Risk Factors for Ovarian Cancer among Libyan Women

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Abstract

Ovarian cancer is the third type of gynecologic cancer in terms of prevalence after cervical and uterine cancer. The disease is known as the silent killer as it is slowly spread without a diagnosis, which leads to the worst prognosis and high mortality rate. Libya shows low disease incidence while the high mortality rate is seen in developed countries due to a lack of proper diagnostic and treatment options. This research aims to understand the various risk factors of ovarian cancer among the women in Libya. A questionnaire is used in a quantitative research methodology using stratified random sample over the population is divided in two classes namely healthy and diseased, based on earlier diagnosis and ovarian cancer care. The diseased and healthy women were targeted in a written survey in different hospitals and clinics in Libya. The data analysis is done in four stages. The first stage is cleaning and coding of the data. The second step is the demographic profile of the respondents. The third stage. Frequency distribution of the data in order to compare the healthy and diseased women. The fourth stage is the linear logistic regression in order to determine the risk factors for ovarian cancer and test the research hypotheses. The logistic regression analysis indicated good fit of the model. The model was able to correctly predicted 81.4 % of the cases which is 19.6 % increase over the null model. The logistic regression analysis was also used to indicate the predictors namely family history, level of obesity, ovulation information, use of birth control and breast feeding unlike awareness, nature of diet which was not predictor in the model.

Keywords: *Ovarian cancer, Risk factors, Binary logistic regression, Libya.*

Introduction

Ovarian cancer is the fifth leading cause of death from cancer in women aged 35-74. An approximate one in 78 women would develop ovarian cancer in the course of their lifetime. The American Cancer Society predicts there will be about 22,280 additional ovarian cancer cases diagnosed by the year 2020, and more than 14,240 people will die from ovarian cancer. The five-year survival rate is over 90 percent when women are diagnosed and treated in the early stages. Owing to the non-specific signs of ovarian cancer and the lack of early detection testing, about 20 percent of all cases are detected early, either in stage I or II. The survival rate may be as low as 28 percent if caught in stage III or higher. Each woman diagnosed with ovarian cancer has a different profile due to the nature of the disease, so it is difficult to provide a general prognosis[1].

In Libya, the number of cancer cases increased from 12.7 in 2008, to 14.9 million in 2012[2]. According to[3], the significant cases are of breast cancer, representing 11.7 % of the cases. The number of cases in 2019 reached 6308, and the number of death due to cancer is 3375. It is significantly important to understand cancer types, distribution, and risk factors in order to provide insights to protect communities and individuals. Ovarian cancer is one of the most severe types of cancer. The primary issue of ovarian cancer is that it is considered a silent disease as early detection is viewed as a challenge. This is the reason many types of research try to examine the risk factors in order to help make the early association of the disease in susceptible individuals. In this research,

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we aim to provide a quantitative approach in order to generalize an understanding of the risk factors of ovarian cancer in women in Libya.

According to[4], Ovarian cancer is considered the seventh most commonly diagnosed cancer among women worldwide. In Libya, ovarian cancer accounts for 4.6% of cancer affecting women, according to the International Agency for Research on Cancer, 2018. may risk factors are associated with ovarian cancer, such as obesity, use of fertility medication, long ovulation cycles throughout life due to lack of children. Some elements showed to reduce the risk of ovarian cancer, such as breastfeeding, pregnancy, and the use of oral contraceptives[5]. The majority of the cases is related to family history through inheritance of mutated autosomal dominant gene [6].

Ovarian cancer is considered one of the most types of cancers affecting women in the world. The incidence of ovarian cancer increased to reach 4.6 % in 2018. The disease does not show symptoms in the early stage, but it becomes symptomatic when it has already spread to other parts of the body. Screening for the condition is not practical due to false-positive, which may lead to unnecessary surgical procedures. Understanding the risk factors is essential to help educate the women community about the risk factors and preventive measures in order to reduce the incidence of the disease and get an earlier diagnosis to provide a better prognosis. The research aims to use logistic regression analysis in order to test the goodness fit of the model and test the research hypotheses to determine which variables are significant predictors as risk factor for ovarian cancer among women in Libya. The research aims to answer the question of: What is the effect of various risk factors for ovarian cancer in women in Libya?. The research study is vital to healthcare workers, doctors, and pharmaceutical companies, and women who are concerned about ovarian cancer. Among the risk factors examined in the study are awareness, obesity, nature of the diet, ovulation information such as the age of menarche and age of menopause, pregnancy, breastfeeding, use of oral contraceptives, and family history. Scholars have controversial opinions about these risk factors and associations with ovarian cancer.

Literature Review: The research is based on four theories that explain the development of cancer in the body which are Incessant ovulation, Gonadotrophin theory, hormonal theory and inflammation Theory. The theories provide a theoretical background on which the research is used to identify the risk factors included in the model framework of the research.

The socioeconomic status has an indirect effect on the diagnosis and prognosis of ovarian cancer. The high social and economic situation is related to increased patient awareness of symptoms, lifestyle, time of response to symptoms, and health care access to the diagnostic and treatment facilities. The increased patient awareness is an essential factor as it plays a role in early diagnosis through regular medical check-ups. Some studies indicated that increased awareness reduces the risk of the development of ovarian cancer[7,8]. Hence, this research postulate that first hypothesis.

H1: Patient awareness has a negative association with the risk of developing ovarian cancer in women in Libya.

The history of the family is the most significant risk factor in ovarian cancer growth. The ovarian cancer case is genetically modified in 5-10 % of cases. The explanation is that genetic variation and chromosome abnormalities were associated with an increased incidence of ovarian cancer. The hypothesis is supported by many types of research such as [5,9–14]. Hence the second research hypothesis is formulated:

H2: Family History has a positive association with the risk of developing ovarian cancer in women in Libya.

Obesity is generally harmful to the general health of the body. The risk of developing many conditions would be that a person is overweight[15]. The effect of obesity is no exception with respect to ovarian cancer. Many reports have demonstrated elevated ovarian cancer mortality in obese individuals[16,17]. Numerous signs for obesity, Body mass index (BMI), and a waist-hip ratio are reported as studies' metrics [18]. In this study the BMI will be used as indication of obesity. Hence the first research hypothesis is formulated.

H3: Obesity has a positive association with the risk of developing ovarian cancer in women in Libya.

Diet and nutrition are essential factors in personal lifestyles that have a significant impact on individuals' overall health. In addition, diets and nutrition are controversial findings in the studies in a similar way to all risks associated with ovarian cancer. In many diseases, including ovarian cancer, food is considered to be a key factor[19].

The link between diet and ovarian cancer development is determined through ecological studies, in which the correlation between the two variables is determined. The nature of food is a significant contributor to ovarian cancer. Bosetti and Edefonti et al. have reported that some of the foods are associated with an increased chance of ovarian cancer, such as meat and certain fats. A reduced risk of ovarian cancer[9,20–22] has been associated with some micronutrients (vitamins and minerals) as well. The number of carbohydrates in the diet also affects the risk of ovarian cancer developing.

In Libya, the diet is a Mediterranean diet, which is one of the guidelines for the reduction of blood glucose and blood pressure [23]. The Mediterranean Diets Program demonstrate increased consumption of foods rich in long-chain n-3 fatty acids and monosaturated fats, mostly present in olive oil[6,9,20]. Hence the second research hypothesis is formulated.

H4: The nature of diet has a positive association with the risk of developing ovarian cancer in women in Libya.

Some of the ovarian cancer risk facts are linked to ovulation time during women's lives. The longer the period of ovulation, the higher the incidence of ovarian cancer. In the absence of children and in pregnancy and breastfeeding,ovulation duration will continue as an ovulation break during pregnancy and sometimes lactation. The risk of developing ovarian cancer is doubled by not having children[5].Other investigators, including[24,25], indicate that the longer the ovulation period for women is, the higher the likelihood of ovarian cancer. Early menstruation and late menopause can extend the ovulation period [24,25].Hence the third research hypothesis is formulated:

H5: Ovulation information has a positive association with the risk of developing ovarian cancer in women in Libya.

The role of oral contraceptives in reducing the risk of ovarian cancer is established in the literature. Many studies support this postulation, such as[26–28] The study also indicated that with each year's use of oral contraceptive pills by 7%[26]. The length of use of oral contraceptives is also an essential factor, and The reduced risk can continue for up to 10–15 years after the cessation of pills[27,29]. Hence, the research postulates the following hypothesis.

H6: The use of hormonal birth control has a negative association with the risk of developing ovarian cancer in women in Libya.

The relationship between breastfeeding and ovarian cancer development is inverse. Luan et al. report that with every five months of breast-feeding, the risk of ovarian cancer decreases by 8 percent[6,9,20,24]. Period of lactation, the number of children, and the risk of ovary cancer is in reverse type[30]. The analysis found that the risk of ovarian cancer was reduced by 22 percent for lactation and lactation, an average of 18 months, according to[31]. Hence the fifth research hypothesis is formulated:

H7: Breastfeeding has a negative association with the risk of developing ovarian cancer in women in Libya.

Methodology

In this study, we aim to investigate the risk factors for ovarian cancer using a quantitative research approach through a survey. The population of the study is the women in Libya between the age of 25 and above. The choice of sampling is Stratified sampling, in which the population is divided into two subgroups, in this research, positive ovarian cancer patients and negative ovarian cancer patients. The sample size is determined to be 196 in total of both healthy and diseased women. The research use questionnaire adapted from [6,32,33] with modification and translation to Arabic language as a mother tongue for people in Libya. The data analysis process is done through frequency distribution comparison between healthy and diseased women and logistic regression analysis. The research framework is demonstrated in figure 1.

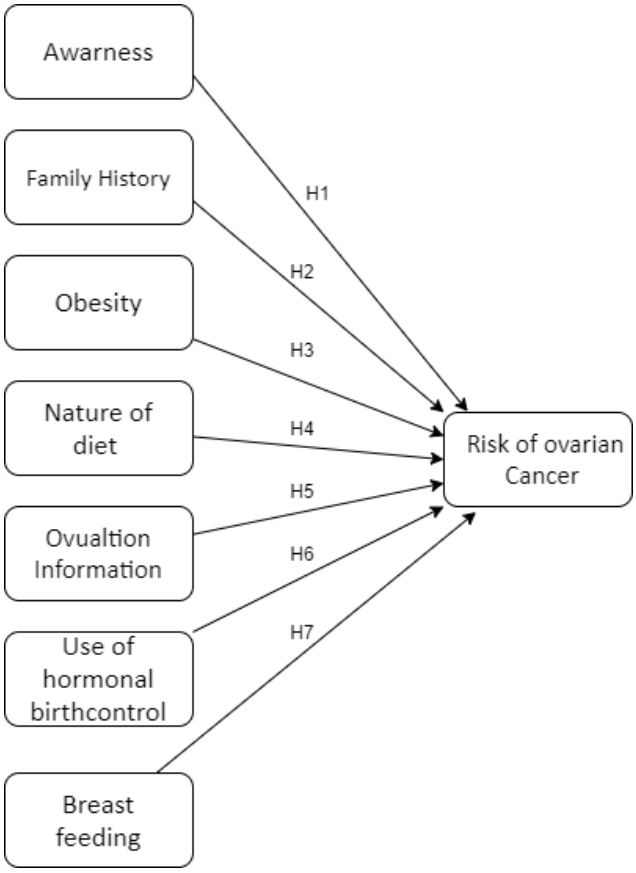

Figure 1: Research framework of ovarian cancer risk factors

The diseased women were targeted in various hospitals and clinics in Libya through a written survey. The healthy women were targeted using a written survey in the same hospitals and clinics. Ovarian cancer indicates in Libya is low. Hence the reverse faced some difficulties in reaching a large number of diseased women, and only 85 surveys were collected. In the case of healthy women, the collected survey was 139 written surveys. After filtering, the number of surveys in diseased women was 73 and for healthy women was 123 hence the total responses were 199. The data is collected from the different location all over Libya, an example of the area are Alagelaat, Benghazi, Misrata, Sabratah, Sorman, Tripoli, Zawiyah and Zealten.

Data Analysis and Results

As the survey was collected through written forms, data cleaning, and data entry was a long process during the data cleaning process BMI was manually calculated for the data as the majority of the patients do not know how to calculate it.. The questionnaire has a number of open-ended questions and a number of questions that have dichotomous categorical variables Frequency distribution of the data in order to compare the healthy and diseased women. and the linear logistic regression is used in order to determine the risk factors for ovarian cancer and test the research hypotheses. The result o the percentage distribution of questionnaire comparing healthy and diseased women is demonstrated in table 1:

For the logistic regression analysis, The First assumption is for the dependent variable to be binary on a dichotomous scale. The Second assumption required for logistic regression is for the observations to be independent of each other, this assumption is met as indicate no relation to the recorded data or observation between the variable groups. In testing for the outliers This relation is examined through observation of the Mahalanobis distance. The result of the maximum Mahalanobis distance is 15.45 that the difference in the result among the most extreme score is 15.45, which is an acceptable variation in the scores indicate that they are no outliers among the group of women [34]. In terms of linearity, this assumption indicates a linear relationship between each of the dependent variables within each group of the independent variable. The linearity is tested through a scatterplot matrix[35].

Table 1 Percentage distribution in response to questionnaire comparing healthy and diseased women

Variable		Healthy	Diseased
(Dependent) Diagnosed ovarian cancer		123	
Awareness	Heard of ovarian cancer	70%	100%
	Read about ovarian cancer	33%	50%
	Regular check-ups	63%	63%

Variable		Healthy	Diseased
History	Ovarian cancer family history	5%	83%
	Breast cancer family history	10%%	68%
	Treated with ovarian cancer in the family	4%	59%
	Relationship	55% second degree relative 8% sister 4% mother	11% mother 7% sister
BMI	Underweight Normal Overweight Higher obese	0% 43% 53% 3%	1% 33% 42% 24%
Nature of diet	Fat and meat consumption	60% moderate 33% low	70% moderate 25% low
	Fruits and vegetable consumption	80% moderate 12% high	60% moderate 33% low
	Carbohydrate intake	65% moderate 30% low	51% moderate 24% low
	Olive oil consumption	51% moderate 38% low	66% moderate 17% low
Ovulation information	Age of menarche (between 12-15)	70%	87%
	Age of menopause (reached at 55)	11%	15%
	Number of pregnancies (up to four times)	30%	17%
	Have children	88%	87%
Use of hormonal birth control	Use of contrapositives	75%	24%
	Type of contraceptives	68% Birth Control Pills	13% Birth Control Pills
	Length of use	56% for one year or less 13.2% for 2 years	52% for one year or less 26% for 2 years 19% for 3 years
Breastfeeding	Breastfeeding (yes)	75%	55 %
	Length of Breastfeeding	74% one year or less 26 % for three years	76% one year or less 17 % for three years

After ensuring that the assumptions required for logistic regression analysis are met, the analysis is performed. The independent variables entered in the model are awareness, history, family history, level of obesity, nature of the diet, ovulation information, use of birth control, and breastfeeding. The resulting output from SPSS. In the null model, the correctly predicted 61.8%. Wald chi-square test, which is a test. The null hypothesis is rejected as the p-value is less than 0.05. The test is done at only 1 degree of freedom as there is only one predictor in the null model. The exponentiation of the B coefficient “Exp(B)” is the odds ratio, which is equal to 0.61, the result is indicated in table 2.

Table 2 Result of null model testing

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-.481	.146	10.889	1	.001	.618

The output of the model of the correctly predicted cases and not correctly predicted based on the model is demonstrated in table 3, compared to the observed cased. The table indicates that 106 cases are observed to have no ovarian cancer and are correctly predicted; 56 of the cases are observed to have ovarian cancer and are correctly predicted. While only 17 were predicted, get ovarian cancer and are wrongly predicted, and 20 were predicted not to get ovarian cancer and were wrongly predicted. The Overall Percentage gives the overall percentage of correctly predicted cases by the model; this model demonstrates 81.4% correct prediction of the model, which is a significant improvement over the null model by 19.6%.

Table 3 Overall predicted percentage of the model

	Observed		Predicted		
			Diagnosed ovarian cancer		Percentage Correct
			No	Yes	
Step 1	Diagnosed ovarian cancer	No	106	17	86.2
		Yes	20	56	73.7
	Overall Percentage				81.4
a. The cut value is .500					

The Hosmer-Lemeshow tests are used to test the null hypothesis for the predictions made by the model fit. The nonsignificant chi-square indicated by the p-value is more significant than 0.05, which indicates a good fitness of the model. The results are indicated in table 4.

Table 4Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	15.883	8	.064

The logistic regression model is used to predict which of the variables provide a statistically significant result. This is used through observation of the Wald chi-square value and p-value used. The overall result is that the logistic regression was used to understand the effect of awareness, family history, level of obesity, nature of the diet, ovulation information, use of birth control, and breastfeeding as risk factors for ovarian cancer in Libya. The results indicated that the logistic regression model was statistically significant, $\chi 2(7) = 85.9$, $p < .0005$. The model predicts 81.4 % of the total variance, which is a 19.6% increase over the null model. The result indicated that Body mass index (BMI), family history, breastfeeding, ovulation information, and use of hormonal birth control all have p values less than 0.05. Hence they are statistically significant predictors for the model. While the awareness and diet have a p-value of more than 0.05 are not statistically significant. Breastfeeding is a significant predictor; an increased breastfeeding period is 2.8 more likely to prevent ovarian cancer. Family history is the second-highest predictor; the result indicates that women with a positive family history are 2.1 more likely to get ovarian cancer. BMI is also a significant predictor; as a result, indicated that women with high BMI are 2 times more likely to develop ovarian cancer. Decreased use of birth control indicates a high probability of developing ovarian cancer, also increase in the ovulation information such as early age of period and late age of menopause, decreased number of pregnancies and children is more likely to develop ovarian cancer. Decreased use of hormonal birth control will increase the chance of ovarian cancer. The result is demonstrated in table 6.

Table 6 Variables in the model

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP (B)	
								Lower	Upper
Step 1[a]	BMIrange	.700	.320	4.780	1	.029	2.015	1.075	3.775
	AWAR	.059	.199	.088	1	.766	1.061	.718	1.567
	HISTO	.722	.232	9.680	1	.002	2.059	1.306	3.245
	FEEDING	-1.026	.164	39.070	1	.000	2.791	2.023	3.850
	OVUL	-.332	.140	5.611	1	.018	.718	.545	.944
	BIRTH	-.800	.126	40.559	1	.000	.450	.351	.575
	DIET	.144	.153	.891	1	.345	1.155	.856	1.559
	Constant	-2.368	1.478	2.568	1	.109	.094		
a. Variable(s) entered on step 1: BMI range, AWAR, HISTO, FEEDING, OVUL, BIRTH, DIET.									

Discussion

The majority of diseased women were between the ages of 41-60. (70% of the respondents). This finding supports the idea that ovarian cancer is an age-related disease that usually occurs after menopause as indicated in the study by[36,37], which demonstrated ovarian cancer incidence is more common in women around the age of 60 years of age and other studies by[38,39], it indicates that the average range of diagnosis of ovarian cancer among women is between 50 to 79 years

Awareness as a risk factor for ovarian cancer: The level of awareness is relatively low among both the diseased and the healthy women, as a result, indicated that only 50% of the diseased and 33% of the healthy women read about ovarian cancer. Both healthy and diseased women receive regular check-ups, which may be explained by the high level of education demonstrated in the demographic profile of the respondents.

The result of the logistic regression analysis indicated that awareness was not a predictor in the proposed model for risk factors. The result shows different findings in comparison to other studies by[7,8,32], which indicated increased patient awareness of symptoms, lifestyle, time of response to symptoms, and health care access to the diagnostic and treatment facilities.

Family history of ovarian cancer as a risk factor: The questionnaire of the healthy and diseased women indicated that the majority of diseased women have relatives that had either ovarian cancer or breast cancer. The result indicated a close association between family history and the risk of developing ovarian cancer. These findings were supported by the logistic regression analysis, which indicated that family history is a predictor for ovarian cancer. The result indicated that Family history is the second-highest predictor; the result indicates that women with a positive family history are 2.1 more likely to get ovarian cancer. The findings of the study are similar to the findings of[5,9–14].

Level of obesity as risk factor for ovarian cancer: The BMI is a good and acceptable indication that can easily be calculated based on the height and weight data collected from the respondents. The result indicates that the diseased women are 68 % overweight and obese compared to only 56% of the healthy women. High percentage of healthy women fall in the normal wight which can be a result of high level of health awareness. Additionally, the result of the logistic regression indicated that BMI is a significant predictor as increased value of BMI among women is 2 times more likely to develop ovarian cancer. The result supports the findings of[16,40,41].

Nature of diet as risk factor for ovarian cancer: The result indicated that diseased women demonstrated high fat and meat consumption and diseased consumption of fruits and vegetables compared to healthy women. Although diseased women indicated high consumption of olive oil compared to healthy women. The result of logistic linear regression indicated that nature of diet is not a significant predictor for the risk factor model proposed in the study. The result is similar to other studies that have examined the role of diet in ovarian cancer which indicate that a complete connection is not established, and it is suggested that the diet does not

have a major impact on the incidence of ovarian cancer occurrence[6].

Ovulation information as risk factor for ovarian cancer: The ovulation information considered in this research are the age of period, age of menopause, number of pregnancies, and number of children. The result indicated that diseased women research puberty earlier than healthy women, the age rage described in the age profile indicate that the majority of respondent were between age of 40-60 which is an early age of menopause. This explain that a small percentage of the sample reached menopause. In relation to the number of pregnancies, diseased women showed decreased in this number in comparison to healthy women. Similar result in relation to the number of children which showed that diseased women had higher percentage of not having children in relation to healthy women. The result of logistic regression indicates that ovulation information is a significant predictor for risk of development of ovarian cancer. The findings is similar to findings discussed in the previous studies as the association between the number of ovulation cycles and the risk of development of ovarian cancer is indicated in[17,42].

Use of hormonal birth control as risk factor for ovarian cancer: The result indicated that the majority of healthy women used contraceptives in comparison to diseased women. The healthy women used birth control pill more than the diseased women, although the length of use was similar in both groups. The result of the logistic regression indicated that use of hormonal birth control is among the predictor variables for the development of ovarian cancer which is indicated as a risk factor. The result indicated that decreased use of birth control indicates high probability of developing ovarian cancer. The findings of the study are similar to findings discussed in the literature. such as[26–28].

Breast feeding. as risk factor for ovarian cancer: The majority of healthy women indicated natural breast feeding and for longer period in comparison to diseased women. the result of logistic regression indicated that breastfeeding is a significant predictor, increased period of breast feeding is 2.8 more likely to prevent ovarian cancer. The findings of the study is similar to findings of other studies such as .[6,24].

Conclusion

This research aimed to understand the risk factors associated with ovarian cancer with focus on the women in Libya. Menarche and menopause, menstrual factors, age at birth. Ovulation information progresses are some of the most important risk factors described by many scholars. While a decreased number of ovulation cycles are generally believed to be associated with low risk based on theory of incessant ovulation.

Family history is the key risk factor in ovarian cancer development. Factors such as obesity is considered a huge risk factor for ovarian cancer. Other factors included in the study include ovarian cancer awareness, the use of hormonal birth control.

The field for future research in the area of risk factors associated with ovarian cancer is filled with many possibilities and topics for the research in order to understand the nature of risk factors for ovarian cancer which many be associated with prevention or easily diagnosis that led to decrease the mortality rate from ovarian cancer. In this research, it was limited to only Libya, other countries in the Mediterranean region should be included in order to completely reject or accept the hypotheses that postulate the relation between ovarian cancer and diet especially the Mediterranean diet. Future research should also consider the association with socioeconomical factors which may lead to increased awareness which helps with early detection and better prognosis of the diseased. The duration of Breast feeding and duration of use of hormonal birth control need additional focus in future research. Other Factors should be included such as the use of fertility medicine or assassination with other drugs. The study was done on a cross-section setting, longitude studies is recommended especially for this type of cancer as it is an age related and it takes time to develop.

Ethical Clearance: The study was conducted in accordance with the ethical standards of College of Medical Technology, Al-Zawiya University, Libya,

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