.001 | 21.74(8.00, 58.82) | <0.001 |
| No | | | | |
| No of Baths a day | 0.49(0.25, 0.97) | 0.041 | 0.43 (0.24, 0.80) | 0.007 |
| Parity | 1.28(0.910, 1.80) | 0.155 | | |
| | | | | |

AQR = Adjusted Odds ratio

DISCUSSION

In this study, lower socio-economic status was highly associated with ovarian cancer, even though there has been no consensus on this association in literature. Possibly, women with low level of education may not have adequate knowledge on ovarian cancer and the associated risk factors. Women who are not working or have low income may not be able seek help in early stages of the disease. Our study findings show a strong association between chronic diseases and ovarian cancer. On possible reason for this could be that chronic diseases may weaken immunity among the women and hence make them more vulnerable. Findings in this study show that use of talcum powder as a risk factor for ovarian cancer. This finding is similar to that of a recent study in England by Gabriel et al (2019). The authors suggested that the combination of talc use and store-bought may modestly increase the risk for ovarian cancer.

In this study, a total of 174 participants (136 cases and 38 controls) had the habit of holding urine. One possible reason could be the scarcity of toilets, as is the case in many underdeveloped countries. As hypothesized by Smith et al (2014) metabolic activity may increase in tandem with the progression of malignancy. A similar finding was reported by Rosenblatt et al (2011) in a study in the state of Washington in the United States. Our findings show that the odds of ovarian cancer decreases with more frequent baths. We hypothesize that this could be associated with cleanliness of the women's perianal area.

Based on our study findings, nulliparous women are at higher risk of ovarian cancer compared to the porous one. This finding is in line with that reported by Xu et al. (2020) that nulliparous women and women with early menopause were at risk.

As this study was conducted at only two hospitals, the generalizability of the findings across Pakistan may not be plausible. In data collection a questionnaire was used. As in all studies using questionnaire, whether the participants answered the questions honestly or not cannot be ascertained. As this study was conducted during the covid pandemic amidst lockdowns, we could not achieve the required sample size. However, in the post hoc power analysis, the power for each one of the significant predictor variables was more than 90%.

CONCLUSION

In this study, the associations between several demographic characteristics, lifestyle factors and reproductive factors were explored. Among the demographic characteristics only low socio-economic status was significantly associated with ovarian cancer. As level of education is one of the components in determining socio-economic status, the women with low or no education seem to be at high risk. These women need to be educated so that

they will be well informed about the disease and the risk factors. Educating the women of preventable risk factors such as the use of telcom power, habit of holding urine and infrequent bathing will help in minimizing the incidence of ovarian cancer. Nulliparous women and those with chronic diseases must take extra precautions in preventing ovarian cancer. For future studies, we recommend a multicentred study, covering the whole country and considering clinical data as well.

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