Int J Clin Exp Pathol 2020;13(2):307-316
www.ijcep.com /ISSN:1936-2625/IJCEP0104355

Original Article

Clinicopathologic significance and treatment of ASC-US in cervical cytology

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Received November 2, 2019; Accepted January 31, 2020; Epub February 1, 2020; Published February 15, 2020

Abstract: Background: In China, cervical cancer is one of the most common gynecologic malignancies. Cervical cytology is an essential method for screening cervical cancer and cervical intraepithelial neoplasia (CIN), and the most common cytological abnormality result is atypical squamous cells of undetermined significance (ASC-US). Therefore, how to effectively deal with ASC-US cytology has become the focus of scholars. Objective: We aim to analyze the final histopathologic results, clinicopathologic significance and current rationale of ASC-US cytology. Methods: All patients with first ASC-US cytological reports who attended our gynecological outpatient clinic in Qilu Hospital of Shandong University during January 2010 to December 2015 were recruited to this study. The data were derived from clinical records and evaluated retrospectively. The results of age, High-Risk HPV (DNA) testing, colposcopy, and pathological outcomes were obtained. Directed biopsy was performed if there were any suspicious cervical lesions under colposcopy, while four quadrant biopsy and/or ECC were performed if no suspicious lesions were noted in colposcopies. Results: A total of 1246 patients diagnosed with ASC-US were involved in the final statistical analysis. Mean age of patients was 41.6 years and the age range between 40-49 years represented 38.52% of all ASC-US women in this study. All patients were evaluated for HPV (DNA) and positive percent for High-Risk HPV was (67.1%). According to the final histopathologic outcomes after ASC-US cytology, 15.6% and 1.1% of patients had ≥ CIN2+ and invasive carcinoma respectively. Patients with invasive carcinoma were associated with HPV16+ and HPV18+. The detection rate of ≥ CIN2+ among the ASC-US/High-Risk HPV+ group was (53.9%) with a negative-predictive-value (NPV) of 100%. Our findings showed that the final pathologic results of ≥ CIN2+ were consistent with colposcopy with a coincidence rate of (77%), and colposcopical impression sensitivity and specificity for ≥ CIN2+ was (91.1% and 96.1%) respectively. Conclusion: Women with ASC-US have a wide range of final pathologic results, and it can be the initial warning of high-grade CIN or cervical cancer. In China, HPV (DNA) testing triage is a useful shunting measure for ASC-US patients, and an immediate colposcopy is a consequential strategy for dealing with ASC-US cytology to increase the detection rate of high-grade cervical lesions or invasive cancer.

Keywords: ASC-US, CIN, HPV, colposcopy, biopsy

Introduction

Globally, it is known that cancer arising from the cervix uteri is the fourth most frequent malignancy for females, and the seventh overall, which causes ~275,000 deaths annually [1, 2]. It is a result of a long process which is preceded by preinvasive cervical lesions i.e. cervical intraepithelial neoplasia (CIN) [3]. It has been demonstrated that infection with one of the oncogenic strains of Human Papillomavirus (HPV) is an important element in the development of cervical cancer and cervical precancerous lesions. According to the prevalence of genital HPV infection in invasive cervical cancer and its preinvasive lesions, these HPV types are categorized as “low-risk” and “high-risk” [4, 5].

The Papanicolaou test (Pap test) coupled with regular screening programs of cervical cancer enable early detection and effective treatment of CIN, which leads to reducing the mortality rate from cervical cancer [6, 7]. ASC-US, first introduced by the Bethesda system classification, is the most frequent abnormal cervical cytology finding which is not sufficiently clear to permit a more definite diagnosis and causes confusion for both clinicians and patients [8].

Although ASC-US is considered as low-risk abnormal cervical cytology, actually about (5-10%) of women with primarily ASC-US diagnosis have an underlying high-level cervical lesion (CIN2+ and CIN3+) on histologic diagnosis and require follow-up [9]. The clinical significance of ASC-US cytology is undetermined, which means that there is a contentious debate regarding its clinical management, given that there is no specific choice for optimal treatment [10, 11]. 30% of women with ASC-US cytology diagnosis have a low-grade cervical lesion, but up to 40% of these cases will progress to a high-grade cervical lesion [12]. The American Society for Colposcopy and Cervical Pathology (ASCCP) released the updated consensus guidelines in 2012 for managing females with positive "or" abnormal cervical screening results [13]. This ASCCP suggested three feasible courses of action for ASC-US cytology: (i) Repeat Pap test in 4-6 months and refer the women for colposcopy exam if the second result of this test is abnormal; (ii) Immediate colposcopy evaluation; (iii) Use HPV (DNA) test as intermediate triage and refer for colposcopy only those who have HPV (DNA) test positive [14].

As HPV is a major causative infection associated with cervical cancer and its precursors, previous studies have denoted the utility of supplemental HPV (DNA) testing as a companion to cervical cytology in initial screening [15]. Moreover, many studies decided that the oncogenic HPV (DNA) testing ("triage") in women with cervical cytology ASC-US has higher accuracy than repeat Pap test in 4 to 6 months, and is considered to be the most cost-effectivene strategy [16], and has proven to be a useful alternative for referring to immediate colposcopy to the detection of ≥ CIN3 and cancer [13]. Also, HPV (DNA) testing may minimize the costs by arranging patients into applicable strategies of management. However, a colposcopic exam with a guided biopsy remains the gold standard diagnostic procedure among women with ASC-US for deciding which patients need treatment. The reason is that the final pathological outcomes revealed cervical squamous cell carcinoma in 0-1%, CIN3 in 3%, and CIN2 in 1-5% respectively in cases of women with Pap test ASC-US [9].

The final pathologic results of ASC-US patients in China are very different from those in foreign countries due to the lack of Chinese cytologic doctors and the difference in their diagnostic level. Thereby, it is recommended that ASC-US diagnosis should be given an importance as it is a wide gynecological diagnostic category in Pap test composed of various aetiologic processes and it can be the initial warning of high grade CIN or invasive carcinoma in China.

In our study we aimed to evaluate the clinicopathologic significance of ASC-US in the diagnosis, the follow up of patient's clinical treatment, and prognosis of cervical lesions, and compared it with final histopathologic outcome.

Materials and methods

Study design and case selection

All patients with cervical cytology ASC-US between the ages of 21 to 78 years old who admitted to our gynecological outpatient clinic in Qilu Hospital from January 2010 to December 2015 were enrolled in this study. The pathologic database was collected retrospectively from medical records by computerized program. Patients that fulfilled the inclusion criteria were involved in the final statistical analysis; all patients with a first ASC-US cytology diagnosis underwent High-Risk HPV (DNA) testing and immediate colposcopy after ASC-US cytology result was performed. If there were any cervical lesions or suspicious lesions, biopsy under the guidance of colposcopy was performed. The four-quadrant biopsy (i.e. examination of the cervix from 12 to 6 o'clock, and from 3 to 9 o'clock) and/or endocervical curettage (ECC) were done in case of inadequately visualized cervical lesions or no suspicious lesions found under colposcopy. Women who were pregnant or immunosuppressed and women who previously had cervical cancer or precancerous lesions treatment were excluded from the present study.

Our study was approved by Human Ethics Committee of the Qilu Hospital of Shandong University (Identifier: KTLL-2017-560).

Cervical cytology slides

The cytology slides were prepared using liquid-based Pap test technique (ThinPrep, Marlborough, MA, USA). Cervical cells were collected from cervical canal of all participants and Pap cytology specimens were collected with an

endocervical plastic cytobrush and placed into 20-ML vials of ThinPrep ®PreservCyt® solution for cytology. The specimens of cytology and histology were read at our hospital's cytopathology laboratory and diagnosed by an expert gynecological pathologist. Criteria for ASC-US were used in accordance with the 2001 Bethesda system classification of cervical cytology report [17]. Briefly, criteria for interpretation of ASC-US included a large nuclei size of 2.5-3 × which is approximately three times that of a normal intermediate squamous cell's nuclei, slightly increased of nuclear/cytoplasmic ratio, chromatin regulation irregularity and minimal hyperchromasia and seldom "atypical parakeratosis" [18].

HPV (DNA) testing

HC2 test: We analyzed the High-Risk HPV (DNA) testing results of all 1246 patients who had diagnosed with ASC-US. Hybrid Capture 2 assay (HC2, Germantown Rd Germantown, MD, USA) was performed for detection of HPV, in which identified 13 types of High-Risk HPV that are known by the numbers (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68). The samples of High-Risk HPV (DNA) and cytology tests were obtained at the same visit and each of these was collected separately. The United States FDA (Food and Drug Administration) endorsed 1.0 pg for HPV (DNA)/ml (equal to 1.0 RLU/CO) as optimal threshold indicating HPV positivity result [19]. Cervical cytology diagnoses were made without knowing HPV status.

HPV genotyping test: Hybribio Rapid GenoArray kit test was used for Genotyping of HPV. HPV genotyping test was done for patients with HC2 positive results, which detects 21 HPV genotypes, comprising of 13 High-Risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68), 6 Low-Risk types (6, 11, 42, 43, 44 and CP8304) and 2 probable High-Risk types (53 and 66). The genotyping HPV samples were obtained by sterile cervical sampling brush and these samples were transported in the storage liquid bottles that contained 0.35 g of Disodium hydrogen phosphate as preservation solution. The test was carried out according to the protocol provided by the manufacturer.

Colposcopic examination

The patients were placed in the modified lithotomy position on the table of examination for performing colposcopy examination. Initially the vulva was assessed, then the vaginal speculum was inserted. Once the vaginal speculum was inserted and good inspection of the cervix was obtained, the cervix was flushed with saline and then the squamocolumnar junction (SCJ) and transformation zone (TZ) were visualized under × 15 magnification. Then 5% of acetic acid solution was applied for assessing a visual inspection of the cervix. The observed changes in colposcopy were assessed as the following: a normal transformation zone and an original squamous epithelium and a columnar epithelium were considered normal colposcopies and acetowhite change without any other alteration, punctuation, iodine-negative epithelial tissue, mosaicism, leukopenia, and atypical vascularization considered abnormal colposcopies. A punch biopsy was performed systemically during colposcopic examination for any suspected cervical lesions. Random four quadrant biopsy and/or ECC were performed in patients where the lesion was inadequately visualized or no lesion was seen during colposcopy. In the current study, the International Federation for Cervical Pathology and Colposcopy (IFCPC) approved the version 2011 IFCPC colposcopic terminology that is preferred by colposcopies. The general assessment for colposcopies starts as the following: adequate/inadequate and according to TZ visibility should be classified as types I, II, III (i.e. completely visible, partial or not visible). Colposcopy diagnostic results involved normal colposcopy findings, minor lesions, major lesions and suspicious for invasion. According to the protocol guidelines, the CIN classification was recommended for histopathologic assessment of biopsies [20].

Statistical analysis

The quantitative variables were analyzed by number, means, and simple percentages. The statistical significance of the categorical variations and comparison between groups had been determined by Pearson's (x^2) test and the significance of two-sided *P*-value was considered at $P < 0.05$. The correlation between colposcopy diagnosis and final pathologic results were assessed by sensitivity, specificity, false negative rate and false positive rate. Statistical analysis of this study was attained by using GraphPad Prism software version 5.01 (GraphPad, Inc, San Diego, CA, USA).

Table 1. Age distribution of ASC-US patients

TCT	Age						
	20-29	30-39	40-49	50-59	60-69	70-79	Total
ASC-US	156	409	480	164	34	3	1246

ASC-US, atypical squamous cells of undetermined significance; TCT, Thin Prep cytologic test.

Table 2. Correlation between cytologic ASC-US and cervical biopsy pathology and the comparison of CIN1 and CIN2-3 detection in ASC-US patients

TCT	Pathology					
	Negative	CIN1	CIN2	CIN3	Cancer	Total
ASCUS	839 (67%)	199 (16%)	98 (8%)	96 (8%)	14 (1%)	1246

TCT, Thin Prep cytology test. ASC-US, atypical squamous cells of undetermined significance. CIN1: low grade cervical intraepithelial neoplasia, CIN2-3: high grade cervical intraepithelial neoplasia.

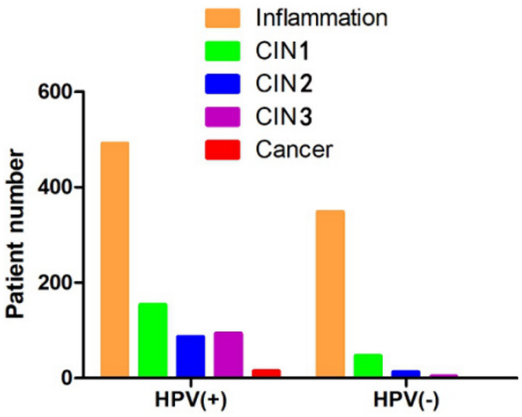

Figure 1. Effect of high-risk HPV status on pathologic outcome in patients with ASC-US. The high-grade CIN detection rate in the High-Risk HPV-negative group was significantly lower than that in the HR-HPV-positive group and cervical cancer detected in the High-Risk-HPV-positive group ($P < 0.0001$).

Results

Basic conditions

A total of 1246 women with the cytologic diagnosis of ASCUS between January 2010 and December 2015 who met the inclusion criteria were included in current study. The mean age of patients who had ASC-US was 41.6 years old, ranging from 21 to 78 years old and the highest age of ASC-US onsets accounted for 480/1246 (38.52%) that ranging from 40 to 49 years as (summarized in **Table 1**).

In total, 39.3% (490/1246) cases in our study had symptoms that mostly included vaginal discharge, bleeding after sexual intercourse, and unexplained vaginal bleeding while 60.7% (756/1246) cases had no symptoms.

ASC-US and high-risk HPV

Detection of high-risk HPV in ASC-US patients: (**Table 2**) reveals the prevalence of positive and negative High-Risk HPV findings for ASC-US. There were (n = 837) of our ASC-US patients had positive High-Risk HPV DNA testing, and 409 of the cases tested negative for High-Risk HPV, with positive and negative rates (67.17% and 32.8%) respectively.

Effect of high-risk HPV on the severity of Cervical Lesion in Case of ASC-US patients: The prevalence of High-Risk HPV was 100% in cervical cancer cases, 96.9% in CIN3, 87.8% in CIN2, 76.9% in CIN1 and 58.5% in an inflammation case with a global NPV (i.e. negative predictive value) for ≥ CIN2+ was of 100%. We noticed that the prevalence of High-risk HPV in ASC-US women was increased with greater severity of cervical lesion diagnosis (Pearson's $x^2 = 101.1$: *P* value = 0.0001) as demonstrated in **Figure 1**.

Our study found that the high-grade dysplasia in ASC-US/High-Risk HPV negative subjects was significantly lower than those ASCU-US/High-Risk HPV positive subjects. Among the High-Risk HPV positive group, 179 patients had ≥ CIN2+ with detection rate (53.9%) which was significantly higher than the group that had a negative result for High-Risk HPV in which only 15 cases had ≥ CIN2+ with detection rate (24%) (Pearson's $x^2 = 17.73$; P = 0.0001) as shown in **Figure 2**.

Effect of high-risk HPV subtypes on pathologic outcome of ASC-US cytology: From our study, we demonstrated that High-risk HPV genotypes were identified on pathologic outcomes of positive High-Risk HPV/ASC-US women; types 16 and 18 in order were identified in cervical cancer, HPV16, 18, 31, 33 and 58 were detected in CIN3, types 16, 31, 33, 58 and 56 were detected in CIN2, types 16, 33, 31, 56, 58 and 18 were detected in CIN1 and HPV16, 58, 53, 18, 31 and 56 were detected in cases of cervical

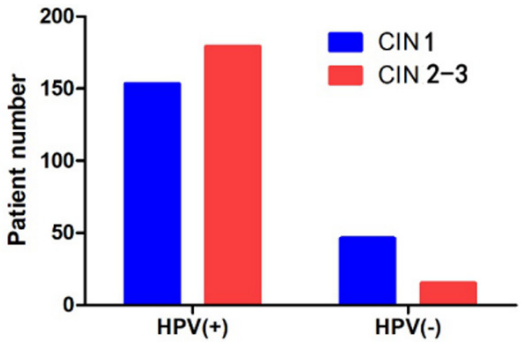

Figure 2. Effect of High-Risk HPV status in ASC-US patients on low-level CIN and high-level CIN detection. The high-grade CIN detection rate in the High-Risk HPV-negative group was significantly lower than that in the High-Risk HPV-positive group (P < 0.0001).

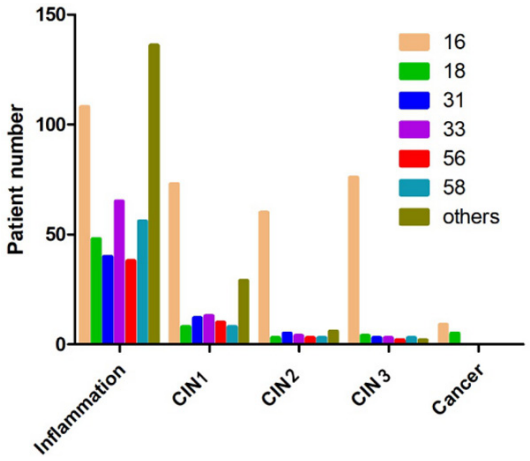

Figure 3. The effect of High-Risk HPV subtypes on final pathologic outcomes in ASC-US patients. The effect of HPV oncogenic subtypes was statistically significant P < 0.0001.

inflammation. Notably, only results of High-Risk HPV types were considered in our analysis. The following final pathologic outcomes that were affected by oncogenic HPV subtype were identified. There were 32.9% of HPV16+ patients who had inflammation, 22.25% had CIN1, 41.46% had CIN2+, and 64.28% (n = 9) had invasive cervical cancer. Among HPV18+ patients there were rates of 9.7% and 5.22% for CIN1 and CIN2+ respectively, and 35.71% (n = 5) had invasive cancer, while 3.9% had inflammation. We observed that 20.1% of patients with other High-Risk HPV+ subtypes had CIN2+ and did not detect any case of cervical cancer in these group of patients (Pearson's x^2 test = 202.24; P = 0.0001) as represented in **Figure 3**; **Table 3**.

ASC-US and biopsy

The detection of CIN grades in ASC-US patients and the correlation between biopsy pathology and ASC-US cytology: According to criteria used for histology in our study, there were 839 of 1246 (67.3%) patients with ASC-US who had inflammation and 393 (31.5%) of the total who had CIN, including 15.9% (n = 199) low-grade CIN (CIN1), 15.56% (n = 194) high-grade CIN (≥ CIN2+); and there were 14/1246 (1.1%) cases who had invasive cancer determined by cervical biopsies. Thus, these results revealed that the detection rate of low-grade dysplasia and high-grade dysplasia, among patients with cytologic ASC-US were nearly the same; so the number of patients with CIN1 was 15.9% (n = 199) that was close to the percent of ≥ CIN2+ which was 15.6% (n = 194) as illustrated in **Table 4**.

Age distribution of cervical lesions in cervical biopsy results of ASC-US women: **Figure 4** depicts the age distribution of each CIN grade and cervical cancer in the final pathology report of the 1246 women with ASC-US cytology diagnosis, in which the peak age of CIN1 was (30-39) while the peak age of ≥ CIN2+ and cancer was (40-49) x^2 = 53.03; P = 0.0001.

Colposcopic diagnosis and biopsy results

All 1246 women with ASC-US in our study were transferred to colposcopic exam and biopsy pathology diagnosis. Depending on the colposcopic terminology used, consensus between colposcopic diagnosis and biopsy pathology was absolutely matched in 959/1246 (77%) of the cases with colposcopic impression sensitivity and specificity of 91.1% and 96.1% respectively. We observed that the rates of false negative and false positive results of the colposcopic impression in our study were 8.8% and 3.9% respectively with Pearson's x^2 = 1898; P = 0.0001 as presented in **Figure 5**.

Discussion

Regular cervical cancer screening is a widely credited strategy for reducingcervical cancer incidence and mortality [21]. In asymptomatic women, the Pap test is the major approach/test used during cervical cancer screening in order to discover the disease at an early stage, so more efficient treatment can be performed.

Table 3. Detection rate of High-Risk HPV in ASC-US patients

TCT	HR-HPV Results				
	Total	HPV (+)	%	HPV (-)	%
ASC-US	1246	837	67.1	409	32.8

TCT: Thin Prep cytology test. ASC-US: atypical squamous cells of undetermined significance. HPV: human papillomavirus.

Table 4. Effect of High-Risk HPV subtypes on pathologic outcome of ASC-US

HPV genotype	Negative	CIN1	CIN2	CIN3	Cancer	Total
16	108	73	60	76	9	328
18	48	8	3	4	5	68
31	40	12	5	3	0	60
33	65	13	4	3	0	85
56	38	10	3	2	0	53
58	56	8	3	3	0	70
Others	136	29	6	2	0	173
Total	491	153	86	93	14	837

Cervical HPV subtypes, high risk human papillomavirus subtypes using Hybribio Rapid GenoArry kit test. CIN1: low-grade intraepithelial neoplasia, CIN2-3: high grade cervical intraepithelial neoplasia.

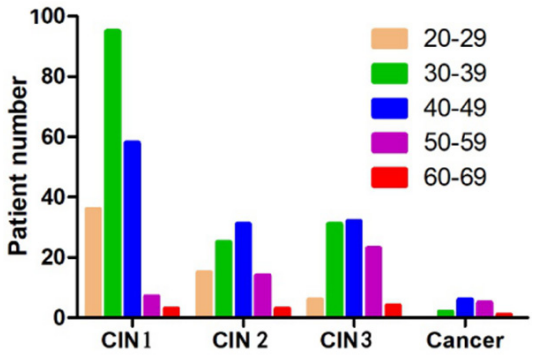

Figure 4. Age distribution of CIN1, 2, 3 and cancer in cervical biopsy pathology. The peak age of CIN1 is 30-39 years old, but the peak age of CIN2, CIN3 and cervical cancer is 40-49 years. CIN, cervical intraepithelial neoplasia ($P < 0.0001$).

However, up to 70% of women with an abnormal Pap test appeared as ASC-US, i.e. uncertain morphology but not precancerous squamous cells [22, 23]. Due to this uncertainty morphology of ASC-US cytology, several questions remain regarding the most appropriate management of women with ASC-US to decide whether these women require early treatment or could be safely observed [9, 24].

From ASCCP guidelines, patients with ASC-US received controversial management strategies [13]. The management of ASC-US cytology includes repeated cytology test in 4 to 6 months, HPV testing, and immediate colposcopy with or without biopsy [25].

Our study demonstrated that the majority of patients whose Pap test was reported as ASC-US received positive results in subsequent examinations. Our findings are in contrast to those reported by the authors in [26], in which the majority of ASC-US patients received negative results in subsequent examinations. Many previous studies concluded that a primarily ASC-US report requires a repeated Pap test over 6 months and within this interval of time outcome of normal and abnormal results was demonstrated [27, 28]. Our study implies that ASC-US patients need more intensive diagnostic strategies in order to accurately attain the final histopathologic result rather than waiting and repeating cytological evaluation after 4 to 6 months as the majority of our patients had high-grade cervical lesions in the final histopathologic outcome. Moreover, a repeat Pap test may cause a delay in the diagnosis of high-grade CIN or cervical cancer and multiple follow up visits may hinder patient adherence.

In females with ASC-US cytology, the incidences of developing CIN2 lesion or worse or CIN3 lesion or worse were distinct among various age ranges. In our study, the incidence rate of CIN2, CIN3, and cervical cancer were higher in the age group of 40 to 49 years. This result is different from that reported by the authors in [29], regarding the incidences of CIN3+, in which the incidences of CIN3+ lesions were higher in women under 30 years old and in those above 60 years old.

Our study confirms that in women with a referral Pap test that observed ASC-US, triage based on High-Risk HPV (DNA) testing for detecting high-grade CIN was useful in order to determine which group of women were at high risk for developing CIN2+ and CIN3+ and require further investigation. These results support the previous published studies [30, 31]. Furthermore, this study assessed the prevalence of High-Risk HPV among women with ASC-US and the result was 76.7%, which is higher than that found in another study [32]. The positivity of High-Risk HPV in our study was statistically sig-

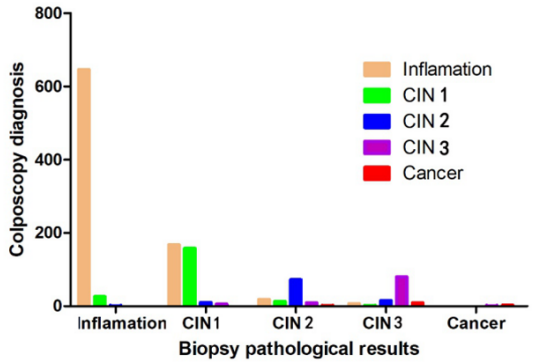

Figure 5. Correlation between colposcopy diagnosis and biopsy results in patients with ASC-US. Consensus between colposcopy diagnosis and biopsy pathology was absolutely matched in cases of ≥ CIN2+ ($P < 0.0001$).

nificantly elevated with increasing severity of the cervical lesion, in which the detection of High-Risk HPV was 100% in cervical cancer cases, 96.9% in CIN3, 87.8% in CIN2, and 76.9% in CIN1.

Also, our study evaluated the detection rate of high-grade CIN among positive and negative High-Risk HPV/ASC-US patients. We found that n = 179 (54%) of positive group had ≥ CIN2+ or worse, and only n = 15 (24.6%) of the negative group had presented with ≥ CIN2+ which was higher than that observed by a Swedish study [33]. In addition, we observed that the NPV of High-Risk HPV for the diagnosis of ≥ CIN2+ was 100% which is closely similar to that reported in previous studies as an NPV for detecting a high-level cervical lesion ranging from 97 to 100% [34-36]. Moreover, in final analysis we detected 14 cases with invasive cervical carcinoma and all of those were associated with HPV16+ and HPV18+ genotypes, which are highly oncogenic HPV strains.

From our results, we showed that high-grade CIN or worse are almost invariably within the positive category of High-Risk HPV (DNA) testing. Generally, ASC-US is reported to be more common in young women than old/postmenopausal women. This study noticed that women aged between (40-49) represent 38.52% of women with ASC-US Pap test result, i.e. the majority of ASC-US patients were diagnosed in young women due to females of young age mostly being affected by HPV infection. In our study, the age range of women affected by ASC-US was (21-78), which was approximately similar to those in Turkey, USA, and Chile, in that the ages of women with a first ASC-US cytology result ranged from teens to adulthood [24, 37]. The average age of our patients with an ASC-US lesion was 41.6 years which was above the average age of those observed in study [38]. In our study, all subjects with ASC-US cytology were referred to colposcopy examination since in China, colposcopy is a more attractive and useful strategy for detecting subsequent ≥ CIN2+ or worse cervical lesions. Also, one of the advantages of colposcopy in cases of ASC-US is that it immediately identifies the presence or absence of significant disease and this is the best way to select of patients who should be treated and monitored to prevent invasive cervical carcinoma. This result supports the result reported by the authors [39] that approve of immediate colposcopy when ASC-US cytology is present. Also, this study revealed that colposcopic impression has a high sensitivity and specificity for detecting high grade CIN. Our analysis showed that there was no statistical significance in the difference in detection rates of CIN1 and ≥ CIN2+ in ASC-US cases, which were 16% and 15.6% respectively as apparent in final pathologic outcome. Furthermore, the variety in detection rates of high-grade dysplasia in ASC-US cytology reported in many previous studies was 6.9-26.4%. The detection rate of high grade CIN in our study appeared to be higher than that reported in prior studies [22, 40]. One of important reasons for the high detection rate of high-grade dysplasia in Chinese ASC-US patients compared to those of foreign countries is the lack of Chinese cytopathology doctors and the difference in their diagnostic ability. From our results, we suggested that women diagnosed with a first ASC-US cytology should be considered with suspicion to exclude the possibility of development and/or progression to ≥ CIN2+ and invasive cancer. The main limitation of this study is the retrospectively collected data and the lack of patient follow-up during the period of the study.

Conclusion

We consider that Chinese women with ASC-US cytology have a wide range of pathology results, and ≥ CIN2+ accounted for a large proportion. ASC-US requires intensive evaluation to detect the women with risk for actual cervical cancer

and its precursors. A colposcopy is a principal approach to deal with ASC-US in China's current national conditions since it immediately identifies the presence or absence of significant disease and this is the best way of selection of patients who should be treated and monitored to prevent invasive cancer. HPV testing is a useful shunting measure for ASC-US patients as the High-Risk HPV detection rate increases with the increase of cervical lesion grade.

Acknowledgements

This study was conducted at Qilu Hospital of Shandong University and was supported by the national key R&D program of China (2016YFC1302900), the Key Research Project of Shandong Province (2017CXGC1210), the National Natural Science Foundation of China (NSFC, 81572559) and the National Science and Technology Project of China (2015BAI13B05).

Disclosure of conflict of interest

None.

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