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Cancer Cervix and Human Papilloma Virus (HPV) among Women Attending Gynecological Out Clinic Patients Al-Azhar University Hospitals: Newly Screening Technique
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ABSTRACT
Background: Most incidences of cervical cancer are caused by the human papillomavirus (HPV), which can be prevented with a vaccination. In around 90\% of cases, HPV infections have no symptoms and disappear on their own within two years. In certain situations, however, an HPV infection might remain and cause warts or precancerous lesions. HPV causes nearly all cervical cancer cases; two strains, HPV16 and HPV18, accounting for 70\% of cases.

Objectives: The study was designed to re-assess the prevalence of HPV infection among women attending the Gynecological Outpatient Clinic Al-Azhar University Hospitals using the new liquid-based cytology technique and our results provide important information for public health authorities considering HPV prevention in Egypt.

Subjects and methods: Our study was conducted on 1000 gynecological patients attending Al-Azhar University Hospitals between March 2021 and December 2021. Their ages ranged from 35 - 70 years old. Cervical samples were collected by a gynecologist using a cytobrush and placed in a liquid-based cytology medium (using the DC LBC from GZLBP) for the presence of HPV DNA using Linear Array HPV genotyping at Cytolab Laboratory, Cairo, Egypt.

Results: Among 1000 women who underwent the LBC test, 97 women were positive for HPV DNA findings (9.7\%), while the rest of women 903 were test free (90.3\%). 57 cases (58.7\%) of positive women showed different degrees of cervical intra-epithelial neoplasia CIN.

Conclusion: The essential need for a proper screening system for cervical pathologies and further multi-central randomized studies are strongly recommended through our study.

Keywords: HPV, Screening Test, Cancer Cervix.

INTRODUCTION
Cancer cervix is the fourth most often diagnosed cancer and the fourth main cause of cancer mortality in women worldwide. It has a tremendous global impact, with over 570,000 new instances of cervical cancer identified each year and 311,000 fatalities reported \cite{1}.

The bulk of cervical cancer-related deaths occurs in developing nations, such as Egypt, where 25.76 million women over the age of 15 are at risk of acquiring cervical cancer. In Egypt, it is projected that 514 women are diagnosed with cervical cancer each year, with 299 dying from the disease; hence, cervical cancer is the second most common cancer among Egyptians\cite{2}.

Human papillomavirus is the most prevalent sexually transmitted infection (HPV). Up to 80\% of sexually active women become infected at some time in their life, with 10-20\% developing a chronic infection \cite{3}.

Human papillomavirus infection (HPV infection) is a sexually transmitted infection (STI) caused by a DNA virus from the Papillomaviridae family that has more than 170 subtypes. It is generally known as the most frequent viral STI globally. Early age of first sexual intercourse, frequent sexual partners, smoking, and impaired immune function are all risk factors for chronic infection by sexually transmitted diseases \cite{4}. HPV is found in more than 95\% of women who develop cervical cancer\cite{5}.

The study was designed to re-assess the prevalence of HPV infection among women attending the gynecological outpatient clinic at Al-Azhar University Hospitals using the new liquid-based cytology technique and our results provide important information for public health authorities considering HPV prevention in Egypt.

PATIENTS AND METHODS
Our study was conducted on gynecological patients attending Al-Azhar University Hospitals during the period between March 2021 and December 2021 and their ages ranged from 35-70 years old.

Inclusion Criteria:
- Age between 35 and 70.
- Asymptomatic women.
- No recurrent vaginal or cervical infection.
- No previous cervical precancerous condition.
- No history of malignant disease including cervical cancer.

Exclusion Criteria:
- History of malignancy including cervical cancer.
- Recurrent vaginal or cervical infection.
- Previous total hysterectomy.
- Virgin.
- Pregnancy.
- Postpartum within 6 months.

Cervical samples were collected by a gynecologist using a cytobrush and placed in a liquid-based cytology medium (using the DC LBC from GZLBP) for the presence of HPV DNA using Linear Array HPV genotyping at Cytolab Laboratory, Cairo, Egypt.
Outcomes:
Our primary outcome was to detect the overall number of infected women with HPV various strains. The secondary outcomes included colposcopy findings of positive infected women and identifying the most common strain of HPV.

Sample size:
Based on an overall prevalence of 10.4% [6], With a confidence interval of 95% and to bypass type I and II errors, a total of 1000 subjects were required. Data were analyzed using the 22.0 SPSS version (SPSS Inc., Chicago, IL, USA).

Ethical Considerations:
The study was approved by the Ethics Committee of the Faculty of Medicine, Al-Azhar University, and was conducted following the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice. Informed consent was obtained from all eligible women before starting the study.

Statistical analysis
The collected data were coded, processed, and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test.
Qualitative data were represented as frequencies and relative percentages. Chi-square test ($\chi^2$) to calculate the difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare two independent groups of normally distributed variables (parametric data). P-value < 0.05 was considered significant.

RESULTS
HPV Prevalence:
Among 1000 women who underwent the LBC test, 97 women were positive for HPV DNA findings (9.7%), while the rest of women 903 were test free (90.3%) (Figure 1).

57 cases (58.7%) of positive women showed different degrees of cervical intra-epithelial neoplasia CIN as shown in Table 1.

They were treated by LLETZ and followed up successfully according to the British society of colposcopy and cervical pathology recommendations BSCCP.

7 cases (12.2%) were diagnosed with invasive cervical cancer stages 1A1 and 1A2 from the positive group of women. HPV (16) was the commonest strain among all tested samples in comparison to other detected subtypes. It was very interesting to find complex infection of more than one subtype of HPV in 23 women (23.7%) out of 97 women who tested positive for HPV (Figure 2).

Table (1): Pathology results of cases.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>CIN 1</th>
<th>CIN 2</th>
<th>CIN 3</th>
<th>Stage 1 A1/2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>23</td>
<td>18</td>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>

Figure (2): It looks obvious that the majority of affected cases were in the age group of 35 to 45-year-old which reflects the important role of raising awareness in women of that age.
DISCUSSION
Our study is the most recent using the most advanced LBC test to estimate the prevalence of HPV among Egyptian women between 35 and 70 years. Our results regarding the HPV positive tests are matching with older studies which revealed a prevalence of 10.3%, 15%, and 10.4% in Egypt[7,8].

The Association of HPV with the development of cancer cervix was only 57/97 (58.7%) in our study.

These results did not agree with many results (93.3%), (99.7%) and (98%)[23,24,25] reported that HPV is the main cause of developing cancer cervix. The discrepancy may be explained by different sociodemographic criteria of our patients and the presence of other risk factors such as smoking, hormones, and infections rather than HPV.

Our study showed that the commonest HPV genotypes associated with the development of cancer cervix were HPV 16. Our study results do not agree with those reported by[26-28]. The interpretation of different genotypes elsewhere was hampered by variation in HPV testing methodology, and sensitivities of different methods used for HPV detection[29].

In our study, single HPV types were observed more frequently (76.3%) than multiple types of infection (23.3%). Our findings are in line with[8-11]. Although HPV is the most prevalent viral sexually transmitted virus, it can also be spread by intimate contact with infected patients’ clothing and autoinfection. Immunity plays a significant role in the progression of the disease, and with adequate immunity, most infections will be eradicated from the body within two years. Many factors directly impact bodily immunity, including mental health, smoking, and autoimmune illnesses, all of which are very widespread nowadays. Moreover, multiple sexual relationships are common, either by the marriage of multiple wives or due to the increased incidence of divorce and re-marriage throughout the entire community[11]. Therefore properly protective strategies and screening plans should be established to protect our patients.

CONCLUSION
In our study, the prevalence of HPV in premalignant and malignant cervical lesions was 58.7%, which means the association between HPV and the development of cancer cervix in Egyptian women is fully established. HPV infection mostly 76.3% in the form of single infections with HPV 16, 18, 31, 11, and 6 genotypes. However, HPV infections in multiple forms, genotypes in 23.3% of positive cases.

RECOMMENDATIONS
Further multi-central randomized studies are recommended to clarify the prevalence of HPV in premalignant and malignant cervical lesions in Egyptian women to determine the benefits of HPV vaccination in Egypt. Our study strongly recommends the essential need for a proper screening system for cervical pathologies.

Conflict of interest: The authors declare no conflict of interest.

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