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The Prevalence of Positive Family History of Malignancy Among Patients with Gynecologic Cancers in the Kingdom of Bahrain: A Retrospective Cross-sectional Study

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Abstract

Introduction: The most common gynecologic cancers are cervical, endometrial and ovarian. Endometrial and ovarian cancer are known to be associated with family history of malignancy. This study aims to explore the prevalence of positive family history of malignancy among patients with different gynecologic cancers in the Kingdom of Bahrain.

Methods: A retrospective cross-sectional study reviewing the family history of malignancy of all gynecologic oncology cases following up in King Hamad University Hospital (KHUH) and Bahrain Oncology Center (BOC) over 5 years, from 2016 until 2020.

Results: A total of 216 women with various types of gynecologic cancer, were included. The most prevalent cancer was endometrial (50.5%), followed by ovarian and cervical cancers. 52 cases (24.1%) had a positive family history of different types of cancers (p=0.2), and 20 patients (9.3%) had a positive family history of breast cancer (p=0.02).

Conclusion: Family history is an important risk factor especially in endometrial and ovarian cancer. Accordingly, determining the family history of malignancy can help guide screening of gynecologic cancer thus attributing to early detection and better management.

Abbreviations: BOC: Bahrain Oncology Center; BRCA1: breast cancer gene 1; BRCA2: breast cancer gene 2; FHM: Family History of Malignancy; GC: Gynecologic Cancers; KHUH: King Hamad University Hospital.

Introduction

The three most common types of gynecologic cancer (GC) include cervical, endometrial and ovarian cancer [1]. Globally, cervical cancer is the fourth most common cancer following breast, colorectal, and lung cancer [2,3]. In fact, in low and middle-income countries, cervical cancer is the second most common cancer in women and the third most common cause of cancer mortality. This is attributed to the lack of well-established screening and vaccination programs [3,4]. The incidence of endometrial cancer is increasing with a lifetime risk of about 3% and this risk is higher in individuals with endometrial cancer in a first or second degree relative [5]. Those with a family history of endometrial cancer are also at an increased risk of developing Lynch Syndrome [6]. Ovarian cancer, sometimes referred to as a silent killer, is the seventh most common cancer in women and has the highest mortality rates amongst GC. The risk of ovarian cancer is observed to increase in women with a family history of breast, endometrial or ovarian cancer in a first-degree relative [7]. 20% of ovarian, fallopian tube and peritoneal cancers are hereditary; some are attributed to the presence of a mutation in the BRCA genes [8]. Other less common GC include vulvar and vaginal cancers [9].

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Table 1. Classification of Gynecologic Cancer Cases Based on Location (n=216)

Year	Vulva	Vagina	Cervix	Uterus	Ovary	Fallopian tubes	Peritoneum	Total
2016	-	-	5 (2.3%)	1 (0.5%)	3 (1.4%)	-	-	9 (4.2%)
2017	-	-	1 (0.5%)	6 (2.8%)	3 (1.4%)	-	-	10 (4.6%)
2018	-	-	9 (4.2%)	27 (12.5%)	7 (3.2%)	-	-	43 (19.9%)
2019	3 (1.4%)	-	9 (4.2%)	37 (17.1%)	27 (12.5%)	2 (0.9%)	1 (0.5%)	79 (36.6%)
2020	2 (0.9%)	1 (0.5%)	7 (3.2%)	38 (17.6%)	24 (11.1%)	3 (1.4%)	-	75 (34.7%)
Total	5 (2.3%)	1 (0.5%)	31 (14.4%)	109 (50.5%)	64(29.6%)	5 (2.3%)	1(0.5%)	216 (100%)

Table 2. Prevalence of Positive Family History of Malignancy According to Degrees of Relatives (n=52)

Degree of Relative	Cervix	Uterus	Ovary	Total
1st degree	2 (3.8%)	24 (46.2%)	11 (21.2%)	37 (71.2%)
2nd degree	3 (5.8%)	6 (11.5%)	2 (3.8%)	11 (21.2%)
3rd degree	-	1 (1.9%)	-	1 (1.9%)
Unknown	-	3 (5.8%)	-	
Total	5 (9.6%)	34 (65.4%)	13 (25%)	52 (100%)

Gynecologic cancers (GC) are mostly preventable with effective screening and lifestyle changes. There are diverse findings as to whether there is a relationship between family history of malignancy (FHM) and cancer screening behavior. Identifying patients with known risk factors, including FHM, can possibly reduce morbidity and mortality associated with GC [1]. There are multiple prediction models designed to determine the risk of developing GC including Pfeiffer, BOADICEA and MMRpro. These models take into consideration the FHM. Family history does not play a major role in the etiology of cervical cancer; however, more extensive screening and vaccination programs have improved detection rates [10].

This study aims to determine whether there is a relationship between the prevalence of GC and the presence of positive FHM. This is the first study in the Kingdom of Bahrain to explore this. Establishing the prevalence of positive FHM in patients with GC can help guide screening to facilitate early detection and treatment to hopefully reduce the rate of progression of cancer.

Methods

We conducted a retrospective cross-sectional study in both King Hamad University Hospital (KHUH) and Bahrain Oncology Center (BOC) from 2016 until 2020. We included all gynecologic oncology cases following up in those two centers during these five years. The gynecologic cancer types evaluated in this study include vulvar, vaginal, cervical, uterine and ovarian cancer. Patients with a known gynecologic cancer are included on the basis of a histologically confirmed biopsy. The patients' medical records have been reviewed in retrospect in search for the presence of family history of malignancy including the relation to the patient and what type of cancer their family members have been diagnosed with.

Statistical analysis was performed with GraphPad Prism (Refer to version 9.3.0). Data was tabulated and represented by percentages. Fisher's exact test was used to determine a relationship between the prevalence of the various types of gynecologic cancers and the presence of family history of malignancy in those patients. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 216 cases were included in our study. Table 1 demonstrates the distribution of GC cases following up in KHUH and BOC throughout the five years. The majority of cases (71.3%) were recorded in 2019 and 2020 (Table 1). Almost half of the GC cases were endometrial (50.5%). The second most common cancer was ovarian (29.6%) followed by cervical (14.4%). Vulvar, vaginal, fallopian tube and peritoneal cancers were less common (Table 1).

52 (24.1%) patients had a positive FHM of various types of cancer, shown on Table 2. Almost one-third of patients with endometrial cancer had FHM. About half of those had a positive family history of breast cancer, a quarter had a positive family history of endometrial cancer and the remaining had positive family history of lung and gastro-intestinal cancer among others. 20.3% of patients with ovarian cancer and 16.1% of patients with cervical cancer had FHM. We did not find a statistically significant relationship between the presence of FHM and the prevalence of endometrial, ovarian or cervical cancer in our patients (p=0.2). Almost all of those with positive FHM reported one type of cancer in their family member(s) while only 8 of those demonstrated a family history of multiple types of cancer (p=0.3).

Table 2 also demonstrates the presence of FHM according to the degree of relatives. Relatives are identified as first, second or third degree. The exact relationship to the patient was not known in 3 cases. 71.2% of patients had FHM in a first degree relative. 21.2% of patients with FHM reported malignancy in a second degree relative and 1 patient had a third degree relative with malignancy. There was no statistically significant relationship between the degree of relative and the prevalence of endometrial, ovarian and cervical cancer (p=0.1).

There were 34 (15.7%) patients with a family history of GC. Family history of GC was noted in only two patients with cervical cancer. And 8 out of 13 patients with ovarian cancer had family history of GC. On the other hand, 73.5% of patients with uterine cancer had family history of GC. Family history of breast cancer was noted in a total of 20 (9.3%) patients; 75% of those developed endometrial cancer, while the rest developed ovarian cancer. Three patients who had ovarian cancer also had a family history of ovarian cancer. 9 (4.2%) patients had family history of endometrial cancer and 8 of those also developed endometrial cancer (p=0.02) (Table 3).

Discussion

The Bahrain Oncology Center (BOC) was established in 2019. We noted the highest number of cases in the years 2019 and 2020. This

Table 3. Prevalence of Positive Family History of Malignancy (FHM) of Breast, Ovarian and Uterine Cancer in Patients with Cervical, Uterine and Ovarian Cancer (n=34)

Gynecologic Cancer / FHM of	Cervix	Uterus	Ovary	Total
Breast	-	15 (44.1%)	5 (14.7%)	20 (58.8%)
Ovary	1 (2.9%)	1 (2.9%)	3 (8.8%)	5 (14.7%)
Uterus	1 (2.9%)	8 (23.5%)	-	9 (26.5%)
Total	2 (5.9%)	24 (70.6%)	8 (23.5%)	34 (100%)

can be attributed to the molecular genetics laboratory and improved diagnostic and screening methods.

Several factors have been linked to the predisposition to hereditary cancer. These factors include the presence of multiple cancers in a family, two or more primary cancers in one person or cancer of earlier presentation [10]. We noted that endometrial and ovarian cancer, the two types of GC known to be associated with family history, were the most prevalent types of GC encountered in our institute. We found no statistically significant results when comparing the risk of developing GC in the presence of one or multiple types of cancer in patients' families. Additionally, endometrial cancer and breast cancer are known to share similar risk factors such as nulliparity and exposure to unopposed estrogen. Moreover, the presence of two primary cancers, such as breast and endometrial cancer, in the same individual, implies a possible etiological association between the two [11].

Breast and ovarian cancers are associated with autosomal dominant cancer syndromes particularly in variants of breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2). Inherited endometrial cancer is mostly associated with Lynch syndrome, which is also linked to colorectal cancer [10]. Negri E et al. (2003) concluded that there is a higher risk of ovarian cancer in women with a family history of ovarian and breast cancers [12]. We found that 20% of women with ovarian cancer had FHM and 62% of those had a family history of either breast or ovarian cancer. Our study did not dwell on the associations between cancer syndromes in families and the prevalence of GC in our patients since we did not explore genetic testing of our patients or their family members diagnosed with malignancy.

A meta-analysis by Win et al. explored the risk of developing endometrial cancer in the presence of a first-degree relative with endometrial, colorectal, breast, ovarian and cervical cancer. They found that women with a first-degree relative with those cancers are at a higher risk of developing endometrial cancer compared to women with no FHM [13]. We established that breast cancer was the most prevalent type when investigating our patients' family history. And we also found that endometrial cancer was associated with positive FHM in almost one-third of patients.

With regards to vulvar, vaginal, or fallopian tube cancer, we did not establish a relationship between their prevalence and FHM. The reviewed literature proves the existence of a link between positive FHM and the prevalence of GC thus highlighting the importance of reviewing a patient's family history. Primary care providers play an important role in prevention by encouraging patients to undergo relevant screening and make necessary lifestyle changes when assessing their individual risk of developing GC [1].

The retrospective design of our study can explain some missing data as we were limited by the data available in the hospital's records. Additionally, we could not determine statistically significant relationships between the prevalence of GC and the presence of FHM possibly due to the relatively small sample size. However, almost a quarter of the patients enrolled in this study demonstrated FHM. Perhaps a larger sample size would allow us to make a more solid conclusion. Furthermore, we did not search for other risk factors that might increase the risk of developing GC besides the mere presence of FHM such as age at diagnosis and genetic testing of relatives as it was not deemed necessary for the current study and also because we are in the process of conducting the prevalence of other risk factors in a future study which will be published in due course.

In conclusion, knowing the FHM can help guide appropriate GC screening thus attributing to early detection and hence, more effective management. It is crucial to increase public awareness of the possible risk of developing GC in the presence of FHM. Executing a study on a larger scale might provide us with a deeper understanding of the possible relationship between FHM, especially family history of GC, and the risk of developing GC thus confirming our findings.

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