Study of Prevalence of Abnormal Cervical Cytology in Al-Shatby Maternity University Hospital

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Abstract

Introduction: Cervical cancer is the most common cause of preventable cancer related deaths; cervical cancer has a long pervasive phase (cervical dysplasia); the prevalence of cervical dysplasia varies according to the socioeconomic characteristics and geographic areas of the population studied. Low-grade lesions regress spontaneously in a significant number of patients, while high grade lesions will progress to an invasive cancer if left untreated. Cervical cancer screening is an important component of the World Health Organization (WHO) strategy for combating cervical cancer. The incidence and prevalence of cervical cancer has reduced remarkably over the last three decades in developed countries where there are effective, well-coordinated screening programs, and treatment of cervical dysplasia, while in developing countries it has been increasing and has constituted major health problems among women where there are no well-coordinated and effective screening programs, also resources are very low and no insurance can cover this programs. Aim of the work: The aim is to assess the prevalence of abnormal cervical cytology in Al Shatby Maternity University Hospital patients using Pap smear. Materials and methods: Inclusion criteria: 1) Married woman from 3 years or more; 2) Women age from 21 to age 65 years. Exclusion criteria: 1) Previously known cervical cancer patient; 2) Virgin females; 3) Woman with active vaginal bleeding. Results: 83% of patients were −ve intraepithelial neoplasia {37.7% was normal cytology and 45.3% was inflammatory}. 17% was +ve intraepithelial neoplasia (abnormal cytology), {11.1% ASCUS, 2.9% LSIL, 1.3% HSIL, 1.1% ASC-H, 0.3% AGS-NO, 0.3% AGS-Favour Neoplastic}. Prevalence of abnormal cervical cytology in age group less than 30 years was 8.4% which is lower than prevalence in the middle age group which was 19.9%. Prevalence of abnormal cervical cytology in women with normal vaginal delivery was higher than those with caesarean delivery. 39.8% of our patients were passive

and active smokers 61.2% of their Pap smear was abnormal cytology. 78.9% of abnormal cytology was among patients from low socioeconomic class (rural areas). Abnormal cervical cytology in patients with high parity was 69% which is higher than abnormality found in lower parity. 60.2% of abnormal cervical cytology was in patients who became sexually active before age of 20 years. Prevalence of abnormal cervical cytology was higher in patients with multiple sexual partners (56.5%) than patients with single sexual partner (13.3%). Conclusion: Cervical cytology remains the gold standard for cervical cancer screening and the use of Bethesda system is a simple and accurate method for diagnosis and management of cases with abnormal cervical cytology.

Keywords

1. Introduction

Worldwide, cervical cancer was the fourth most common cancer among females in 2012, accounting for 7.5% of all female cancer deaths. About 87% of cervical cancer deaths occurred in the less developed regions [1]. In Egypt, according to the World Health Organization (WHO) most recent estimates, every year 866 women are diagnosed with cervical cancer and 373 die from the disease. Cervical cancer ranks as the 13th most frequent cancer among women in Egypt and the 10th most frequent cancer among women between 15 and 44 years of age in 2012 [2]. CIN is a spectrum of intra-epithelial cellular abnormality suggestive of neoplasia. The process of dysplasia of cervical cells means abnormal maturation. [3] According to Bethesda system 2014, CIN is classified into three grades which include mild, moderate and severe degrees (CIN 1, 2 and 3 respectively). The main risk factors for cervical dysplasia include HPV infection with serotypes 16, 18, 31, 33, 35 [4]. Other risk factors include early sexual activity, smoking, high parity and immunosuppression. Screening of pre-invasive disease of the Cervix aims to prevent morbidity and mortality from cervical cancer. Screening starts at the age of 21and continues till the age of 65years. Methods for cervical screening: The main screening methods of cervical cancer are: 1) Cervical cytological screening (Pap smear); 2) Visual inspection with acetic acid (VIA); 3) Visual inspection with Lugol's iodine (VILI); 4) Colposcopy; and 5) Cervical biopsies. The conventional method (Pap smear): The Pap test was developed by Dr. George Papanicolaou in 1941. Cervical screening always requires an endocervical and an ectocervical sample, using wooden or plastic spatulas: Ayre and extended tip or Aylesbury [5]. Exfoliated cells are collected from the transformation zone of the cervix and transferred directly to the slide and fixed using the conventional technique. In practice, there are several problems with the Pap test. They include the adequacy of the samples, the difficulty of microscopic screening, based on

recognizing few abnormal cells among many thousands of cells in each sample as well as high rate of false negative results. Liquid-based technology (LBC) is a newer technique that employs liquid-based cytology (e.g. Thin Prep) have been developed to improve the sensitivity of screening. LBC involves placing the cervical sample directly into a liquid fixative; slide preparation occurs in the laboratory. Improved slide preparation can allow for a more even distribution of cells and decreased background artifact and overlapping of cells. Disadvantages of LBC approach are lack of availability and being more expensive than conventional Pap testing. The Bethesda System the standard universal system used for interpretation of Pap smear results [6]. Types of results using Betheseda system include: Negative for intraepithelial lesion or malignant atypical squamous cells. 1) Atypical squamous cells of undetermined significance (ASC-US); 2) Atypical squamous cells-cannot exclude HSIL (ASC-H); 3) Low grade squamous intraepithelial lesion (LGSIL or LSIL); 4) High grade squamous intraepithelial lesion (HGSIL or HSIL); 5) Squamous cell carcinoma; 6) Atypical Glandular Cells not otherwise specified (AGC-NOS); 7) Atypical Glandular Cells, suspicious for AIS or cancer (AGC-neoplastic); 8) Adenocarcinoma in situ (AIS); 9) Adenocarcinoma. Low grade lesions correspond to CIN1 and high grade lesions correspond to CIN 2 and 3.

2. Aim of the Work

The aim of work is to assess the prevalence of abnormal cervical cytology in Al Shatby Maternity University Hospital of Alexandria, Egypt, patients using Pap smear.

3. Subjects and Methods

1000 women, median age 43 years (range 21 - 65), attending the Gynecology Clinic at El-Shatby Maternity Hospital, Alexandria University Hospital over a 12-month period, starting from February 2019 to January 2020 were enrolled in the study after taking a written consent and approval of ethics committee.

The sample size was determined by the medical research institute, department of statistics to evaluate the accuracy of this statistical work.

Statistical analysis of the data [7]:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) [8] Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level

3.1. Inclusion Criteria

1) Married woman from 3 years or more;
2) Woman age from 21 to age 65 years.

3.2. Exclusion Criteria

1) Previously known cervical cancer patient;

2) Virgin females;

3) Woman with active bleeding.

3.3. Methods

All ladies that participated in this study had the following:

1) A written consent of agreement of study participation;

2) A full booking procedure which include a detailed history taking, general and pelvic examination;

3) Pap smearing.

3.4. Collection of Specimen Steps

1) A sterile dry speculum is inserted into vagina and the cervix clearly visualized. The cervical os should be located.

2) The pointed end of the Ayers spatula is inserted into the cervical os in a nulliparous cervix and the rounded end of the spatula inserted into the patulous os of a parous woman. The device rotated 360 degrees to remove the cells from the region of the transformation zone, squamocolumnar junction and endocervical canal.

3) The material on the spatula or brush spread immediately on a glass slide which has been previously labeled with the patient's name.

4) The fixation is done by 95% ethyl alcohol. Spray fixation is used; the specimen fixed immediately by spraying at a right angle from a distance of 20 cm. The slide is placed on a flat surface for spray fixation. Very fast fixation, within a few seconds, was done which is essential to prevent drying artifacts the slides transported to the cytology laboratory in a container for processing.

The Pap smears were examined by staff of the Pathology Department, Faculty of Medicine, Alexandria University using Bethesda system 2014 [5].

4. Results

4.1. Statistical Analysis of the Data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp) (75). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

4.2. The Used Tests Were

1) Chi-square test:

For categorical variables, to compare between different groups.

2) Student t-test:

For normally quantitative variables, to compare between two studied groups.

3) Mann Whitney test:

For abnormally quantitative variables, to compare between two studied groups.

4.3. Sample Size

Sample size was calculated based on a previous study and by using Med Calc statistical software. Assuming area under ROC to be 0.80, an alpha of 0.05 and power of study 90.0%, a typical advice is to reject the null hypothesis H0 if the corresponding p-value smaller than 0.05, a minimum sample size required was 50 patients will be required for this study.

4.4. Socio-Demographic Data

Distribution of studied patients regarding age:

According to patients' ages, 321 (32.1%) patients' ages were <30 years, 480 (48%) patients' ages ranged between 30 - <40 years, 154 (15.4%) patients' ages ranged between 40 - <50 years, 27(2.7%) patients' ages ranged between 50 - <60 years and 18 (1.8%) patients' ages were ≥60 years, in general patients' ages ranged between 20 - 63 years with mean ± S.D. 34.18 ± 7.825 years (Figure 1; Table 1).

4.5. Marital Data

As regard of patients marital status 970 (97%) patients were married while 30 (3%) patients were not married at that time as 14 (47%) patients were divorced and 16 (53%) patients were widow (Table 2).

Age of 1st intercourse: As regard to age of first Intercourse of patients were ranged between 15 - 30 years with mean ± S.D. 22.981 ± 3.528 years (Table 3).

Number of previous marriages: According to number of marriage of patients it was ranged between 1 - 3 husband with mean ± S.D. 1.120 ± 0.352 (Table 4).

Table 1. Distribution of studied sample according to patient's age (years).

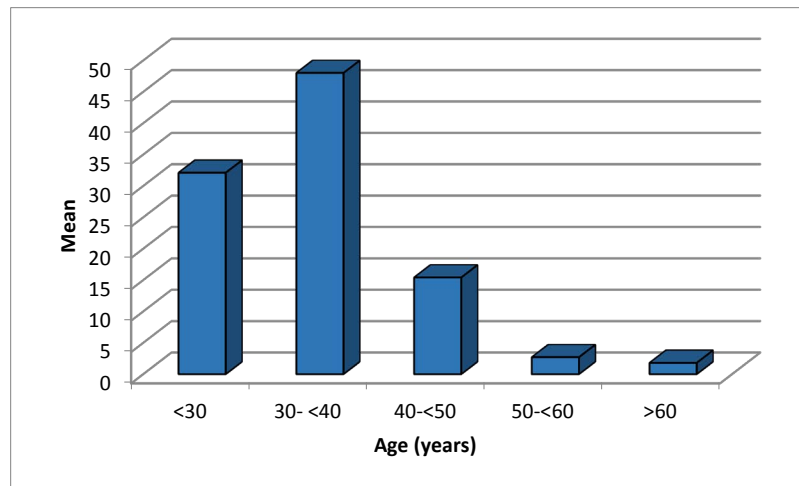| Age	No	%
<30	321	32.1
30 - <40	480	48
40 - <50	154	15.4
50 - <60	27	2.7
≥60	18	1.8
Total	1000	100
Min-Max	20 - 63	
Mean ± S.D	31.18 ± 7.825	

Figure 1. Distribution of studied sample according to patient's age (years).

Table 2. Distribution of studied sample according to marital status.

Marital Status	No	%
Married	970	97
Not married now	30	3
Divorced	14	47
Widow	16	53
Total	1000	100

Table 3. Distribution of studied sample according to patient's age of First Intercourse.

Marital Status	Age of first Intercourse
Min.	15
Max.	30
Mean.	22.981
S.D	3.528

Table 4. Distribution of studied sample according to patient's No. of marriage.

Marital Status	No. of marriage
Min.	1
Max.	3
Mean.	1.120
S.D	0.352

4.6. Delivery Status

As regard to mode of previous deliveries showed that 432 (43.2%) patients had CS delivery, 449 (44.9%) patients had NVD, 77 (7.7%) patients had NVD then CS delivery and 42 (4.2%) patients had no previous deliveries (**Table 5**; **Figure 2**).

Table 5. Distribution of studied sample according to mode of previous deliveries.

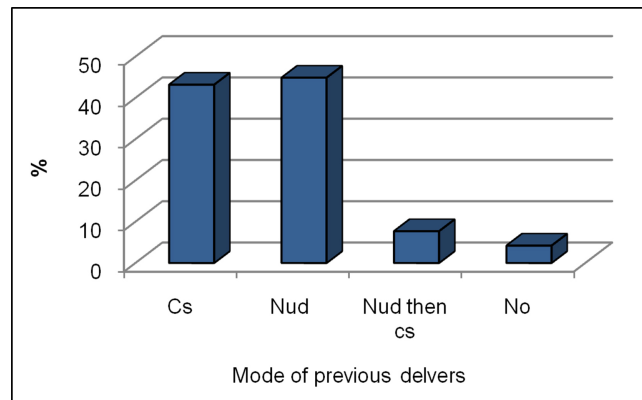| Mode of previous delvers	No	%
Cs	432	43.2
NVD	449	44.9
NVD then CS	77	7.7
No	42	4.2
Total	1000	100

Figure 2. Distribution of studied sample according to mode of previous deliveries.

Table 6 is distribution of studied sample according to mode of previous deliveries Distribution of studied sample according to patient's parity:

Patient parity ranged between 0 - 10 delivaries with mean ± S.D. 2.62 ± 1.460 (Table 6).

4.7. Smoking Status

According to cigarette smoking showed that 602 (60.2%) patients were non smokers, 260 (26%) patients were passive smokers and 138 (13.8%) patients were active smokers (Table 7).

4.8. Contraception Status

- As regard to oral contraceptive pills (OCPs) usage, 360 (36%) patients were on OCP while 640 (64%) patients were non user (Table 8).
- As regard to IUD usage, 216 (21.6%) patients were IUD user and 784 (78.4%) patients were non user (Table 9).

4.9. Gynecological Data

As regard to related gynecological symptoms there were 660 (66%) patients were normal, 286 (28.6%) patients had vaginitis, 53 (5.3%) patients had abnormal vaginal bleeding, and 1 (0.1%) patients had cervical bleeding on touch (Table 10; Figure 3).

Table 6. Distribution of studied sample according to patient's parity.

	Parity
Min.	0
Max.	10
Mean.	2.26
S.D	1.460

Table 7. Distribution of studied sample according to cigarette smoking.

Cigarette Smoking	No	%
No	602	60.2
Passive	260	2.6
Active	138	13.8
Total	1000	100

Table 8. Distribution of studied sample according to OCP user.

OCP user	No	%
Yes	360	36
No	640	64
Total	1000	100

Table 9. Distribution of studied sample according to IUD user.

IUD User	No	%
Yes	216	21.6
No	784	78.4
Total	1000	100
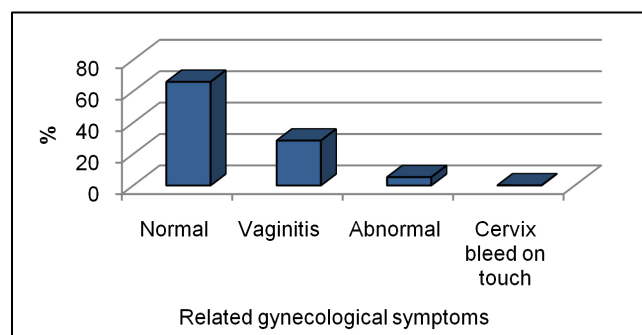
Figure 3. Distribution of studied sample according to related gynecological symptoms.

4.10. Cervical Findings

As regard to cervical finding, 655 (65.5%) patients were normal, and 345 (34.5%) patients were abnormal as 183 (18.3%) patients had cervical infection; 83 (8.3%) patients had Nabothian follicle; 28 (2.8%) patients had cervical polyp; 19 (1.9%) patients had cervical bleeding on touch; 18 (1.8%) patients had ectropion; 12 (1.2%) patients had cervical ulcer and 2 (0.2%) patients had cervical nodule (Table 11; Figure 4).

4.11. Pap Smear Results

According to result of Pap smear, 830 (83%) patients were negative intraepithelial neoplasia as 377 (37.7%) patients were normal smear and 453 (45.3%) patients were inflammatory smear, while 170 (17%) patients were positive intraepithelial neoplasia as 111 (11.1%) patients were ASCUS; 29 (2.9%) patients were LSIL; 13 (1.3%) patients were HSIL; 11 (1.1%) patients were ASC-H; 2 (0.2%) patients were AGS-US; 2 (0.2%) patients were AGC; 1 (0.1%) patients were AGS-NO and 1 (0.1%) patient was AGS-Favour Neoplasia (Table 12; Figure 5).

Table 10. Distribution of studied sample according to related gynecological symptoms.

Related gynecological symptoms	No	%
Normal	660	66
Vaginitis	286	28.6
Abnormal	53	5.3
Cervix bleed on touch	1	0.1
Total	1000	100

Table 11. Distribution of studied sample according to patient's cervical finding.

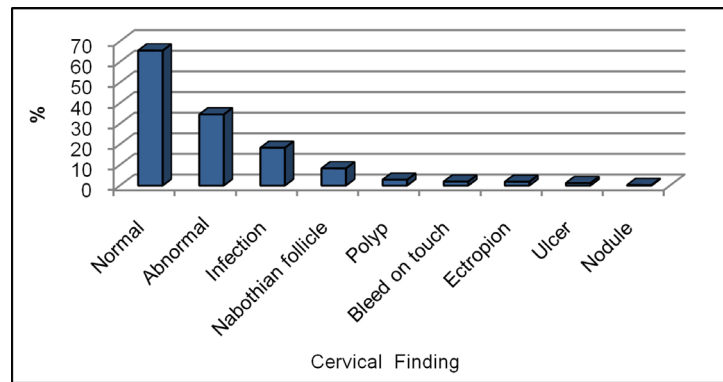| Cervical finding	No	%
Normal	660	65.5
Abnormal	345	34.5
Infection	183	18.3
Nabothian follicle	83	8.3
Polyp	28	2.8
Bleed on touch	19	1.9
Ectropion	18	1.8
Ulcer	12	1.2
Nodule	2	0.2
Total	1000	100

Figure 4. Distribution of studied sample according to patient's cervical finding.
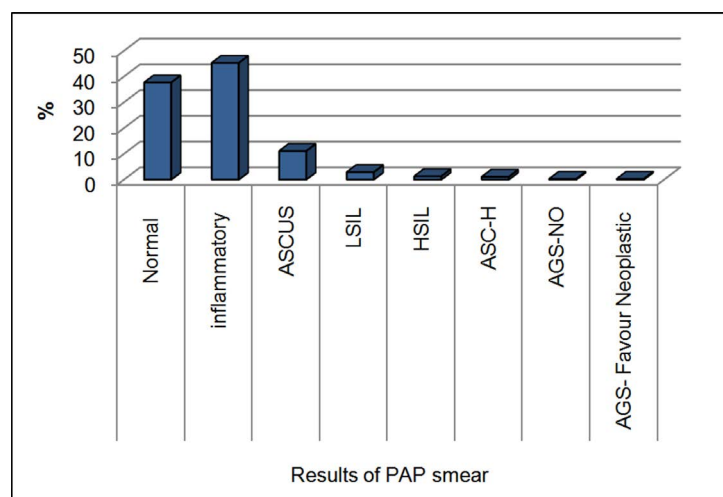

Figure 5. Distribution of studied sample according to patient's result of Pap smear.

Table 12. Distribution of studied sample according to patient's result of Pap smear.

Results of Pap smear	No	%
−ve intraepithelial neoplasia	830	83
Normal	377	37.7
inflammatory	453	45.3
+ve intraepithelial neoplasia	170	17
ASCUS	111	11.1
LSIL	29	2.9
HSIL	13	1.3
ASC-H	11	1.1
AGS-NO	3	0.3
AGS-Favour Neoplastic	3	0.3
Total	1000	100

According to relation between patient's age and result of Pap smear, negative intraepithelial neoplasia group were 294 (35.4%) patients and their age were <30 years, 395 (47.6%) patients' ages ranged between 30 < 40 years, 113 (13.7%) patients' ages ranged between 40 < 50 years, 14 (1.7%) patients' ages ranged between 50 - <60 and 14 (1.7%) patients' ages were ≥60 years while in positive intraepithelial neoplasia group 27 (16.1%) patients' ages were < 30 years, 85 (49.8%) patients' ages ranged between 30 < 40 years, 41 (24.4%) patients' ages ranged between 40 < 50 years, 13 (7.5%) patients' ages ranged between 50 < 60 years and 4 (2.2%) patients' ages were ≥60 years. There was statistically significant difference between two groups where P = 0.001 (**Figure 6**).

According to relation between patient's cigarette smoking and result of Pap smear, there were negative intraepithelial neoplasia group (536 (64.6%) patients were non-smokers; 187 (22.5%) patients were passive smokers and 107 (12.9%) patients were active smokers) while in positive intraepithelial neoplasia group, 66 (39.1%) patients were non-smokers, and 73 (42.7%) patients were passive smokers and 31 (18.2%) patients were active smokers. There was statistically significant difference between two groups where P = 0.001 (P significant as P < 0.05) (**Figure 7**).

As regard to relation between patient's residence and result of Pap smear there were negative intraepithelial neoplasia group (169 (20.4%) patients were from rural areas and 661 (79.6%) patients were from urban areas) while in positive intraepithelial neoplasia group, 134 (78.9%) patients were from rural areas and 36 (21.1%) patients were from urban areas. There was statistically significant difference between two groups where P = 0.001 (P significant as P < 0.05) (**Figure 8**).

5. Discussion

Cervical cancer (CC) is a preventable neoplasm with known etiology and precursor lesions of slow evolution, could to be screened. Cervical cancer remains a huge burden in developing countries where cervical cancer screening rates are currently low, ranging between 6% - 8% [9].
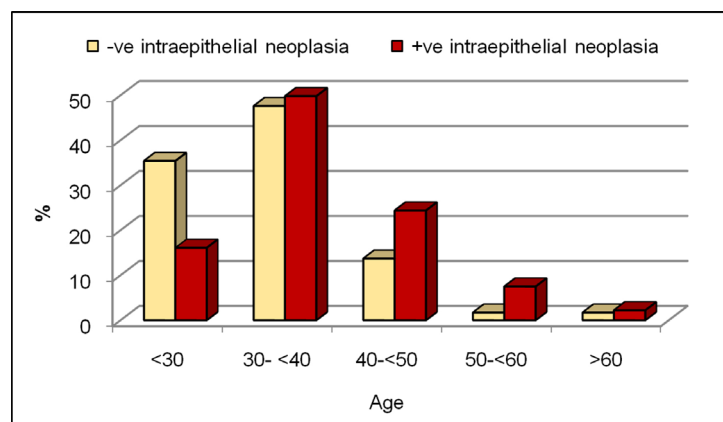

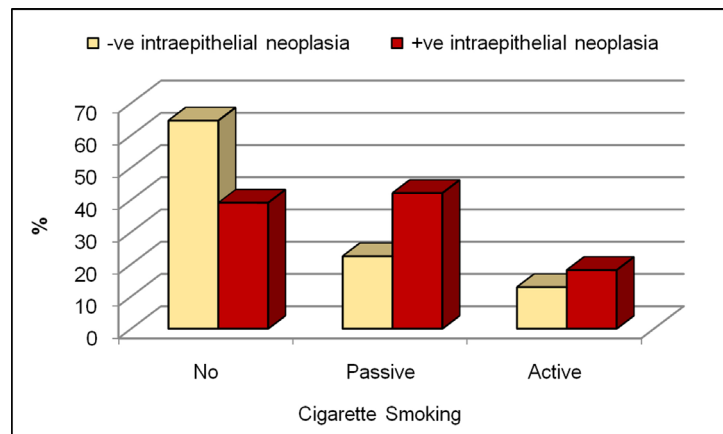**Figure 6.** Relation between patient's age and result of PAP smear.

Figure 7. Relation between patient's cigarette smoking and result of Pap smear.
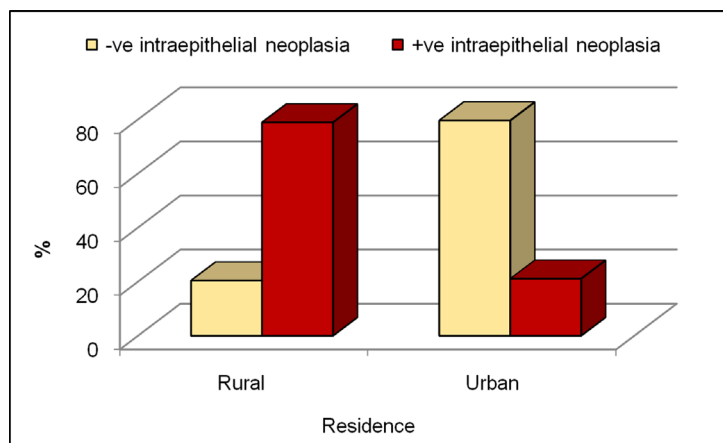

Figure 8. Relation between patient's residence and result of Pap smear.

A systematic analysis of cervical cancer in 187 countries between 1980 and 2010 found that developed countries with comprehensive cancer screening programs have recorded sustained declines in cervical cancer incidence and mortality while many developing countries in sub-Saharan Africa have experienced upsurges in new cases [10].

In Egypt early detection of precancerous cervical lesions through screening remains a critical health care service intervention for reducing cervical cancer incidence and mortality particularly in low-resource settings where HPV vaccination coverage is poor [11].

Cytology-based screening is a highly effective method of secondary prevention and control of cervical cancer in developed countries. (82, 83) Nearly all cervical cancer cases arise from CIN lesions, but not all CIN lesions progress to cancer. Actually, many persist without change or even regress. (84) It is believed that CIN I and II are more likely to regress than to progress; only 10.0%-15.0% of CIN I lesions are progress to CIN II and III/CIS, and 50.0% of CIN II and 30.0% of CIN III regress spontaneously [12] [13] [14] [15].

Our current study was conducted on 1000 patients from Al-Shatby Maternity University Hospital outpatient clinic. Smear results were categorized into 3 main groups; normal, inflammatory and abnormal (+ve intraepithelial neoplasia). 37.7% of patients were normal, 45.3% of them showed an *inflammatory* smear (the majority of cases) and 17% of them showed abnormal cytology results. Cases with abnormal cervical cytology (ACC) were due to ASCUS in 11.1%, LSIL in 2.9%, HSIL in 1.3%, ASC-H in 1.1%, AGS-NO in 0.3% and AGS-favour neoplasia in 0.3% of cases. This means that the majority of cellular abnormality we found was ASCUS which represent almost one tenth of cases of cases of abnormal cytology. This was agreement with Mosuro *et al.* (2015) and Richter *et al.* (2013) who reported that 59.3% of smears were inflammatory and 16.4% were abnormal cervical cytology [16] [17].

The prevalence of abnormal cytology in the age group from 30 to 40 years in our study was much more predominant than any other age category. This finding was in accordance with Sanad *et al.* (2014) who found that prevalence of ACC in age group <30 was significantly lower than in middle age group [18].

High parity was always been a risk factor for ACC. The American Cancer Society [19] and Mahalli *et al.* [20] reported that women with high parity (≥3) have increased risk of ACC and CC. We reported the same finding in our study where 69% of abnormal cytology was reported in females having high parity ≥ 3. This finding may be attributed to HPV exposure with unprotected intercourse and immunosuppression that occurs during pregnancy which may contribute to oncogenesis.

In our study we found a significant association between young age of first intercourse and abnormal cervical cytology, as 60.2% of ACC was found in patients who were sexually active before age of 20, so there was agreement with El-Moselhy *et al.* (2015) [21] who reported the same significant association between early age of marriage (<20) and cytological abnormality.

In our study there was 53% of cervical cytological abnormality in patients who had normal vaginal delivery which was more than other patients group (nullipara, had CS delivery), as these women were exposed to more cervical trauma during vaginal delivery especially multipara women, this with agreement with Skegg *et al.* (2013) [22] who found that women who had vaginal delivery were at higher risk of cervical cancer than who deliver by CS especially multiparous women with low social class.

Cigarette smoking is established as a cofactor of HPV for cervical cancer. The prevalence of HPV is increased in associated with active smoking it seems that the risk is dose-dependent and disappears after smoking cessation [23]. In our study 60.9% of ACC was among smoker patients (active and passive), 42.7% of abnormal cervical cytology found among passive smoker patients, this was agreement with Min, Kyung-Jin *et al.* (2017) [24] who reported that passive smoking among non-smokers is associated with the risk of CIN, especially non-smoking women who exposed to passive smoking for 2 or more hours per

day.

Lower social class women are more likely to develop cervical cancer than those with higher social class. In Egypt, most patients with low social classes reside in rural areas. We found in our study that women from rural areas have higher incidence of ACC than those who reside in urban ones. We found that 78.9% of those patients come from rural areas with low social status. These findings were also in accordance with those found by El-Moselhy *et al.* (2017) who reported that there is a strong correlation between socioeconomic class and abnormal cytology results [25].

In our study there was a significant difference regarding number of previous marriages and development of cervical cell abnormalities. The incidence of ACC in patients who married only once was 13.3%, and it was 56.5% in women who had twice or more previous marriages. This was in agreement with Mosuro *et al.* (2015) [16] who reported higher cervical cytological abnormality between patients with multiple life time partners.

In our study we found that there was decrease incidence of ACC between IUD users was lower than non IUD users. Castellsague *et al.* (2011) [26] also found that the use of IUD use is a protective factor against ACC. This was explained by the cellular immunity triggered by the IUD. Researchers have theories that could explain how the IUD protects from developing CC. One theory states that the procedure of inserting the IUD may destroy HPV lesions before they become cancerous [27].

We found some decrease of abnormal cytology between condom to male this with agreement with El. Mahalli *et al.* (2015) [20] as it reported that usage of condom to male will lower the risk of STD infection and also abnormal cytology So, the condom was reported a statistically significant protective factor.

Our study reported that the use of oral contraceptive pills (OCs) was associated with increase of ACC. We reported that 42.9% of patients with ACC were pill users. El-Moselhy *et al.* (2016) [25] and other studies also reported that OCs usage for long duration was a significant risk factors for development of ACC. This effect may be due to increasing the susceptibility of cervical cells to persistent infection with high-risk HPV types.

6. Conclusion

Cervical cytology remains the gold standard for cervical cancer screening and the use of the Bethesda system is a simple and accurate method for diagnosis and management of cases with abnormal cervical cytology.

7. Recommendations

- Cervical cancer screening programs need to be applied to women in our country to decrease the burden of CIN and cancer cervix.
- We need to teach all females in our country about importance of cervical screening.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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