



# Assessment of Cervical Smears according to The Bethesda System (TBS) 2014 in a Sample of Patients. A Clinico-pathological Study

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## **ABSTRACT:**

### **BACKGROUND:**

Cervical cancer develops slowly, raising the possibility of early recognition of pre-neoplastic lesions using Papanicolaou test and consequently avoiding deaths. Cervical screening system seeks to identify females who have an epithelial abnormality that could; if untreated, take the lead to the progress of cervical carcinoma. Extremely applied test for cervical carcinoma screening is cervical cytology which is effective in decreasing the occurrence of cervical cancer deaths by 70% since 1950.

### **OBJECTIVE:**

To assess cervical pap smear from a sample of Iraqi patients according to The Bethesda System (TBS) 2014 and to study the relation of different categories of TBS with clinicopathological parameters include (patients age, clinical presentation, parity, and lower female genital tract infection).

### **MATERIALS AND METHOD:**

A cross sectional study was conducted in the Department of Pathology/ Collage of Medicine/ Al-Nahrain University, Baghdad, Iraq (For a period from January 2021 to January 2022). Cases were collected from Medical Consultant Office/ College of Medicine/ Al- Nahrain University (For a period from May 2017 to December 2020). There were 209 patients referred at that period. The data that were analyzed for patients according to five general factors: (age of the patient, clinical presentation, parity, types of lower female genital tract infection, microscopic examination and final diagnosis according to The Bethesda System 2014).

### **RESULTS:**

The mean age was  $40 \pm 9.95$  years .According to The Bethesda System 2014: Negative for intraepithelial lesion or malignancy was (57 cases 27%), Atypical squamous cells of undetermined significance composed (4 cases 2%), Low grade squamous intraepithelial lesion was (96 cases 46%), High grade squamous intraepithelial lesion was (51 cases 24%), Atypical glandular of undetermined significance was (1 case 0.5%). There was significant correlation between The Bethesda System 2014 categories and age P value = 0.014. There was no correlation with clinical presentation, number of parities and types of lower genital infections, P value was (0.806, 0.277, 0.063) respectively.

### **CONCLUSION:**

The most frequent category of The Bethesda system 2014 categories in this cross – section study was low grade squamous intraepithelial lesion (46%), High grade of cervical intraepithelial lesion is significantly associated with older age group and there was no significant association of The Bethesda System 2014 categories and clinical presentation, number of parities and types of cervico-vaginal infections.

**KEY WORDS:** The Bethesda system 2014, pap smear.

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## **INTRODUCTION:**

Cytology-based screening remains the cornerstone of the global preventive measures for cervical cancer, as screening programs have achieved a significant reduction in the incidence and

mortality of cervical cancer, especially when screening is done in a well-organized program with enough coverage, high-quality screenings, and suitable frequency<sup>(1)</sup>.

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Evidence-based methods for cervical cancer screening are available in a wide range of settings. Early detection of early-stage dysplasia and pre-cancerous lesions may be achieved with cytological screening using Papanicolaou (Pap) smears, followed by colposcopy and biopsy, in high-resource settings. The employment of cytopathologists for cytological screening might be expensive because of the need for specialized specimen preservation and high technical knowledge.<sup>(2)</sup>

For more than half a century, the Pap smear cytology test has been widely utilized across the world. The ectocervical and endocervical cells are collected and prepared for smear using a brush or spatula.<sup>(3)</sup>

Changes in cervical squamous cells discovered during sampling have been described using a variety of cytological reporting methods. The Bethesda system (TBS) is the standardized cytology reporting regarding sample adequacy and its clinical findings, especially squamous intraepithelial lesions (SILs) which are graded as low or high grade. As for glandular cells, the Bethesda system describes their changes as atypical glandular cells (AGC) and adenocarcinoma in situ (AIS).<sup>(4)</sup> Regarding atypical glandular cells, they show nuclear atypia which renders it difficult to distinguish between benign and in situ/invasive malignant cells. As for adenocarcinoma in situ, it is pre-invasive adenocarcinoma that has not yet penetrated the basement membrane into the deeper cervical tissue.<sup>(5)</sup>

### MATERIALS AND METHOD:

A cross-sectional study was conducted in the Department of Pathology/ College of Medicine /Al-Nahrain University, Baghdad, Iraq (For a period from January 2021 to January 2022). Cases were collected from the Medical Consultant Office/ College of Medicine/ Al-Nahrain University. There were 209 patients referred during that period. The data that were analyzed for patients according to five general factors which are listed: (Age of patient, Presentation, Parity, Types of lower female genital tract infection, Final diagnosis and microscopic examination were obtained).

### The practical workup of the current study includes:

Collection of 209 cervical smear reports, and clinical data listed above. Collected slides were stained by routine hematoxylin and eosin (H&E) stain. This procedure was done in the Medical Consultant Office/ College of Medicine/ Al-Nahrain University. Hematoxylin and Eosin (H&E-stained) slides were assessed and classified according to TBS 2014. Slides were revised by the student and the supervisor of student.

### RESULTS:

#### Age Distribution

The age distribution of 187 cases (excluding cases with missing data about age) with TBS categories showed that the peak number of cases (41.1%) in 40-49 years (1.6%) were ≤ 19 years (13.3%) were 20 - 29 years (25.1%) were 30 - 39 years (16%) were 50 - 59 years (2.6%) were ≥ 60 years. The median age was 42 years (range 16 - 71 years) as shown in Figure 1. Mean age was 40.47 ± 9.95 years.

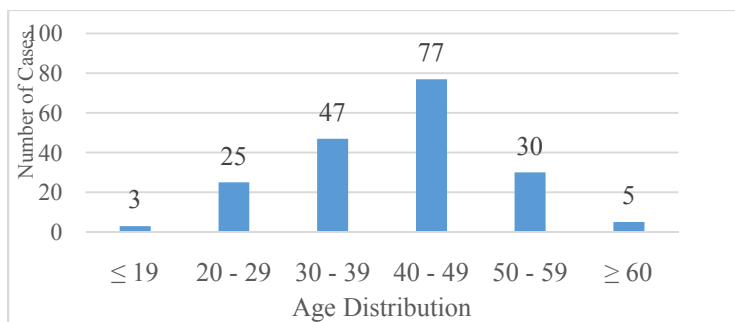


Figure 1: Age Distribution of patients.

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### The Clinical Presentation

The clinical presentation of 184 cases (exclude cases with missing data about clinical presentation) showed that (50.5%) had vaginal discharge, (19.5%)

had post coital bleeding, (14.1%) had check-up, (13%) had vaginal bleeding, (2.7%) had Dyspareunia as shown in Figure 2.

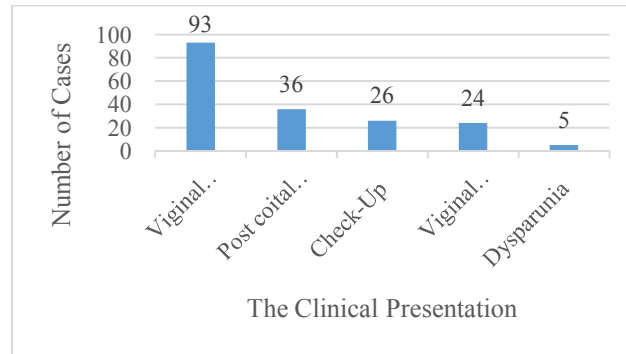


Figure 2: Frequency of different clinical presentation for the studied cases.

### Parity of patients included in this study.

The number of parities of 96 cases with TBS categories showed that (4.1%) had Nil Parity P0, (11.4%) had P1, (16.6%) had P2, (16.6%) had P3,

(19.7%) had P4, (15.6%) had P5, (10.4%) had P6, (3.13%) had P7, (2.1%) had P8 as shown in Figure 3.

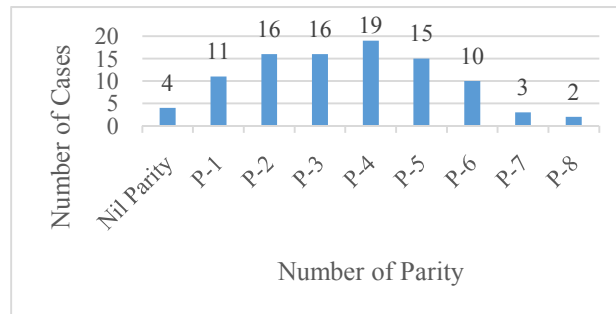


Figure 3: Number of parity for the patients included in this study.

### The TBS Categories

According to TBS 2014, LSIL Figure 4 had the highest percentage of cases (96 cases, 46%), NILM was seen in (57 cases, 27%), HSIL Figures

5, 6 were seen in (51 cases, 24%), ASCUS was seen in (4 cases, 2%), and AGUS was seen in (1 case, 0.5%). Figure. 7.

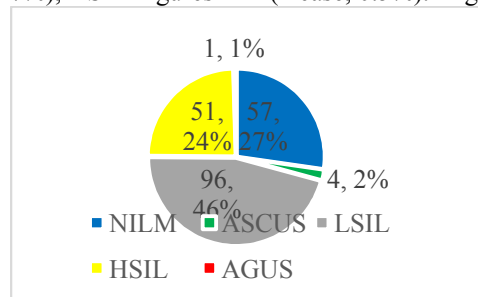


Figure 7: Frequency of categories of the Bethesda system 2014 in the patients included in this study.

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### Types of cervico-vaginal infection in the studied patients

The number of patients presented with cervico-vaginal infection was 239 cases (patient may had more than one infection) divided into specific infection seen in 110 cases (40.0%) and non-specific infection seen in 129 cases (53.9%).

Individually, for a specific infection (24.65%) had Candida, (13.3%) had Lactobacilli, (4.6%) had Trichomonas, (2%) had a shift in flora suggestive of bacterial vaginosis, (1.2%) had Actinomyces. For the nonspecific infection, (28.8%) had mild infection, (25.1%) had severe infection as shown in Figure 8.

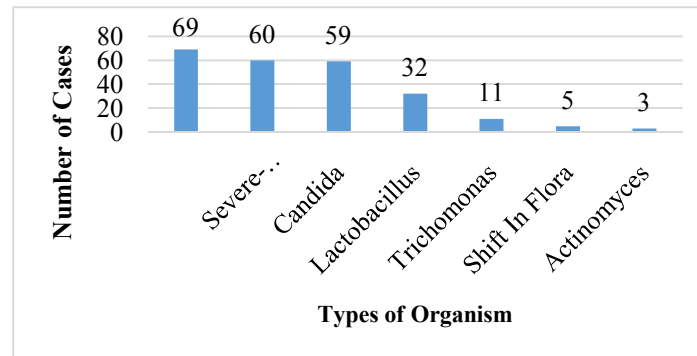


Figure 8: Frequency and severity of different types of cervico-vaginal infection in studied patients.

### Relations Between Clinical Parameters and TBS 2014 Categories

#### Relation of age to TBS 2014 Categories

In NILM category the highest percentage of cases lie in the 40-49 group (20 cases), all cases of ASCUS category lie in the 40-49 group (3 cases), LSIL category had highest percentage of cases lie

in the 40-49 group (29 cases), HSIL category had highest percentage of cases lie in 40-49 group (25 cases) It is noteworthy that all patients of the age group 70-79 had a cytological diagnosis of HSIL and the AGUS within 30-39 group (1 case), There was significant association P value = 0.014; figure 9.

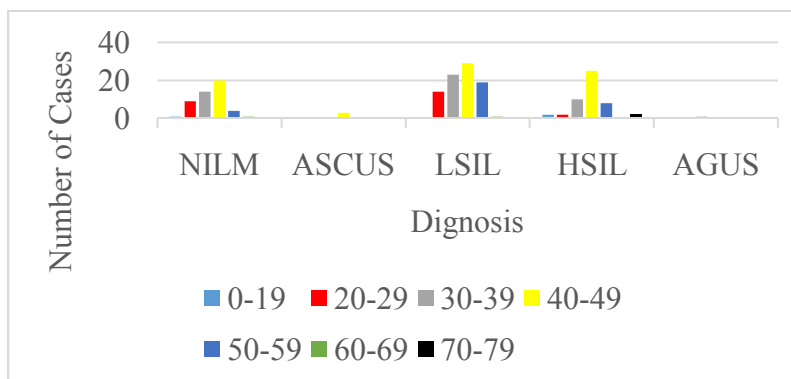


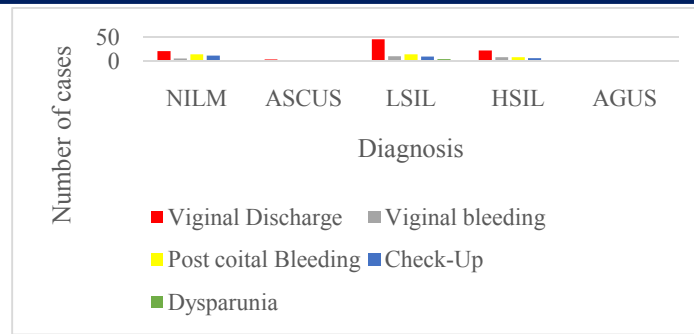
Figure 9: Relationship between categories of ages with TBS categories.

### Relation of clinical presentation to TBS 2014 Categories

In NILM category, highest percentage of clinical presentation was vaginal discharge (21 cases). The clinical presentation in ASCUS category was vaginal discharge (3 cases) and vaginal bleeding

(1 case); in LSIL and HSIL categories highest percentage was vaginal discharge (46,22 cases) respectively; AGUS case presented with vaginal discharge (1 case). There was non-significant association P value = 0.806 figure 10.

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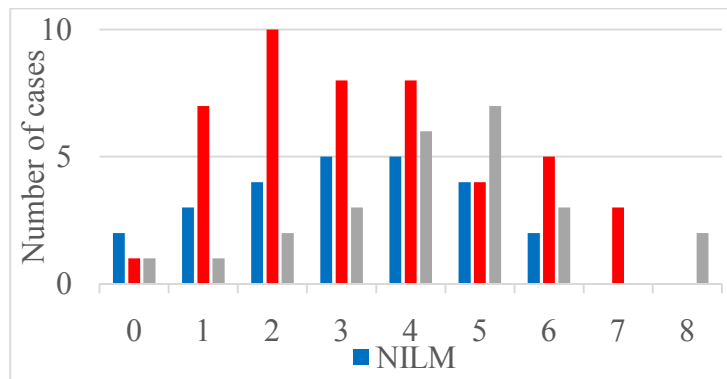


**Figure 10: Relation clinical presentation with TBS 2014 categories.**

**Relation of Parity to TBS 2014 Categories**

In patients with P0 group highest percentage to NILM (2cases), in P1,P2,P3,P4 groups highest percentage to LSIL category (7,10,8,8) cases respectively ,in P5 the highest percentage was

HSIL (7 cases), P6 group increase in number LSIL (5 cases), P7 group just LSIL (3cases), P8 group just HSIL (2 cases). There was no significant association P-value = 0.277 Figure 11.

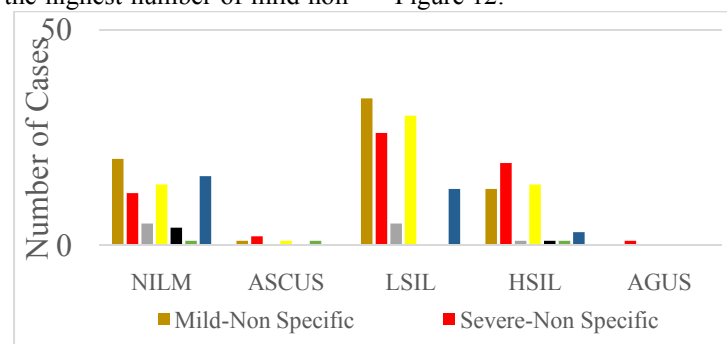


**Figure 11: Relation of parity with TBS 2014 categories.**

**Relation types of cervico-vaginal infection to TBS 2014 Categories**

For the NILM category, the predominant infection type was mild non-specific cervicitis (20 cases); ASCUS category showed the highest percentage of severe non- specific infection (2cases); LSIL category revealed the highest number of mild non-

specific cervicitis (34 cases); HSIL category reported the highest number of severe non-specific cervicitis (19 cases) ; AGUS case was associated with severe non- specific infection (1 case). The relation of cervico-vaginal infection to TBS 2014 categories was non-significant P value = 0.063 Figure 12.



**Figure 12: Relation of types of cervico-vaginal infection TBS 2014 categories.**

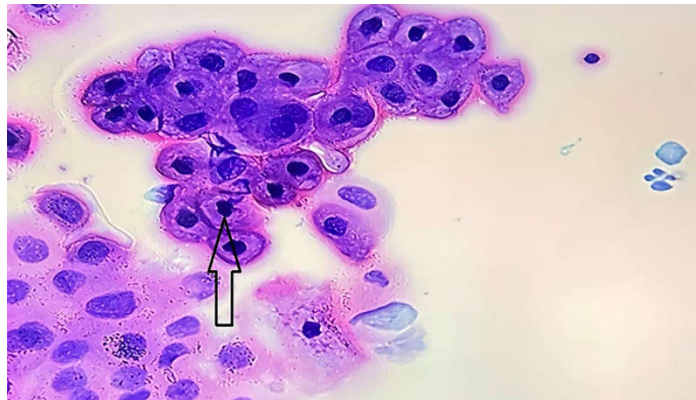


Figure 4: Low grade squamous intraepithelial lesion. smear show classical koilocyte (black arrow): large, hyperchromatic, slight irregular nuclear membrane and have large sharply defined perinuclear halo (40x twice magnification, H&E).

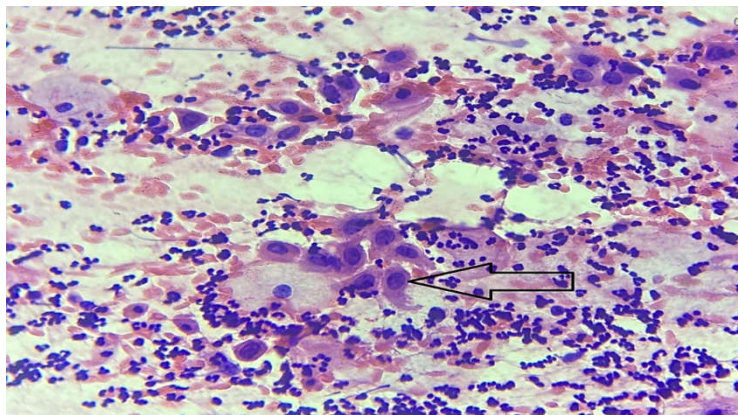


Figure 5: High grade intraepithelial lesion, moderate dysplasia or CIN II (black arrow), cells with moderate amount of cytoplasm and enlarge nuclei one half of cell size with hyperchromatic (40x H&E),

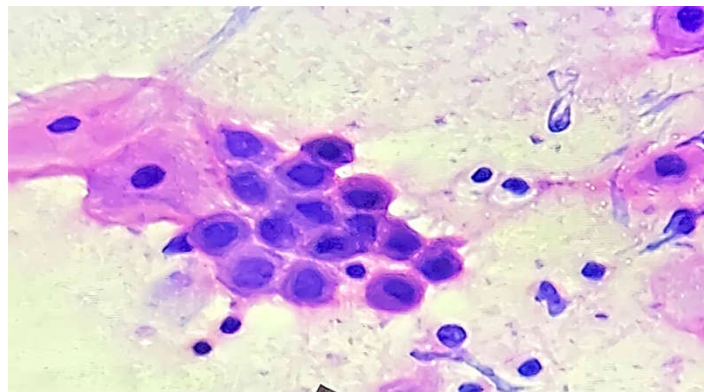


Figure 6: High grade intraepithelial lesion, severe dysplasia CIN III, smear show syncytium-like group, small cells have scant cytoplasm and hyperchromatic nucleus with irregular nuclear contours (40x twice magnification, H&E).



### DISCUSSION:

In the present study, the frequency of NILM was (27%) while that of abnormal pap smears was 73%. The frequency of abnormal pap smears was 4.3% in a study done at Saudi Arabia<sup>6</sup> and only 1.28% of the cases have abnormal pap smear in a large study done at Kirkuk governorate in Iraq.<sup>(7)</sup> The high frequency in this study is explained by the inclusion of nearly all women who were visiting the gynecology clinic complaining of symptoms related to cervical pathology during the study period.

On comparing this finding with other studies performed in Iraq using similar selection criteria, the frequency of abnormal pap smear was slightly lower than that found by Abdulla *et al.*, 2016 in Baghdad (86%)<sup>8</sup> and slightly higher than that found by Abdulrazaq A *et al.*, 2017 in Anbar province (66.7%).<sup>(9)</sup>

There were no CA cases of cervical carcinoma in current research. This in concordance with the study by Mahmoud and Khalid, 2012 in which the incidence of cervical cancer was 0.08%.<sup>(7)</sup> This reflects the low incidence of cervical carcinoma in conservative societies as sexually transmitted human papilloma virus is responsible for the majority of cervical cancer cases.<sup>(10)</sup> However, the small sample size of present study and the possibility of false negative diagnosis should be taken in to account when explaining the zero incidence of cervical carcinoma in our study. A 2017 study in Anbar Province by Abdulrazaq *et al.*, 2017 found a 5.6% incidence of cervical carcinoma.<sup>9</sup>

#### Association of TBS 2014 categories with age groups

In the present study, the most common age group was 40-49 years (41%) which is in concordance with Abdulrazaq *et al.*, 2017.<sup>9</sup> A statistically significant association has been found between cytological diagnosis and age group (P value = 0.014) as the majority of cases of LSIL and HSIL were above 40 years old which is also in concordance with Abdulrazaq *et al.*, 2017.<sup>9</sup> One probable explanation is that women in developing countries start cervical cancer screening later in life, when premalignant lesions have reached their peak.<sup>11</sup>

However, this discordance with Abdulla *et al.*, 2016<sup>8</sup> and the study by Fatin Al-Mosawi, 2015<sup>12</sup>, which found no statistical association between age group and cytological abnormalities.

This difference may be attributed to different in sample size and selection criteria.

#### Association of TBS 2014 categories with parity

According to a large cohort research done in Taiwan, high vaginal parity is not a significant reason unless the women are also infected with HPV., however, vaginal parity doesn't matter whether it is high or low because birth trauma can heal by itself.<sup>(13)</sup>

The study showed no significant association between parity and Pap smear cytological findings which agrees with other Iraqi study Hassan *et al.*, 2009<sup>(14)</sup> This lack of association can be explained by the low prevalence of sexually transmitted HPV infection in the traditional Iraqi society.

#### Association of TBS 2014 categories with clinical presentation

In the present work, vaginal discharge was the most common clinical presentation 93 (50.5%) cases followed by post-coital bleeding 36 (19.5%) cases and vaginal bleeding 24 (13%) cases. This agrees with the studies by Fatin Al-Mosawi, 2015<sup>12</sup> and . This high presentation reflects that vaginal discharge is the leading cause of consulting gynecology clinician in the Medical Consultant Office of Collage of Medicine/ Al-Nahrain University.

#### Association of TBS 2014 categories with cervico-vaginal infection

In this study, non-specific inflammation was seen in 129 (62.2%) cases, which is higher than the percentage found by Abdulrazaq *et al.*, 2017 (33.3%).<sup>9</sup> Nonspecific inflammation is characterized as negative smear as it carries no risk of future progression to cervical cancer.<sup>15</sup> Studies have demonstrated that 47% of women who showed inflammatory changes on cervical smear testing had a microbiologically verified infection.<sup>16</sup> Another study showed that Inflammation on Pap smear has been associated with a 30–50% incidence of bacterial vaginosis.<sup>17</sup> Our study showed that 59 (28.5%) cases had candida. Baka *et al.*, 2013 reported a much lower incidence of 11.6% of which the most were diabetic.<sup>18</sup> This high incidence of candida may be due to high prevalence of inadequately treated DM in Iraq as around 1.4 million of Iraqis have diabetes.<sup>19</sup> Other risk factors for vulvovaginal candida include rise in endogenous estrogen level (due to obesity or pregnancy), use of estrogen, immunosuppression (e.g. being on antimetabolite

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drugs or chemotherapy, patients with organ transplant, HIV infection), and use of broad-spectrum antibiotics<sup>20</sup>.

### CONCLUSION:

The most frequent category of The Bethesda system 2014 categories in this cross – section study was low grade squamous intraepithelial lesion (46%), High grade of cervical intraepithelial lesion is significantly associated with older age group and there was no significant association of The Bethesda System 2014 categories and clinical presentation, number of parities and types of cervico-vaginal infections.

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