

Cervical dysplasia: assessment and risk factors among women attending the Maternity Teaching Hospital in Erbil, Kurdistan-Iraq

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Abstract

Background and objective: Cervical cancer is the second most common female cancer in the world. It is the commonest cause of female cancer deaths in South-East Asia and Africa and accounts for 15% of all female cancers in developing countries. The aims of this study was to determine the frequency of abnormal cervical cytology among women underwent Pap smear and assess for the presence of risk factors related to abnormal Pap smear results.

Methods: A hospital-based cross sectional study, using a questionnaire and involved 2,146 women at the Maternity Teaching Hospital in Erbil city from January to December 2009. All Pap smears cytological examinations were conducted using Bethesda classification system.

Results: Histological reports were found to be normal in 88.4% of women; meanwhile, 248 (11.6%) women had abnormal cytological findings with a mean age of 36.84 years, significantly older than those with normal results ($p < 0.05$). The duration of marriage was also found to be significantly longer among those with abnormal Pap smear (18.34 years versus 15.72 years, ($p < 0.05$).

Conclusion: This study was able to indicate that during reproductive life, the older ages of women and longer duration of marriage were associated with an increased risk of abnormal Pap smear results.

Keywords: : Cervical Dysplasia, Pap smear

Introduction

Cervical cancer is the second most common female cancer in the world that affects some 489000 women and kills 268000 women each year. It is the commonest cause of female cancer deaths in South-East Asia, Africa and other parts of the developing world¹. It accounts for 15% of all female cancers in developing countries². The World Health Organization record of cervical cancer incidence in Iraq, estimated to be 2.1 per 100,000 populations³. Invasive cancer of the cervix results from the progression of pre-invasive precursor lesions called cervical intraepithelial neoplasia (CIN), or dysplasia. Not all precursor lesions will progress to invasive can-

cer many of the mild and moderate lesions may regress¹. The cytological changes which appear in pre-invasive lesions are nuclear enlargement, multinucleation, hyperchromasia with thin cytoplasm and perinuclear halo, in addition to the koilocytotic atypia⁴. Bethesda classification reporting system which was first developed in 1988, classified these cytological abnormalities as atypical squamous cells of undetermined significance (ASCUS) which is synonym of the terminology cellular atypia, low grade squamous intra-epithelial lesion (LSIL) which is synonym of the terminology mild dysplasia or cervical intraepithelial neoplasia I (CIN I), here the

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abnormality is confined to 1/3 of the cervical squamous epithelium and high grade squamous intra epithelial lesion (HSIL) comprising cervical intraepithelial neoplasia II (CINII) or moderate dysplasia (approximately two thirds of cervical squamous epithelium involvement) and cervical intraepithelial neoplasia III (CINIII) or severe dysplasia with cervical carcinoma insitu (more than two thirds to a full thickness of cervical squamous epithelium involvement without involvement of basement membrane)⁵. Cervical cancer can be prevented through screening programs, designed to identify and treat the precancerous lesions. Pap smear which was introduced in 1943 remains the main cervical cancer screening test. Population screening with cervical Pap smears performed regularly for all women who are or have been sexually active every 1 to 3 years until age 35 and then at 5 years intervals can reduce both incidence and mortality rate from invasive cervical cancer². Successive mass screening using the Pap test to diagnose premalignant cases decreased the incidence and mortality from cervical cancer over 40 percent in U.S and UK since 1973⁶. In situations with abnormal cervical cytology, further evaluation by colposcopy is needed which generally performed along with colposcopy-directed biopsies. The biopsy is performed to rule out invasive disease and to determine extent of pre invasive lesion². Women can lower their risk for developing cervical dysplasia by quitting smoking, waiting to have intercourse until age 18 to 20, having only a few sexual partners in a lifetime, not using contraceptive pills for long time, and preventing infection with sexually transmitted diseases especially persistent infection with human papilloma virus (HPV), as these certain health problems with lifestyle choices may raise a woman's risk for cervical dysplasia⁶. With early detection, treatment, and close follow-up care, nearly all cervical dysplasia can be cured. If untreated, the mild to moderate stages of dysplasia often grow more severe and up to 30% to 50% of

carcinoma in situ cases progress to invasive cancer of the cervix². To the best of our knowledge, there hasn't been any similar study performed on a large sample size to look at the rate of abnormal Pap smear findings among women in Erbil city. The aim of this study was to determine the frequency of abnormal cervical cytology among women underwent Pap smear and to find the most common risk factors associated with abnormal Pap smear results.

Methods

This hospital-based cross sectional study included asymptomatic women for whom cytological examination of the Pap smears taken from cervix was performed at the Maternity Teaching Hospital, Azady primary health care center, and Kurdistan primary health care center in Erbil, Iraqi Kurdistan in the period from January to December 2009. The study population involved 2,146 women who were married for more than one year, including those in menarche or during menopause; Women who received any vaginal treatment or douches 48 hours prior to the Pap smear were excluded from the study. Pap smears collected between 10th -20th day of the menstrual cycle and were obtained by rotating Ayer's spatula 360 degrees around transformation zone of cervix, then the spatula sample was spread evenly on the glass slide which was inserted into 95% ethyl alcohol for fixation. The data used in this study included different socio-demographic variables such as age, age at marriage, duration of marriage, number of marriages, sequence among wives, gravidity, religion, occupation of women and her husband as well, smoking and alcohol consumption and finally types of contraception used by women. Socioeconomic status was assessed using a scale derived from a study by Al-Mashhadani⁷. Five parameters used to score the socioeconomic status of the family such as type of living home (rented or owned), the occupation of the head of family, monthly income, and number of family member per bedroom. Based

on these parameters, socioeconomic status was classified into Low (0-4), Intermediate (5-7) and High (>7) ⁷. Current smokers were defined as having one or more cigarettes per day. All Pap smears cytological evaluation were conducted by the same cytologist in the maternity teaching hospital laboratory unit using Bethesda classification system to classify the cytological abnormalities to normal, ASCUS, LSIL, HSIL and invasive carcinoma ⁵. Data were analyzed using SPSS Statistical software (version 17.0 for windows, SPSS Inc., Chicago, IL, USA). For descriptive purposes, continuous and discrete variables were presented as mean \pm SD and rates and proportions, respectively. For analytic purposes, independent sample t-test and chi-square test were used. When Chi-square test wasn't applicable, Fisher's exact test was used instead. Logistic regression analysis was used to predict the independent variables. A P-value of ≤ 0.05 was considered statistically significant.

Results

The total number of women included in the study was 2,146 women. The mean age was 34.68 ± 8.8 years, ranging between 12 to 65 years. The mean age at marriage was 18.79 ± 4.4 years, starting as young as 10 years and reaches up to 40 years. The average duration of marriages at time of taking Pap smear was 16 ± 9.1 years (ranging from 1 to 50). The mean age of women at time of first baby delivery was 19.8 ± 4.2 years (range between 12 to 39 years). Only 9.3% of the cases were nulliparous at time of data collection, meanwhile, the mean number of pregnancies among the studied sample was 4.2 ± 2.7 with the number of pregnancies reaching as high as 15 gravida. Up to 38.4% of the cases had history of miscarriages with an average number of miscarriages 0.71 ± 1.1 . Among the examined women, 4.8% were second wives, while third wives constitute only 0.5% of the total number of women. On the other hand, 3.3% of the women were married for the second time.

The proportion of Christian women involved in Pap smear was very scarce (0.7%). Regarding socioeconomic status, the majorities (92.5%) of the women were of intermediate economic status, and 65.8% of the cases can't read and write, while only 8.1% of the cases finished intermediate and high school education. Tobacco use was recorded among (2.9%) of the cases and only (0.1%) of the cases drank alcohol. The cytological examination of the Pap smears was found to be normal in (88.4%) of women; meanwhile, 247 (11.4%) women had abnormal findings which varied from ASCUS (2.9%) to the presence of LSIL (6.3%), HSIL (2.1%) and invasive carcinoma (0.1%). Cervical exudates of variable severities were found in about 1% of the cases. Meanwhile, cervicitis was also found, ranging from mild (1.7%) to severe one (0.7%). The most common microorganisms detected on the cervical smears were *Haemophilus vaginalis* (3.3%) and *Candidiasis* (2.8%) as seen in Table 1. Regarding hormonal background of the cervical epithelium, the mean for the superficial layer \pm SD was 32.18 ± 19.6 ; while the intermediate layer was 61.19 ± 20.5 and the parabasal layer 5 ± 12.14 . Patients with abnormal findings on Pap smear had a mean age of 36.71 years, which was significantly older than those with normal results ($p < 0.001$). The duration of marriage was also found to be significantly longer among those with abnormal Pap smear (18.40 years versus 15.60 years, $p < 0.001$). There was no significant relation between abnormal results on Pap smear and age at marriage, at first delivery, and gravidity, Table 2. Among the studied group, 62 (3%) women admit to have history of cigarette smoking, Table 3. Cigarette smoking was reported among 17.8% of those with abnormal Pap smears, especially among women who had ASCUS, which was significantly higher among 8.1% of the smokers compared to 2.7% of the cases seen among non-smokers ($p=0.031$). No significant association was seen between

the grade of the Pap smear and patients having more than one marriage, religion, alcohol drinking, socioeconomic status and education. While only 7.3% didn't use contraception, the rest used different contraceptive methods such as Oral Contraceptive Pills (16.5%), intrauterine contraceptive device (43.5%), condoms (4.6%), and other methods (28.1%). Table 4 demonstrates the distribution of contraceptive method used according to the Pap smear results. No significant association

was seen between using contraception and the presence of abnormal cervical smear findings ($p > 0.05$). among the three significant associated factors (Smoking, Duration of marriage and Age of patient) with abnormal Pap smear as tested by Chi-square, we have found that two factors (marriage for more than 20 years and patients older than 30 years) are regarded as significant predictive factors of positive Pap smear Table 5.

Table 1: Laboratory Findings of Pap smear analysis.

Examination		Frequency	Percent
Grading	Negative	1885	87.8
	ASCUS	63	2.9
	LSIL	136	6.3
	HSIL	46	2.1
	Invasive Carcinoma	2	0.1
	Missing	14	0.7
	Total	2146	100
Background	Normal Endocervical Cells	1957	91.2
	Metaplasia	46	2.1
	Reactive Pattern	40	1.9
	Exudate+	24	1.1
	Exudate++	1	0.03
	Exudate+++	3	0.1
	Mild Cervicitis	36	1.7
	Moderate Cervicitis	19	0.9
	Severe Cervicitis	16	0.7
	Missing	4	0.2
Biology	Total	2146	100
	No biological causes	1969	91.8
	Trichomonus Vaginalis	2	0.1
	Hemophilus Vaginalis	71	3.3
	Listeria	11	0.5
	Candidiasis	61	2.8
	Mycoplasma	7	0.3
	Herpes Virus 2	7	0.3
	CMV	4	0.2
	Others	14	0.7
Total	2146	100	

Table 2: Pap smear finding among the studied group according to patient age, age at marriage, duration of marriage, age of mother at the time of first delivery and number of pregnancies and miscarriages.

	Pap smear Findings	N	Mean ± Std. Deviation	P value	95% CI
Age of patients (in years)	Negative or reparative pattern	1875	34.40±8.778	<0.001*	(-3.5 to -1.05)
	Abnormal findings	245	36.71±9.414		
Age at marriage (in years)	Negative or reparative pattern	1873	18.79±4.387	0.721	(-0.47 to 0.7)
	Abnormal findings	243	18.68±4.681		
Duration of marriage (in years)	Negative or reparative pattern	1869	15.60±8.972	<0.001*	(-4.13 to -1.47)
	Abnormal findings	240	18.40±9.958		
Age at the time of 1st delivery (in years)	Negative or reparative pattern	1517	19.85±4.241	0.09	(-0.1 to 1.20)
	Abnormal findings	181	19.30±4.207		
Number of Pregnancies	Negative or reparative pattern	1885	4.16±2.729	0.09	(-0.73 to 0.05)
	Abnormal findings	247	4.50±2.982		
Number of miscarriages	Negative or reparative pattern	1885	.70±1.173	0.3	(-0.22 to 0.08)
	Abnormal findings	247	.77±1.173		

*Statistically significant

Table 3: Smoking and Pap smear findings among the studied group.

Grading		Tobacco Use		Total	P-value
		Non Smoker	Smoker		
Negative	No.	1828	51	1879	0.152
	%	88.7%	82.3%	88.5%	
LSIL	No.	132	4	136	1.00
	%	6.4%	6.5%	6.4%	
HSIL	No.	44	1	45	1.00
	%	2.1%	1.6%	2.1%	
Infiltrative Carcinoma	No.	1	1	2	0.058
	%	.0%	1.6%	.1%	
ASCUS	No.	56	5	61	0.031*
	%	2.7%	8.1%	2.9%	
Total	No.	2061	62	2123	
	%	100%	100%	100%	

*Statistically significant

Table 4: Contraceptive method use and Pap smear findings among the studied group.

Contraceptive method used	Pap smear results		P-value
	Negative or reparative pattern	Abnormal findings	
OCP	234 (16.5%)	24 (14.8%)	0.580
IUCD	615 (43.5%)	66 (40.7%)	0.505
Condom	65 (4.6%)	8 (4.9%)	1.00
Others	397 (28.1%)	49 (30.2%)	0.581
No contraceptive method used	103 (7.3%)	15 (9.3%)	0.429
Total	1414	162	

Table 5: The relation between smoking, duration of marriage and age of patient with the presence of abnormal Pap smear results using logistic regression analysis

Independent variables	B	S.E.	df	P-value	Exp(B)
Smoking	-0.536	0.340	1	0.114	0.585
Duration of marriage (> 20 Years)	-0.617	0.139	1	<0.001*	0.540
Age of patient (>30)	-0.356	0.148	1	0.016*	0.700

*Statistically significant

Discussion

The Pap smear results in the studied group were abnormal in 11.4% of all cases, but only 0.1% of the females found to have an invasive cervical carcinoma. Increasing women age has been considered a principal risk factor for cervical cancer. In this study, women with abnormal Pap smear findings had a mean age of 36.71±9.414 years, and this was significantly older than the mean age of women having normal pap smear findings (34.40±8.778 years). A similar relation between women age and presence of cervical cancer has been drawn from other similar studies⁸. Invasive cervical cancer develops over many years, even decades, with a peak or plateau in risk around 35-55 years of age⁹⁻¹⁰. Women who were older than 30 years were significantly more likely to have abnormal

Pap smear results, (p=0.016), and this is consistent with the recommendation of cervical cancer screening programs by the World Health Organization (WHO) which recommend performing screening for cervical cancer to all women after 30 years of age⁷. although there was a limited number of women in this sample (3%) who admit to smoke in relation with the total number of the study population, but this study was able to find a significant association between smoking and the presence of abnormal Pap smear cytology (ASCUS). Many previous studies concluded association between cervical cancer and smoking¹¹⁻¹³. Nicotinic metabolite has been found on the cervical mucus of smokers, leading to a direct carcinogenic action of cigarette smoking¹⁰. While the age marriage, which in this society reflects

the age at first intercourse, was not significantly different between women with normal and those with abnormal Pap smears, the duration of marriage was proven in this study to be a significant factor even after controlling for age difference. Those women who were married for more than 20 years were more likely to have abnormal Pap smear results and this association was statistically significant ($P < 0.001$). The mean number of pregnancies was slightly higher among those with abnormal Pap smear; however it wasn't significantly different from those with normal findings. Studies in North America and Central and South America showed that the number of pregnancies is a risk factor for cervical cancer¹⁴. According to this study, there was no significant association between the use of different contraceptive methods (IUCD, Condom, OCP and others) and the presence of abnormal Pap smear results. However, the data used didn't involve the duration of contraceptive use. There is an excess risk of cervical cancer associated with long-term use (12 years or more) of oral contraceptives, and this association is somewhat stronger for adenocarcinomas than for squamous cell carcinomas¹⁰. The association with oral contraceptive use observed in studies in which precancer was an outcome may have been due to detection bias, since women who use oral contraceptives undergo more frequent gynecological examinations, and are thus more likely to have disease detected early, than those who do not use them¹⁴. Identifying the factors that contribute to the development of cervical cancer in addition to HPV infection is important because most women who receive a positive HPV test result do not go on to develop disease and therefore it is important to indicate what other factors are considered to be associated with cervical cancer in this community. Furthermore, by identifying which women have a lower risk of disease it may be possible to reduce the number of unnecessary colposcopies. These results could have important implications for future

screening activities for the prevention of cervical cancer in Erbil and other provinces in Iraq. Recently, prophylactics and therapeutic vaccination has shown promising results for preventing HPV infection and thus reducing the incidence of cervical neoplasia. However, development of effective vaccines would require a comprehensive study of the HPV genotypes in different regions of the world¹⁵. Further studies would be needed to measure the HPV infection serotype commonly present in Kurdistan and Iraq and the combined effect of viral infection together with other risk factors in initiating precancerous changes detected by Pap smear.

Conclusion

This study was able to indicate that during reproductive life, the older ages of women and longer duration of marriage were associated with an increased risk of abnormal Pap smear results. Therefore, it is recommended to target these groups of women when planning for the future screening programs for cervical cancer in this community. There was no significant difference between abnormal results on Pap smear and age of women at marriage, age at time of first delivery, and the gravidity.

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References

1. Arbyn M, Sankaranarayanan R, Muwonge R, Keita N, Dolo A, Mbalawa CG et al. Pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India. *Int J Cancer* 2008;123(1):153-60.

2. Parkin MD, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; 55:74-108.
3. World Health Organization [homepage on the Internet]. Catala d' Oncologia. Human Papiloma Virus Information Center Report-Iraq. [Updated 2010 Sept 15; cited 2011 Feb 15]. Available from: <http://apps.who.int/hpvcentre>.
4. Rosai J. Rosai and Ackermani surgical pathology. 9th ed. St.Louis:CV Mosby;2004.
5. Scott JR, Gibbs RS, Karlan BY, Haney AF, editors. Danforth's obstetrics and gynecology. 9th ed. Philadelphia,: Lippincott Williams and Wilkins; 2003.
6. Patro BK, Nongkynrih B. Review of screening and preventive strategies for cervical cancer in India. *Indian J Public Health* 2007;51:216-21.
7. Al-Mashadani JS. Hepatitis B virus markers in diabetic.[MSc Thesis]. Baghdad: Baghdad University; 1988.
8. Flores YN, Bishai DM, Shah KV, Lazcano-Ponce E, Löörincz A, Hernández M, et al. Risk factors for cervical cancer among HPV positive women in Mexico. *Salud Publica Mex.* 2008;50:49-58.
9. Muñoz N, Bosch FX, De Sanjosé S, Herrero R, Castellsagué X, Shah KV Snijders PJF and Meijer CJLM. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med.* 2003;348: 518-27.
10. Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical Cancer. *Asian Pac J Cancer Prev.* 2010;11:537-8.
11. Winkelstein W. Smoking and cervical cancer: current status — a review. *Am J Epidemiol* 1990;131:945-57.
12. Castellsague X and Muñoz N. Cofactors in human papillomavirus carcinogenesis-role of parity, oral contraceptives, and tobacco smoking. *J Natl Cancer Inst Monogr.*2003;31: 20-28
13. Tay SK and Tay KJ. Passive cigarette smoking is a risk factor in cervical neoplasia. *Gynecol Oncol.* 2004;93: 116–20.
14. Franco EL, Duarte-Franco E, Ferenczy A. Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. *CMAJ* 2001;164 (7):1017-25.
15. Ghaffari SR, Sabokbar T, Mollahajian H, Dastan J, Ramezanzadeh F, Ensani F, Yarandi F, Mousavi-Jarrahi A, Mohagheghi MA, Moradi A Prevalence of Human Papillomavirus Genotype in Women with Normal and Abnormal Cervical Cytology in Iran. *Asian Pacific J Cancer Prev.* 2006,7:529-32.