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Original Research

Pregnancy Associated Cancer in Yemen: An Observational Study

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Abstract

Background: Cancer in pregnancy is not uncommon and represents a complex problem requiring consideration for both the mother and fetus.
Aim: The objective of this study is to analyze the frequency, the clinical feature of cancer diagnosed during pregnancy and the obstetric outcomes.
Methods: This is a single-center, retrospective analysis of women who were diagnosed with cancer during pregnancy at Saudi Hospital Hajjah (SHH) between Jan 2016 and Dec 2017. Maternal sociodemographic, and obstetrical data including age, parity, gestational age at diagnosis, type, stage, symptoms and signs of cancer for each patient were retrieved from the hospital database.
Results: Among 32400 pregnant women seen in antenatal care clinic, there were 17 women diagnosed with cancer. The mean age of women was 33.94 ± 4.80 years, the mean gestational age was 26.88 ± 7.5 weeks and the mean parity was 4.0 ± 2. The most frequent cancer found was ovarian cancer (23.5%), gastrointestinal cancer (23.5%) and cervical cancer (17.6%). Stage II was the most frequently found in 9 women (52.9%). Therapeutic abortion was performed for 9 cases (52.9%) and induced preterm labor for 8 cases (47.0%). Among those induced birth, 6 fetuses were liveborn and 2 deaths. (25.0%). All patients were referred to specialized centers after delivery.
Conclusion: Based on these results, the incidence of cancer complicated pregnancy was 0.052 % (52.4/100000 pregnancies). Gynecological cancer such as ovarian, cervical and breast are more frequent and the gestational age at diagnosis is the most important factor both for the choosing the appropriate obstetrical management and also for the mother prognosis.

Keywords Cancer in pregnancy, Yemen, Outcome

1. Introduction

Pregnancy associated cancer (PAC) is uncommon but nowadays is increasing because there is a trend for women to delay child bearing [1]. Also, the increasing prevalence of obesity contributes to the increasing risk of several age-dependent malignancies [2]. PAC is defined as the cancer diagnosed from the first day of pregnancy to one year postpartum [3]. The incidence of PAC ranges from 0.02 to 0.1% (1:200 to 1 in 1000) of pregnancies [4].

Breast cancer, cervical, thyroid, melanoma, lymphoma and acute leukemia are the most common diagnosed malignancies during pregnancy [5,6]. Coexistence of cancer with pregnancy is a complex and challenge in terms of diagnosis and treatment as both mother and fetus are affected.

The diagnosis of PAC is frustrating for many reasons: firstly, earlier detection of cancer seems difficult because they are often asymptomatic, even if symptoms and signs do appear, they may be overlapped with the signs and symptoms of normal pregnancy. Fatigue, nausea and vomiting are common in the first trimester of normal pregnancy. Additionally, breast tenderness and engorgement make palpable lump is difficult and small lump might be confused with breast engorgement [7,8]. Slight rectal bleeding could be overlooked or attributed to hemorrhoids which are common in pregnancy. Secondly, some diagnostic tools are not always safe. For example, X-ray, CT scan, and to lesser extent magnetic resonance

imaging (MRI) should be avoided during the first trimester [9,10]. Gadolinium used with CT scan found to cross placenta resulting in high fetal concentration and therefore, it is contraindicated [11,12]. Moreover, nuclear medicine such as positron emission tomography (PET), bone scan and thyroid scanning are contraindicated [13]. Finally, tumor markers such as α-fetoprotein, hCG, CA– 125 among others are elevated in pregnancy thus, have no diagnostic value and should not be used during pregnancy [13].

In Yemen as well as many other countries, there is no local data about the size of PAC problem, and there has been limited experience in the management of this clinical situation. The objective of this study is to analyze the frequency and clinical features of PAC in a single-center.

2. Methods

This is a retrospective study conducted in Saudi Hospital Hajjah (SHH) carried out between Jan 2016 and Dec 2017. The hospital records of pregnant women who diagnosed with cancer were reviewed and the medical charts of those women were retrieved. Women who had cancer before pregnancy or developed cancer after delivery was excluded from this study.

Maternal age, parity, gestational age at diagnosis, and the type, stage, symptoms and sings of cancer were retrieved from the patients' charts. The cancers were grouped into ovarian, cervical. gastrointestinal, breast, hematologic and thyroid cancers. Each cancer was staged initially according to the universal staging system. Obstetrical management was classified into two approaches; 1) termination of pregnancy (TOP) defined as therapeutic abortion before fetal viability (24 weeks of gestation) for the purpose of acceleration of cancer management; 2) Iatrogenic (induced) preterm labor (IPL) after fetal viability and then immediate referral for comprehensive management. Pregnancy outcomes included abortion, preterm delivery, sex and birth weight of the neonates, and perinatal mortality were identified.

Data analysis

Data analysis was performed using SPSS statistical version 21. Evaluated variable were analyzed using descriptive statistics. Data are shown as frequencies, mean ± standard deviation (SD) and percentage.

3. Results

There were 17 cases diagnosed with cancer during pregnancy giving prevalence as 0.052%. The most common cancer was ovarian cancer (n=4), and gastrointestinal (n=4), followed by cervical (n=3), hematologic (n=2), breast (n=2), and thyroid (n=2). The site, type, and clinical presentation are described in Table 1. The mean age of patients is 33.94±4.87 years and gravidity between 2-5 was the most frequently affected accounted for 70.6%. The stage II was observed among 52.9% (9/17), Table 2.

Table 1: Site, type and clinical presentation of women having PAC

Site	Type	Clinical features
Ovarian (n = 4)	Serous (n = 2)	Accidently mass by US [4]
	Mucinous (n = 1)	Minimal ascites [2]
	Dsygerminoma (n = 1)	
GIT (n = 4)	Gastric adCa (n = 1)	Nausea, vomiting [3], indigestion [2]
	HCC (n = 2)	Jaundice [2], abdominal pain [2]
	CRC (n = 1)	palpable mass [2], loss of weight [3], bloody stool (1), diarrhea [2]
Cervical (n = 3)	SCC (n = 2)	Vaginal bleeding [2], contact bleeding [3], non-specific
	adCa (n = 1)	
Hematology (n= 2)	HL (n = 2)	Neck swelling [2], dyspnea [1], sore throat [1], wt. loss [2], fever, chills [2]
Breast (n = 2)	Ductal Ca (n = 2)	Palpable lump [2], bloody nipple discharge [1]
Thyroid (n = 2)	Papillary nodCa (n = 2)	Accidental thyroid nodule left [2]

HCC: Hepatocellular carcinoma, CRC: Colorectal carcinoma, US: ultrasound; SCC: Squamous cell carcinoma, adCa: Adenocarcinoma, HL: Hodgkin`s lymphoma, nodCa: nodular carcinoma.

Table 2: Characteristics of women with PAC

Variable	Frequency	%
Age (year)	33.94±4.8	
Gravidity		
Primigravida	1	5.9
2 –5	12	70.6
> 5	4	23.5
Gestational age (week)		
First trimester	1	5.9
Second trimester	8	47.0
Third trimester	8	47.0
Staging		
I	2	11.8
II	9	52.9
III	1	5.9
IV	0	0.0
N/A	5	29.4

Table 3: Distribution of women with PAC according to the obstetric variable

Cancer histology	Age	Gravidity	Gestational age	Stage
Ovarian				
Serous	40	4	26	IIb
Serous	38	5	35	IIa
Mucinous	39	3	34	Ic
Dysgerminoma	21	1	19	IIa
GIT				
Gast adCa	39	9	25	N/A
HCC	35	4	18	II
HCC	27	3	32	III
CRC	38	6	36	N/A
Cervical				
SCC	36	2	33	Ib1
SCC	29	2	27	IIb1
AdCa	34	3	34	IIa
Hematology				
HL	30	4	17	N/A
HL	38	7	21	N/A
Breast				
Ductal	32	2	32	II
Ductal	36	3	12	N/A
Thyroid				
Papillary	33	6	34	II
Papillary	36	5	22	II

The distribution of cancer type according to the obstetric variables is shown in Table 3. The mean gestational age is

26.88± 7.5 weeks. Therapeutic abortion was carried out for 53% while induced preterm birth was performed for 47% of patients. Table 4 describes the obstetric management and outcomes.

Table 4: Obstetric management and outcome

Variable	Value
Mean gestational age (week)	26.88 ± 7.5
Therapeutic abortion	9 (53 .0)
Induced preterm delivery	8 (47.0)
Cesarean section	4 (23.5)
Vaginal delivery	4 (23.5)
Gender	
Male	3 (17.60)
Female	5 (29.40)
Birth weight (g)	2225 ± 755
Perinatal mortality	2 (25.0)

Data presented as n (%) or mean ± SD.

4. Discussion

Based on the findings of this study the incidence of PAC is 0.052% (52.4 per 100000) pregnancies. The most frequent PAC in this study was the ovarian cancer (OC). Gastrointestinal tract (GIT), cervical, breast and hematological cancers ranked as the other most common types of cancer. Although malignancy during pregnancy can arise from any site, the most common cancer reported are breast, cervical, lymphoma, ovarian cancer and melanoma [14,15,16]. It is reported in most studies that the incidence of ovarian malignancy among all adnexal tumors detected by ultrasound during pregnancy is 1: 15000 to 1: 32000 [17], which is lower than that noted in our study (> than2: 15000). We have no local data to compare both the actual rate as well as the trend, however, the genetic and environmental factors in our setting could contribute to this difference.

The high frequency of OC in this study could be explained by the wide use of ultrasound during antenatal care for evaluating the pregnancy and fetal status therefore, the accidentally finding of adnexal mass is increasing as supported by another study [18]. In review of the literature, up to one third of OC during pregnancy were identified incidentally by ultrasound, making it the most common method of tumor detection [19,20]. Results of this study showed the most histologic type of OC was epithelial ovarian cancer (EOC) 75% and germ cell dysgerminoma (25%), and most patients (75%) had stage II. These findings are in contrast to other studies reported the most common OC during pregnancy are non-epithelial germ cell, sex-cord and tumors of low malignant potential [21,22,17]. These differences could be explained by the relatively older age of women (mean = 39 years), by asymptomatic characters of these cancers and lack of women`s periodic health check-up. However, other unknown risk factors could be present and further larger studies are required.

In the present study, 50% of patients with OC had induced preterm labor (IPL) and had live birth. The result of this study shows that 17.6% of all PAC were cervical cancers with mean age of 33 years indicating an increase of the prevalence of cervical cancer (CC) among younger women which could be attributed to the advancement in the diagnostic methods and early age of the first sexual activity. Generally, the incidence of CC during pregnancy is 0.1 to 12 / 10000 births [23] and at least 1 – 3% of all CC are diagnosed in pregnancy [24]. In our situation, Pap smear is not routinely performed in most centers during prenatal check-up thus, this test is strongly recommended for each pregnant woman unless screening has been recently updated. Taking in account that at least 5 – 8 % of cervical cytology during pregnancy are abnormal [24], we suggest that the pregnancy is the best time for obstetrician to make early diagnosis of abnormal cervix.

The current study found one pregnant patient had advanced gastric cancer (GC) at 25-week gestation. Termination of pregnancy was decided and referred for further management. GC during pregnancy is very rare accounting for only 0.025% to 0.1% of all pregnancies [25]. While most patient are middle aged or elderly, approximately 10% are under 45 years of age [26]. The diagnosis of GC is often delayed during pregnancy due to non-specific symptoms that are similar to that of the normal pregnancy, invasive endoscopy and biopsy are often deferred either by physician or patient, and tumor marker such as α-fetoprotein is increased during pregnancy [27]. The prognosis of GC during pregnancy is poor [28].

Breast cancer (BC) is the second most common cancer diagnosed in pregnancy and post-partum. It occurs in approximately 1 in3000 pregnant women. The average age is between 32 to 38 years old [29], and the incidence is likely increasing. BC in pregnancy is often present in advanced stage since small lump cannot be easily detected due to natural tenderness and engorgement during pregnancy [30]. The present study found two women with BC, in advanced stage and their average age was 34 years old. Breast ultrasound is the ideal diagnostic tools because it can distinguish between cystic and solid mass along with axillary lymph node evaluation without risk of radiation exposure [4]. Breast MRI during pregnancy is not yet evaluated and mammography is associated with a high rate of false negative and low sensitivity [4]. The definitive diagnosis is achieved by tissue biopsy which should be performed for any clinically suspicious lump [4].

Hepatocellular carcinoma (HCC) is extremely rare during pregnancy, since 1957 less than 50 cases have been reported worldwide [31] but must be considered in population with a high prevalence of exposure to hepatitis B virus (HBV). The results of this study found 2 cases with HCC, one of them diagnosed before 20 weeks gestational age and the another after 30 weeks, both of them have advanced disease at diagnosis and one patient had history of long use of combined contraceptive pill more than 12 years. Moreover, it is noted that this hospital serves patients mainly from plains of Hajjah and Al Hudaydah governorates where there are many instances of HBV prevailed.

The first case of colorectal carcinoma (CRC) during pregnancy was diagnosed in 1842 [32] and fewer than 350 cases have been reported till now [33]. The incidence of CRC is 1 in 13000 gestations (34), and the mean age was 31 years [35] with range of 16 – 48 years [36]. For its rarity, there is a limited experience on the management of CRC during pregnancy. The current study found one patient with CRC aged 39 years and virtually at 36 weeks of gestation.

Lymphoma is the fourth most frequent cancer seen in pregnancy with Hodgkin lymphoma (HL) being more commonly seen compared with non-Hodgkin lymphoma (NHL) perhaps because HL generally occurs in younger adulthood [37] and approximately 3% of HL are pregnancy associated [13]. Despite the symptoms which might be confused with that of normal pregnancy such as dyspnea and hyper metabolism, HL in pregnancy is mostly first diagnosed at about the same disease stage as in non-pregnant patients [13]. This study found two pregnant women with HL during early second trimester. TOP was performed and referred for proper staging and management.

Thyroid cancer (TC) is the most frequent endocrine malignancy, usually detected in women of child bearing age and about 10% of TC are diagnosed during pregnancy or early after delivery [38]. At present, there are still no reliable data available supporting a specific management of pregnancy associated TC. During pregnancy, patient with TC do not require surgery except in case of rapid nodular growth, and / or the appearance of lymph node metastasis [38]. Two patients found in this study with TC, at 34- and 22-weeks gestations, one delivered vaginally alive female 2.4 kg, while TOP was performed for another patient.

Generally, when PAC is diagnosed, coordination of team approach is required and the most important step is deciding whether to terminate or continue the pregnancy. This major decision depends on the gestational age, stage and type of cancer, the treatment option, and the mother`s wish [38].

However, the treatment of PAC is beyond the scope of this study because the hospital is an emergency one, and all patients were referred to specialized centers which considered a major limitation of this study.

5. Conclusion

Coexistence of malignancy during pregnancy represents two opposite phenomena, the developmental of a new life one and life threatening of the other one. Cancer complicating pregnancy is a rare health problem but needs more attention to differentiate between the signs and symptoms of pregnancy and those related to cancer. Missing such recognition could lead to delay of the cancer management and therefore poor prognosis.

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

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