Risk Factors of Cervical Epithelial Cell Abnormality in Baghdad

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Abstract

Knowledge of risk factors associated with cervical epithelial cell abnormality help in tracing cervical cancer incidence. This study aimed at identifying risk factors associated with ECA.

A retrospective case control study was done in the Women cancer Center. All complete patient records from January 2016-July 2019 were reviewed; (2176) women's records were included in the study. Epithelial cell abnormality was found among 508(23.3%). Cervical epithelial cell abnormality was higher among those aged > 45 years 199(39.2%), widowed 9(1.8%) and divorced 4(0.8%). About 102 (20.1%) of those with epithelial cell abnormality had their 1st sexual contact at age < 15 years, in comparison with those with normal cytology 285(17.1%). Post coital bleeding as a presenting symptom was higher among those with ECA 105(20.7%). Bivariate logistic analysis showed significant relation with age groups of 45 years or older (Adjusted odds ratio (AOR) 1.4, 95 % CI: 1.1 – 1.81.), post coital bleeding (AOR 1.92, 95 % CI: 1.1 – 3.43). A high percentage of women had ECA. The most common risk factors were age older than 45 years, the first sexual contact at age < 15 years, and high parity >3, and post coital bleeding.

Key words: cervical cancer, clinical presentation of ECA, Epithelial cell abnormality, Risk factors, Pap Smear.

Introduction

Cervical cancer [CC] is the 2nd leading cause of cancer morbidity and the 4th leading cause of cancer death among women globally; the majority of cases occur in developing countries [1] .

In Iraq the incidence rate of cervical cancer is 2.1 per 100.000 population [2], while the ECA prevalence was (23.2%) [3]. Cervical cancer screening decreased the incidence of invasive cervical cancer to 50% of previously reported levels [4] .

Cervical epithelial cell abnormality (ECA) is a term that refers to a sequence of cervical abnormality ranging from mild to severe Squamous intraepithelial dysplasia to invasive squamous cell carcinoma [5] .

The precursor lesions gradually develop to invasive cancer [6] . Not all precursor lesions will progress to invasive cancer; many of the mild and moderate lesions may regress [1] . On a global level, 75 % of women have abnormal cervical cytology at least once in their life time which may progress to cervical cancer. The cytological changes which appear in pre-invasive lesions are nuclear enlargement, multinucleation, hyperchromasia with thin cytoplasm and perinuclear holo, in addition to koilocytotic atypia [7].

Abnormal growth of squamous epithelial cells of the ectocervix is known as Squamous intraepithelial lesions (SIL). A spectrum of SIL that lies along the footpath (mild, severe dysplasia and invasive cancer) is known as cervical epithelial cell abnormalities (ECA) [1]. Precursor lesions develop gradually to form cervical carcinoma [1]. Greater than 99.7 % of cervical cancer is attributed by human papillomavirus (HPV) infection.

Multiple risk factors are associated with CC. These include: age of 30-55 years, socioeconomic status, smoking, abnormal Papanicolaou (Pap) smears, HPV infection and vaginal inflammatory changes, number of previous pregnancies,[8] number of sexual partners, and age at first intercourse [9] . About 6% of CC reported using of barrier methods of contraception (condom and diaphragm) [10]. Women diagnosed with cervical intraepithelial neoplasia grade 3 had an accelerated increased risk of acquiring invasive cancer [11].

Pap smear screening test is the method of preventing CC. The danger of CC development was reduced by early detection of cervical cell abnormalities. This is due to timely response to abnormal changes in cervical cytology [12].

Few reports have described the frequency and pattern of abnormal Pap smears in developing countries [13] and in Iraq [14, 15]. No researcher in Iraq has studied the risk factors associated with ECA. This study aimed to determine the associated risk factors for an abnormal pap smear cytology. The knowing of associated risk factors helps in prevention strategies implementation.

Patients and methods

A retrospective case control study was done in Al-Alwiyaa Maternity Teaching Hospital, Women cancer Center. Patient records from January 2016-July 2019 were reviewed and those with complete information waere selected. A total of 2,176 women's records were included in the study, 1,668 with normal cytology compared with 508 cases with abnormal cytology.

Al-Alwiyaa Maternity Teaching Hospital, Women cancer Center, is one among the main cervical cancer early detection centers, and drains areas of the Al Rusafa part of Baghdad city, as well as some patients referred from the Salahaddin and Al Anbar governorates.

Excluded was any record with incomplete information, or without Pap Smear cytology results. The spatula with the sample was rapidly but lightly stroked, thinly and evenly across the surface of the slide and cytology spray fixatives were used without delay. All slides were evaluated at the cytology laboratory of the hospital using light microscopy. Smears were prepared by cytotechnologists and every slide was read by the consultant cytopathologist.

Socio-demographic data, age, marital status, age at marriage and gynecological and obstetrical history was obtained from the records.

Results

Epithelial cell abnormality was found among 508(23.3%) of the total sample of 2,176 patients.

Cervical epithelial cell abnormality (ECA) was higher among those aged > 45 years 199(39.2%), while most of those with normal cytology were aged 34-45years 653(39.1%). This relation was statistically not significant.
Marital status analysis showed that widowed 9(1.8%) and divorced 4(0.8%) were among those who had epithelial cell abnormality higher than those among normal epithelial cytology 18(1.1%), 8(0.5%) respectively. This relationship was not statistically significant.

About 102 (20.1%) of those with epithelial cell abnormality had =their first sexual contact at age < 15 years, in comparison with those with normal cytology at the same time of sexual contact 285(17.1%) This relation was statistically not significant, as shown in Table 1.

Post coital bleeding as a presenting symptom was higher among those with ECA 105(20.7%), while it was lower among those with normal epithelial cell cytology 245(14.7%).

Bivariate logistic analysis showed that the prevalence of ECA was significantly higher among patients within the age groups of 45 years or older (Adjusted odds ratio (AOR) 1.4, 95 % CI: 1.1 – 1.81, p = 0.027) as compared to women aged < 34 years. Age at marriage, status of marriage, and parity was not associated with increased

Table 1: The relation of Pap smear test results and different patient characteristics.

		Pap smear results		Total	P value
		Normal	Epithelial cervical abnormality		
Age	<34	436	118	554	0.157
		26.10%	23.20%	25.50%	
	34-45	653	191	844	
		39.10%	37.60%	38.80%	
	>45	579	199	778	
		34.70%	39.20%	35.80%	
Marital status	Married	1642	495	2137	0.331
		98.40%	97.40%	98.20%	
	Widow	18	9	27	
		1.10%	1.80%	1.20%	
	Divorced	8	4	12	
		0.50%	0.80%	0.60%	
Marriage age	<15	285	102	387	0.261
		17.10%	20.10%	17.80%	
	15-18	415	116	531	
		24.90%	22.80%	24.40%	
	>18	968	290	1258	
		58.00%	57.10%	57.80%	
Parity	<2	361	98	459	0.5
		21.60%	19.30%	21.10%	
	3-4	471	151	622	
		28.20%	29.70%	28.60%	
	>4	836	259	1095	
		50.10%	51.00%	50.30%	

risk of ECA. Post coital bleeding was associated with increased risk of ECA (AOR 1.92, 95 % CI: 1.1 – 3.43, p = 0.028), the crude OR was significantly higher among those who presented with post coital bleeding as compared to the screening 1.8, 95 % CI: (1.01-3.2, p = 0.048)

Discussion

Little has been written about the correlation of presenting symptoms of the patient with cytological abnormality of the cervix in Iraq, therefore it is important to know the most prevalent risk factors to predict the risk of cervical ECA. Epithelial cell abnormality was found among 508(23.3%); this goes with that reported previously in Iraq [15] and Ethiopia (16.4 %) [16].

This was lower than the figure reported in Baghdad by Abdulla K N et al (86%), [17] and Aloan H.H, and Issa Z.A. (85.4) [18] . This difference is due to the difference in selection of the sample as they selected only symptomatic patients and those in need of colposcopy, resulting in a higher prevalence of cervical ECA .

Cervical epithelial cell abnormality (ECA) was higher among those aged > 45 years (39.2%). This was supported by previous studies that showed increased prevalence and grade of ECA with increasing age, mostly women aged >45 years (46.04%). Patients older than 40 years had the greatest incidence of invasive cancer [19] . Prevalence of high-grade lesions was high and not surprisingly was commonly seen in older age group women [20].

El. Mahalli Azza Ali found that mean age for those with (ECA) (45.97 ± 8.012) was higher than with normal cytology (42.25 ± 10.047), and patients of age (40-50 years), had the highest prevalence of ECA (52.4%), and for those above 50 years it was (26.9%) [21].

The adjusted logistic regression showed that those aged > 45 years had significantly higher risk of ECA(OR=1.4) This is supported by Shield's et al., (2004) who showed that risk of developing CC was high among patients aged (35-44), (45-54), and (≥55) with OR = 1.2, 1.7 and 1.5 respectively [22].

Table 2: The relation of Pap smear cytology results and presenting symptoms

Presenting symptom	Normal	Epithelial cervical abnormality	Total
Screening	71	17	88
	4.30%	3.30%	4.00%
Vaginal discharge	884	261	1145
	53.00%	51.40%	52.60%
Abdominal pain	32	10	42
	1.90%	2.00%	1.90%
Irregular vaginal bleeding	311	71	382
	18.60%	14.00%	17.60%
Post coital bleeding	245	105	350
	14.70%	20.70%	16.10%
Post-menopausal bleeding	83	26	109
	5.00%	5.10%	5.00%
Other	42	18	60
	2.50%	3.50%	2.80%
Total	1668	508	2176
	76.70%	23.30%	100.00%

Chi-Square= 15.9, df=6, P value <0.014

Table 3: Bivariate analysis of risk factors for cervical ECA among women attending cervical cancer screening unit

		AOR (95% C.I.)	95% C.I.		P value
			P value	COR (95% C.I.)	
Age	<34	1		1	
	34-45	1.1(0.8-1.44)	0.476	1.1(0.8-1.4)	0.5
	>45	1.4(1.1-1.81)	0.027	1.3(0.98-1.6)	0.07
Age at marriage	>18	1		1	
	15-18	0.9(0.73-1.2)	0.568	0.9(0.7-1.2)	0.578
	<15	1.2(0.9-1.6)	0.17	1.2(0.9-1.6)	0.182
Parity	<2	1		1	
	3_4	1.17(0.9-1.6)	0.297	1.2(0.9-1.6)	0.259
	>4	1.1(0.8-1.4)	0.518	1.14(0.8-1.5)	0.325
Marital status	Married	1		1	
	Widow	1.73(0.8-3.9)	0.196	1.7(0.7-3.7)	0.219
	Divorced	1.6(0.4-5.3)	0.468	1.65(0.5-5.5)	0.410
Presenting symptom	Screening	1		1	
	Vaginal discharge	1.3(0.75-2.3)	0.348	1.23(0,7-2.1)	0.453
	Abdominal pain	1.4(0.6-3.3)	0.484	1.31(0.5-3.2)	0.556
	Irregular vaginal bleeding	0.95(0.53-1.7)	0.875	.95(0.5-1.7)	0.874
	Post coital bleeding	1.92(1.1-3.43)	0.028	1.8(1.01-3.2)	0.048
	Post-menopausal bleeding	1.1(0.5-2.2)	0.816	1.31(0.6-2.6)	0.444

This study found that those with high parity 3-4 or > 4 pregnancies had higher prevalence of ECA while the logistic regression showed a non-significant relation between ECA by Pap smear and parity of > 3 full term deliveries. This goes along with Munoz et al., (2002) who reported that high parity is a risk factor for developing CC (OR in women who had ≥ 7 full term pregnancies was 3.8) [23]. In addition, the Alliance for Cervical Cancer Prevention reported in their 'Risk Factors for Cervical Cancer: Evidence to Date' that women with (3 or 4) full term pregnancies had 2.6 times the risk of developing CC than nulliparous women [24]. The American Cancer Society reported 'Women who have had 3 or more full-term pregnancies have an increased risk of CC' [25]. These figures go with the present findings where patients who had ≥ 3 pregnancies were at higher risk of developing CC.

The real reason for this fact is not known. One theory states that these women may have had more exposure to HPV infection due to having unprotected intercourse. Other studies have attributed this to hormonal changes during pregnancy, as it makes women more vulnerable to HPV infection or cancer development. A further thought is that the weaker immune system during pregnancy allows contracting of HPV infection and cancer growth [25]. The lower and non-significant OR in this study may be explained by the cultural difference in Islamic countries in which most of women are restricted to one partner and have restricted use of family planning which can confound the relation or may be prove the fact that multiple partners increase risk of HPV which is the main cause of cervical cancer, therefore, further studies should investigate why this risk factor increases the likelihood of developing abnormal cervical cytology.

Marital status analysis shows that widows (1.8%) and the divorced (0.8%) among those who had epithelial cell abnormality was higher than those among normal epithelial cytology (1.1%) and (0.5%) respectively.

About 102 (20.1%) of those with epithelial cell abnormality had their first sexual contact at age < 15 years, in comparison with those with normal cytology at the same time of sexual contact 285(17.1%) with an AOR of 1.2 compared with those whose first sexual intercourse was at age > 18 years old. This finding is supported by findings of Louie, K., et al [26], Compared with women with >1 years, OR was 1.80 (95% CI: 1.50–2.39)). The process by which the first sexual contact could influence the cervical carcinogenesis risk may be clarified by the effect of steroid during adolescence on HPV infection and host's immunity. The transformation zone of the cervical epithelium is the site in which dysplastic changes tend to occur as a result of HPV infection. Stripping of the stratified epithelium in this area increases susceptibility and facilitates the exposure of the basal layer to HPV with minimal trauma. The acidification of vaginal cavity which is stimulated by the high levels of oestrogen during adolescence, play a role in squamous metaplasia. HPV infection during these metaplastic changes increase risk of cell transformation, and neoplastic changes [27,28].

The common presenting symptom among those with ECA was vaginal discharge (51.4%), and post-coital bleeding (20.7%), and irregular vaginal bleeding (14%) This figure was higher than that found by Shapley M (11%) [29]. Srivastava S, [30] found that the most prevalent clinical finding was abnormal vaginal discharge (13.4 %). Vaginal discharge is usually a normal and regular evidence; the type of discharge may suggest an underlying infective cause. Such abnormal discharge was considered when the vaginal discharge was yellow or green in color, chunky in consistency, and having a foul odour. Most abnormal discharges in the study were caused by yeast or bacterial infection.

The prevalence of PCB among those with abnormal cytology was 20.7%. This was higher than that found in India 6.7% [30]. The crude logistic regression was 1.8, and adjusted OR was 1.9 for post coital bleeding. This goes with previous studies that reported increased probability of cancer among patients with postcoital bleeding [15,16,29].

From the above we noted that all risk factors indirectly affect the ECA development through increasing the susceptibility to HPV infection. This fact makes the effect of these risk factors lower in countries with lower HPV prevalence. More research isneeded to evaluate the effect of these risk factors in Middle East countries and communities with low prevalence of HPV infection.

Conclusions and Recommendations

Epithelial cell abnormalities wer high (23.3%). The most common risk factors were >45 years, post coital bleeding, the first sexual contact at age < 15 years, widowed and divorced, and high parity >3. Attention should be paid to patients presenting with post coital bleeding and should be sent for Pap smear examination.

Ethical consideration and acknowledgment:
No ethical concerns were present. The study was approved by the research ethics Committee of Rusafa health directorate. We acknowledge all the patients and staff of women cancer center for their cooperation and help.

Conflict of interest
There is no conflict of interest except for increase the knowledge and research quality regarding cervical cancer.

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