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(RESEARCH ARTICLE)

RISK FACTORS AND HISTOLOGICAL TYPES OF ENDOMETRIAL CARCINOMA AT SHENDI UNIVERSITY TUMOR THERAPY CENTER, SUDAN

Sami Hummeda Elnour Hummeda [1,*], Elaf Elfakei [2] and Ibrahim Bakhit Yousif Elemam [3]

[1] Department of Obstetrics and Gynecology Faculty of Medicine, Shendi University, Shendi, Sudan.
[2] Department of Obstetrics and Gynaecology, Al Mak Nimir Hospital, in Shendi locality, Sudan.
[3] Department of Histopathology and Cytology, Faculty of Medical Laboratory Sciences, Shendi University, Shendi, Sudan.
* Corresponding Author

ORCID Details
Sami Hummeda Elnour Hummeda: https://orcid.org/ 0009-0005-7097-3734
Elaf Elfakei: https://orcid.org/0009-0002-2999-5593
Ibrahim Bakhit Yousif Elemam: https://orcid.org/ 0009-0006-3591-0049

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ABSTRACT

Background: Uterine endometrial cancer is the most prevalent gynaecologic malignancy, representing a significant cause of morbidity and mortality, worldwide. Understanding the risk factors, diagnosis, and management of endometrial cancer necessitates a comprehensive approach from an interprofessional team. This study aimed to evaluate the risk factors and histological types of endometrial carcinoma among patients at the Tumor Therapy and Cancer Research Center at Shendi University. The study was conducted between September 2022 and March 2023.

Methods: A descriptive cross-sectional hospital-based study was conducted involving 80 participants diagnosed with endometrial carcinoma.

Results: Out of the 80 patients, 2 (2.5%) were using estrogen, 21 (26.2%) had hypertension, and 13 (16.3%) had diabetes mellitus (DM). Other risk factors included polycystic ovary syndrome (2.5%) and a history of prior pelvic radiation (1.3%). Family histories of cancers were notable, with 14 (17.5%) having a family history of breast cancer, 14 (11.2%) for endometrial cancer, and 8 (10.0%) for colorectal cancer. Disease staging revealed IA and IB stages in 26 patients each (32.5%). The predominant histopathological subtype was endometrioid adenocarcinoma, accounting for 67 (83.7%) cases.

Conclusion: In summary, early marriage was significantly associated with a higher prevalence of endometrial adenocarcinoma, emphasizing the potential need for targeted education and screening for women who marry at a younger age. while advanced age was associated with advanced tumor grade, and the associations were statistically significant.

Keywords: Endometroid Adenocarcinoma, Uterine Cancer, Endometrial Cancer, Sudan

1 INTRODUCTION

Endometrial carcinoma is the most common and the second most lethal gynecologic cancer in the developing countries, causing over 8,000 deaths annually. The majority of these tumors are low-grade, endometrioid carcinomas that present with stage 1 disease and portend an excellent prognosis. However, nonendometrioid carcinomas are important because they often present with late-stage disease and are fatal [1]. Overall evidence suggests that there are etiologic differences between Types I and II endometrial carcinomas, but conclusions are limited by small sample sizes and the lack of prospective data [2].

Bokhman proposed that endometrial cancers could be divided into two broad types based on fundamental differences in endocrine and metabolic functioning and accepted endometrial cancer risk factors [2]. Specifically, he proposed that the numerically predominant endometrioid form of endometrial cancer has a hormonally driven etiology (i.e., relative excess estrogen exposure), develops from endometrial hyperplasia, pathologically is more well-differentiated, and portends a favorable prognosis. In contrast, other endometrial cancers were viewed as unrelated to typical endometrial cancer risk factors, not associated with endometrial hyperplasia, and pathologically high grade, often resulting in death [3]. Studies reporting an association between higher BMI and increased mortality more frequently controlled for stage, histologic subtype, and adjuvant therapy compared with studies that did not detect relationships, although exceptions are evident. Most studies did not include sufficient numbers of non-endometrioid carcinomas to fully examine relationships among rare aggressive subtypes, and differences in categorization of BMI, small sample sizes, and short follow-up times hamper interpretation of the literature [4].

Many pathologists and gynecologists have embraced the view that there are at least two main biological types of endometrial cancer (and possibly more), but most epidemiologic studies have assessed risk factors for endometrial cancer overall—which essentially represent the risks for the predominant Type I tumors, especially in largely Caucasian populations. Registry data consistently have shown Type II cancers to more frequently occur among older and non-white women. In addition, some epidemiologic investigations have found that Type II cancers are less strongly linked to classic Type I risk factors, such as obesity, nulliparity, and hormones [5]. Accepted prognostic factors for endometrial carcinoma include tumor characteristics, such as histology, grade, lymphovascular space invasion, and stage. Less is known about the role that etiologic risk factors may have on survival following an endometrial carcinoma diagnosis, which could be of use to clinicians to guide treatment decisions and inform surveillance schedules [6]. This study aimed to evaluate the risk factors and histological types of endometrial carcinoma among patients at the Tumor Therapy and Cancer Research Center at Shendi University.

2 MATERIALS AND METHODS

This was a prospective descriptive, hospital-based study. The study was conducted in the Tumor Therapy and Cancer Research Center, Shendi University, Sudan. The study included 80 women diagnosed with all types of endometrial cancer during the period from September 2022 to March 2023. The data were collected by a well-designed questionnaire, which was used for this study, including questions that fulfilled the objectives of the study. Data was collected by the principal investigator. Both primary and secondary data collection was applied by the author herself. Data was entered into an Excel sheet and then exported to SPSS version 25 for analysis.

3 RESULTS

A total number of 80 patients were investigated in the present study. The most encountered risk factors were 2 (2.5%) who were using estrogen, 21 (26.2%) were known cases of hypertension, and 13 (16.3%) had diabetes mellitus. There were 2 (2.5%) who had polycystic ovary syndrome and 1 (1.3%) who reported a history of prior pelvic radiation. There were 7 (8.8%) reported histories of ovarian cancer, 6 (7.4%) reported breast cancer, and 1 (1.3%) reported a history of hereditary nonpolyposis colorectal cancer. 14 (17.5%) had a family history of breast cancer, 14 (11.2%) had a family history of endometrial cancer, and 8 (10.0%) had a family history of colorectal cancer. As shown in Fig. 1, the main reported disease stages were IA and IB, as reported by 26 (32.5%) and 26 (32.5%), respectively, and stages II (8.8%), stage IIIA (7.4%), stage IIIB (8.8%), stage IVA (6.2%), and stage IVB (3.8%). Regarding disease grade as shown in Fig.2, 34% were grade X, followed by 27% grade 1, 19% grade 2, and 20% grade 3. Endometroid adenocarcinoma was the main reported histopathological subtype, as reported by 67 (83.7%), followed by 5 (6.2%) metastatic, 3 (3.8%) mucinous, 2 (2.5%) squamous, 2 (2.5%) mixed, and 1 (1.3%) clear cell, as shown in Fig. 3.

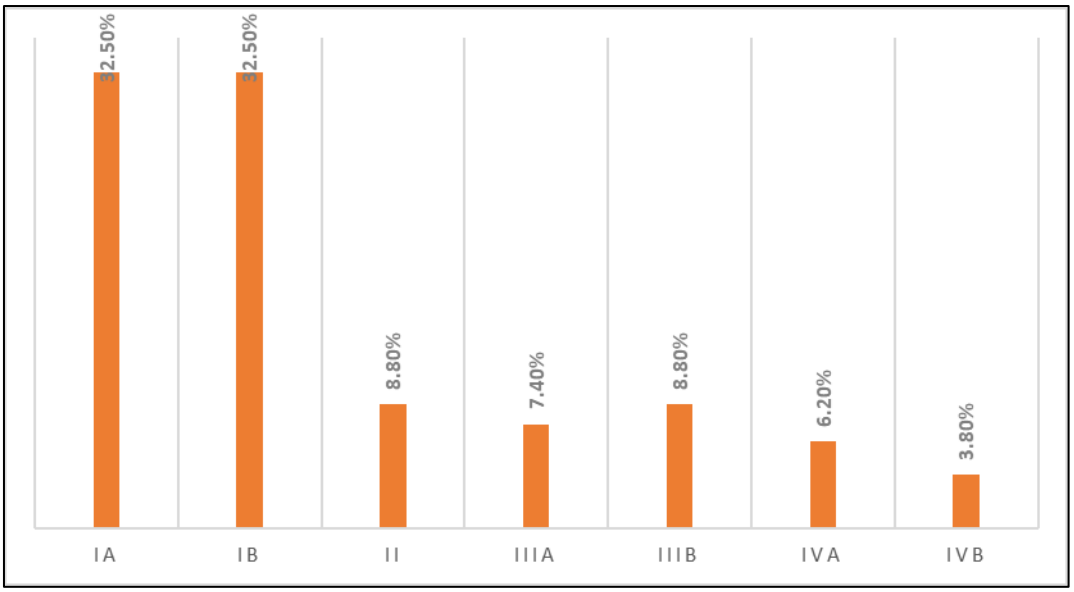


Figure 1: Description of proportions of the study subjects by disease stage

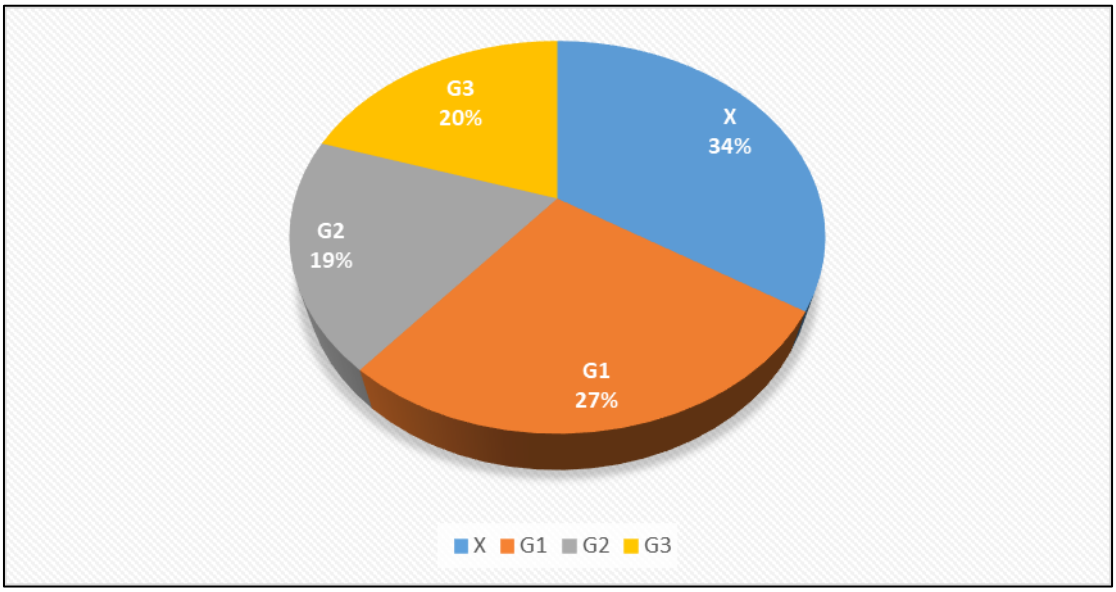


Figure 2: Description of proportions of the study subjects by disease-grade

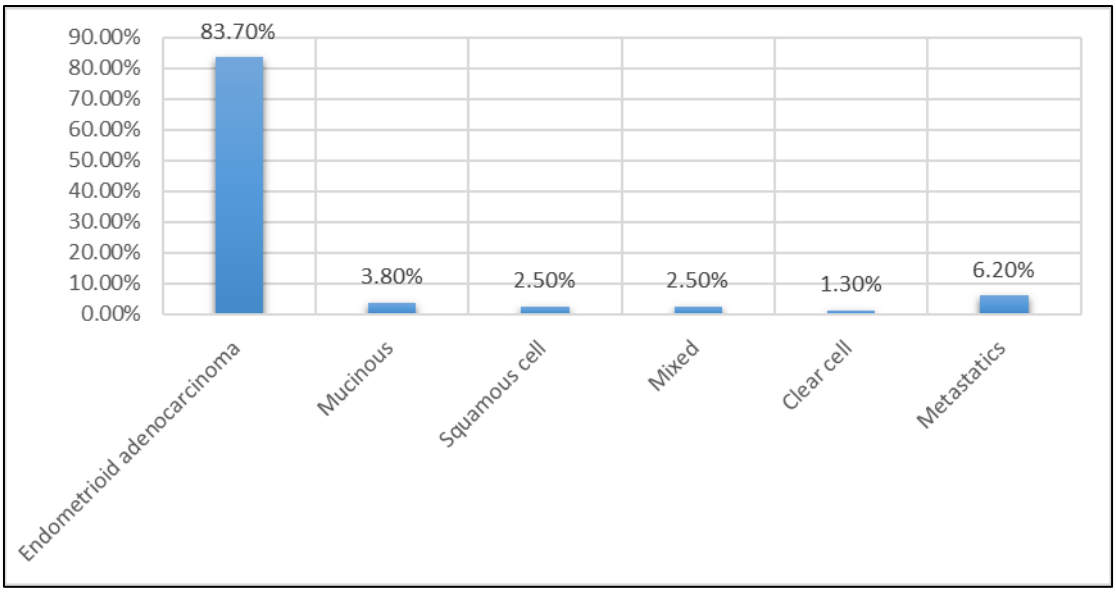


Figure 3: Description of the patients by histopathological subtype

< 15 years**:** Only 1 patient (1.3%) was reported, classified as Grade X. 15-35 years: This group constituted the majority with 59 patients (73.8%). The distribution of grades was as follows: Grade X: 19 (23.8%), G1: 15 (18.8%), G2: 11 (13.8%), and G3: 14 (17.6%), as indicated in Table. The p-value of .028 indicates a statistically significant association between age and tumor grade, highlighting younger age groups as more likely to present with Grade X tumors. This underscores the need for targeted surveillance and intervention strategies in younger populations at risk for endometrial carcinoma.

Table 1: Correlation between age in years and disease grade among study participants (n=80)

Age		**Grade**				**Total**	**P value**
		X	G1	G2	G3		
< 15 years		1	0	0	0	1	.028
		1.3%	0.0%	0.0%	0.0%	1.3%	
15-35		19	15	11	14	59	
		23.8%	18.8%	13.8 %	17.6 %	73.8%	
> 35 years		7	7	4	2	20	
		8.8%	8.8%	5.0%	2.5%	25.0%	
Total		N	22	15	16	80	
		%	27.5%	18.8%	20.0%	100.0%	

The analysis of histopathological subtypes of endometrial carcinoma in relation to the age at marriage involved 67 patients, with results as follows:

Endometrial Adenocarcinoma: The predominant subtype, accounting for 59 cases (88.1%). Age at marriage distribution was observed with 8 patients (<19 years, 11.9%), 48 patients (19-25 years, 71.6%), 3 patients (25-40 years, 4.5%), and none (>40 years). The findings revealed a statistically significant association (p = .001), indicating a strong correlation between early marriage age and the incidence of endometrial adenocarcinoma.

Mucinous Carcinoma**:** This subtype included 3 patients (4.5%) with one case each in the age categories of 19-25, 25-40, and >40 years, and no cases for those married <19 years. Other Subtypes: Encompassing 5 patients (7.5%), with 1 case each in the age groups of <19, 19-25, and 25-40 years, and none for >40 years, as indicated in Table 2.

Table 2: Correlation between age of marriage in years and histopathological subtype among study participants (n=80

Histopathology Subtype		Age of Marriage				Total	P value
		< 19	19 - 25	25 - 40	> 40		
endometrial adenocarcinoma		8	48	3	0	59	.001
		11.9%	71.6%	4.5%	0.0%	88.1%	
mucinous		0	1	1	1	3	
		0.0%	1.5%	1.5%	1.5%	4.5%	
Others		1	3	1	0	5	
		1.5%	4.5%	1.5%	0.0%	7.5%	
Total		N	52	5	1	67	
		13.4%	77.6%	7.5%	1.5%	100.0%	

4 DISCUSSION

This study aimed to determine the risk factors and histological types of endometrial carcinoma among patients at the Tumor Therapy and Cancer Research Center, Shendi University (September 2022 - March 2023), and covered 80 study participants who enrolled in it. With the cancer burden rising in sub-Saharan Africa, countries in the region need surveillance systems to measure the magnitude of the problem and monitor progress in cancer control planning. In this current study regarding socio-demographic characteristics, 59 participants (73.7%) were aged 15-35 years, while 20 participants (25.0%) were older than 35 years, which is consistent with the findings of Pamela et al. that addressed risk factors for young premenopausal women with endometrial cancer. In the reported period, the twelve percent (188/1531) of all patients with endometrial adenocarcinoma were younger than 50 years. The mean age at diagnosis was 41 years (range 21-49 years). Reversely, Faina et al. reported that most of their cases involved patients who were older than 40 years [32]. In this present study, 23 (28.8%) were underweight, followed by 44 (55.0%) with a normal body mass index, 9 (11.2%) overweight, and 4 (5.0%) obese, in a similar context to Hannah et al., where obesity is a strong, modifiable risk factor for endometrial carcinoma, which is implicated in approximately 40% of cases. Obesity is a stronger risk factor for Type I as opposed to Type II carcinomas, but some increase for the latter has been noted [8]. This observation could be justified by the fact that postmenopausal obesity is consistently linked to increased circulating levels of estrogens, which likely accounts for part of the excess endometrial cancer risk among heavier women. However, obesity is also related to diabetes, metabolic syndrome, and a proinflammatory state, which could contribute to endometrial carcinogenesis via elevated exposure to growth factors and other nonestrogenic mechanisms. Furthermore, Pamela et al. found that the mean BMI was 34 kg/m^2 (range 18-68); 58% of patients had a BMI of 30 or greater [7]. Moreover, S. M. Shoff et al. compared overweight and non-overweight women who reported diabetes with non-overweight nondiabetic subjects, and no overweight women who reported diabetes had nonsignificant elevated risks of endometrial cancer (no overweight, odds ratio (OR)=1.10, CI 0.66-1.86; overweight, OR=1.58, CI 0.81-3.05). In contrast, elevated risk estimates were observed for obese diabetic women (OR=2.95, CI 1.60-5.46). These data contradict earlier reports and suggest that diabetes confers no additional risk of endometrial cancer in women who are neither overweight nor obese. In our study, 18 (22.5%) of the participants were nulliparous, consistent with the findings of Faina et al., who similarly indicated that the majority of their participants were nulliparous [10]. Furthermore, Pamela et al. reported that fifty-five percent were nulliparous and 39% reported irregular menstrual cycles [33]. We revealed that 2 (2.5%) were using estrogen; similarly, Pamela et al. found that less than a quarter of their cases were using it [33]. In this study 7 (8.8%) reported a history of ovarian cancer, 6 (7.4%) reported breast cancer, and 1 (1.3%) reported a history of hereditary nonpolyposis colorectal cancer. In a similar context to Ashley et al., Type II cases had an OR of 1.56 for having a history of an additional primary cancer compared to Type I cases (p = 0.03). The most common additional primary cancer in this cohort was breast cancer. Of the Type II cases with an additional primary, 59.5% had breast cancer, compared to 44.6% for the Type I cases (p = 0.07). Several hypotheses for an association between Type II EC and additional cancer primaries exist. First, these cancers may share similar risk factor profiles. Second, radiation treatment for proximate cancers may increase the incidence of radiation-induced ECs or vice versa. Third, the presence of multiple cancers may be a manifestation of inherited cancer syndromes, such as hereditary nonpolyposis colorectal cancer syndrome; however, these genetic disorders are relatively rare in the population. Finally, multiple cancer primaries may be a result of mutations in unidentified cancer-predisposing genes [11]. Furthermore, Pamela et al. revealed that thirty-six patients (19%) had synchronous ovarian cancers. Found that the majority [7]. We reported that 14 (17.5%) had a family history of breast cancer, 14 (11.2%) had a family history of endometrial cancer, and 8 (10.0%) had colorectal cancer, in agreement with Hannah et al., where a relation between a first-degree family member with

breast cancer and Type II endometrial carcinomas was noted, although this result was based on a limited number of events [30]. Although endometrial and breast cancers share some of the same reproductive and hormonal risk factors, most studies have not assessed the relationship between family history of breast cancer and endometrial cancer risk according to tumor subtype. In support of our finding, a recent study has reported that BRCA mutations may be common among uterine papillary serous cancers. Although an inherited factor could explain the association between a family history of breast cancer and Type II endometrial carcinoma, nongenetic causes are also possible. In addition, the association may reflect a chance finding or differential recall bias by tumor type, suggesting the need for further study. In our study, endometroid adenocarcinoma was the main reported histopathological subtype, as reported by 67 (83.7%). Similarly, Pamella et al. reported that endometroid adenocarcinoma was the most prevalent type of endometrial cancer [7]. Additionally, SM Shoff et al. reported that endometroid adenocarcinoma was a highly frequent type, especially among the premenopausal group [9]. In this current study, cross tabulations were done to assess the possible association between participants' characteristics with types of endometrial cancer and outcome using the chi-square statistical test.

The results showed that younger age, married ladies, history of estrogen exposure, and positive family history of breast cancer and endometrial cancer were associated with endometrial adenocarcinoma type, while advanced age was associated with advanced tumor grade, and the associations were statistically significant (p values < 0.05 in all). Moreover, Veronica et al. reported that parity, oral contraceptive use, cigarette smoking, age at menarche, and diabetes were associated with type I and type II tumors to similar extents. Body mass index, however, had a greater effect on type I tumors than on type II tumors: odds ratio (OR) per 2 kg/m^2 increase was 1.20 (95% CI, 1.19 to 1.21) for type I and 1.12 (95% CI, 1.09 to 1.14) for type II tumors (Pheterogeneity < .0001). Risk factor patterns for high-grade endometrioid tumors and type II tumors were similar. The results of this pooled analysis suggest that the two endometrial cancer types share many common etiologic factors. The etiology of type II tumors may, therefore, not be completely estrogen-independent, as previously believed [12]. Lastly, Olivia et al. documented that body mass index and waist-to-hip ratio were associated with increased cancer risk in premenopausal women (RR per 5 kg/m^2 1.49; CI 1.39–1.61) and for total endometrial cancer (RR per 0.1 unit 1.21; CI 1.13–1.29), respectively. Parity reduced risk of disease (RR 0.66, CI 0.60–0.74). Of many proposed risk factors, only three had a strong association without hints of bias. Identification of genuine risk factors associated with endometrial cancer may assist in developing targeted prevention strategies for women at high risk [13].

5 CONCLUSION

In summary, early marriage was significantly associated with a higher prevalence of endometrial adenocarcinoma, emphasizing the potential need for targeted education and screening for women who marry at a younger age. while advanced age was associated with advanced tumor grade, and the associations were statistically significant.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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