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Referral patterns and incidence of cervical intraepithelial neoplasia in adolescent and pregnant patients: The impact of the 2006 guidelines:

Cervical intraepithelial neoplasia

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Abstract

Objective—The 2006 American Society for Colposcopy and Cervical Pathology (ASCCP) consensus guidelines for management of abnormal cervical cytology made significant changes to referral recommendations for adolescent and pregnant populations. In this study, we sought to review the impact of these new guidelines on referral patterns, along with the incidence of cervical intraepithelial neoplasia (CIN) 2/3 and cervical cancer in these two populations.

Materials and Methods—After obtaining IRB approval, a retrospective chart review of 12,333 patients referred to a single colposcopy clinic between January 2004 and November 2009 was performed. This colposcopy clinic serves as a statewide referral center. All adolescent patients (<21 years old) and pregnant patients were included for analysis. Patients were analyzed in two groups with respect to implementation of the 2006 guidelines. Statistical analysis was performed using chi square and Student's T-test.

Results—Between 2004–2007, prior to implementation of the 2006 guidelines, 9,346 patients were referred to colposcopy clinic. Overall, 1398 adolescents and 958 pregnant patients were identified and included in the analysis. The mean age was 23.0 (range 10–60). Of the 1398 adolescent patients, ASC-US pap smears accounted for 406 referrals (29.0%). Of the 958 pregnant patients, ASCUS cytology accounted for 284 referrals (29.6%). One case of squamous cell carcinoma (SCC) was identified in the pregnant population (0.1%) and no cases of SCC were diagnosed in the adolescent population. After implementation of the 2006 guidelines, between 2008 and 2009, a total of 2,987 patients were referred including 113 adolescent patients and 168 pregnant patients. The average age was 25.5 (range 16–54) which was not significantly different from 2004–2007, $p=0.79$. ASCUS accounted for 6 referrals in the adolescent population (5.3%) and 15 referrals in the pregnant population (8.9%). The decrease in the proportion of ASCUS cytology referrals in these populations was statistically significant at $p<.001$. No adolescent or pregnant patients were diagnosed with SCC during their colposcopic evaluation.

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Conclusions—The 2006 ASCCP consensus guidelines decreased the number of ASCUS cytology referrals to colposcopy in the adolescent and pregnant populations. The overall number of patients with SCC in these populations is quite small, therefore practitioners can be reassured that the new screening guidelines are unlikely to miss this diagnosis.. These guidelines provide an efficient, evidence-based approach to the cytologic evaluation of these special populations.

Keywords

cytology; pregnancy; adolescents; colposcopy

Background

Previous studies have attempted to develop a triage method for patient referral to colposcopy to minimize the risks associated with over-treatment of CIN1 while maximizing recognition and evaluation of advanced CIN. In 2006, the American Society for Colposcopy and Cervical Pathology (ASCCP) reviewed recent literature and formulated guidelines to streamline referral recommendations for patients with abnormal cervical cytology, and addressed management with regards to special populations, specifically pregnant and adolescent patients. The 2006 ASCCP consensus guidelines established that it is acceptable to repeat cytology in one year for these patients and forego immediate colposcopic evaluation, citing the high rate at which these low-grade lesions spontaneously regress [2]. Similarly, the 2006 guidelines also established that colposcopic examinations of pregnant patients with ASCUS or LSIL cytology can now be deferred until the postpartum period. Such remarkable changes in referral recommendations would logically lead to drastic alterations in the both the number and referral cytology of patients in a university-based colposcopy clinic, and we sought to evaluate the impact of these guidelines on our patient population.

Materials and Methods

After obtaining Institutional Review Board (IRB) approval from the University of Alabama at Birmingham, we identified all patients who were referred to a single colposcopy clinic between January 2004 and November 2009. All adolescents (defined as < 21 years of age) and pregnant patients were included in the analysis. Diagnosis of CIN was made via colposcopic impression and/or pathologic confirmation with cervical biopsy or loop electrosurgical excision procedure (LEEP). The 2006 guidelines were implemented into our referral practice beginning in January of 2008, and thus patients were analyzed as two groups: one group consisting of patients referred prior to 2008, and the second group consisting of patients referred after 12/2007. Abstracted data included age, referral cytology, colposcopic impression, pathology, and follow-up recommendations. The two groups were compared using [chi]2 test and Student's t test where appropriate. Because the duration of time included in the two groups differed, the proportions of total referrals were used in the statistical analysis. CPT codes were also queried for any pregnant or adolescent patients diagnosed with cervical cancer during this time frame, to identify any pregnant or adolescent patients referred to the University of Alabama at Birmingham's gynecologic oncology center who may not have had evaluation for CIN at this site.

Results

A total of 12,333 patients were identified. Prior to implementation of the 2006 guidelines (2004–2007), 9,346 patients were referred. 1398 (15.0%) adolescents (see Table 1.) and 958 (10.3%) pregnant patients (see Table 2.) were included in the analysis. The mean age was 23.0 (range 10–60).

After implementation of the guidelines, between 2008 and 2009, a total of 2,987 patients were referred for colposcopy. 113 adolescents (3.8%) and 168 (5.6%) pregnant patients were identified. The average age at referral was 25.5 (range 16–54) which was not significantly different from 2004–2007 ($p=0.79$). There was a statistically significant difference between the two groups in relation to referral cytology. Following the implementation of guidelines, a higher proportion of patients were referred for ASC-H and HSIL pap smears ($p<0.0001$ for both) and a smaller proportion of patients were referred for ASCUS pap smears ($p<0.0001$).

Of the 1398 adolescent patients referred between 2004–2007, ASC-US pap smears accounted for 406 referrals (29.0%). 578 (41.3%) adolescent patients had normal colposcopic impressions and/or no dysplasia on biopsy. 125 (8.9%) patients were diagnosed with CIN2, and 117 (8.4%) patients had CIN3. Forty-five (3.2%) patients in the adolescent cohort underwent a LEEP, and no cases of SCC were diagnosed in this population. After implementation of the guidelines, 113 adolescents were referred. ASCUS pap smears accounted for only 6 (5.3%) referrals ($p<0.0001$). A total of 43 patients were diagnosed with CIN2/3 (38.1%). This was a significantly larger proportion when compared with the earlier group (CIN2/3 combined=10.2%), $p<0.0001$. Again, no cases of invasive cancer were diagnosed in the cohort following implementation of the 2006 guidelines.

Between 2004–2007, ASCUS cytology accounted for 284 referrals (29.6%) within the pregnant population. 739 (77.1%) patients had a normal colposcopic impression or biopsy, 52 (5.4%) had pathology consistent with CIN2, and 47 (4.9%) patients had CIN3. One case of squamous cell carcinoma (SCC) was identified in the pregnant population (0.1%). Between 2007–2008, 15 (8.9%) pregnant patients were referred for ASCUS cytology. 37 (22.0%) were diagnosed with CIN 2/3 and no cases of squamous cell carcinoma were identified, which was again a significantly higher proportion than before the guidelines (CIN2/3 combined=10.3%), $p<0.0001$.

Discussion

The 2006 consensus guidelines were assembled to address referral guidelines for special populations including adolescents and pregnant patients. The changes from the 2001 guidelines primarily impacted the recommendations for adolescent patients with ASCUS cytology. The prevalence of high risk HPV in the adolescent population is approximately 20% [3]. In addition, it has been estimated that more than 90% of new HPV infections will be cleared within two years of acquisition in this population, supporting a less aggressive protocol for evaluation [4]. According to the 2006 ASCCP consensus guidelines, adolescent patients with ASCUS or LSIL cytology may be monitored conservatively with repeat cytology at 12 months for up to 24 months, without biopsy or excisional procedure for

pathologic diagnosis. Excisional procedures are still recommended for high-grade lesions (CIN3) [2]. Given the prevalence of HPV in this population, and the frequency with which HPV is cleared, the new guidelines have established a less aggressive algorithm for treatment and evaluation of low-grade lesions in this population.

The incidence of CIN is similar in pregnant and non-pregnant patients [5]. Prior to the 2006 ASCCP consensus guidelines, pregnant patients with abnormal cytology were referred for immediate colposcopy regardless of cytology result secondary to concerns for progression during pregnancy. However, cervical biopsy and excisional procedures during pregnancy are theoretically higher risk procedures given the increased cervical vascularity associated with pregnancy. The rate of progression of all squamous intraepithelial lesions during pregnancy is approximately 14%, while approximately 50% will regress [5]. The 2006 guidelines took into account this high rate of regression and have recommended that patients with antepartum ASCUS or LSIL cytology may now defer colposcopy until post-partum evaluation.

Our data illustrate the expected decrease in the proportion of pregnant patients and adolescents with ASCUS cytology referred for colposcopic evaluation. In addition, these results demonstrate that despite deferring evaluation for 1 year in the adolescent population and until 6 weeks post partum in the pregnant population, the incidence of cervical cancer in these populations did not increase. This supports recent guidelines that conservative management for ASCUS or LSIL cytology and low-grade cervical intraepithelial neoplasia in these special populations is medically reasonable, and not likely to result in increased rates of squamous cell carcinoma.

Our data did show an increase in the proportion of CIN2/3 diagnosed in the adolescent and pregnant population after institution of the 2006 guidelines, without an increase in the incidence of carcinoma. This is not reflective of a delay in screening and progression of CIN, but rather it reflects the appropriate shift toward referral of those patients who are at highest risk of significant lesions based on screening cytology and truly need colposcopic evaluation.

Although this study is strengthened by the wide referral base and large study population, one of the limitations of this study is that it did not elucidate which referrals were for first time or recurrent abnormal cytology. In addition, the less aggressive guidelines raise concern regarding compliance and follow-up with delayed evaluation, especially in the adolescent population. Historically, follow-up is as low as 24% in this population [5], and although not abstracted in this study, rates in the study population are likely equivalent given the broad, state-wide referral base from which the patients were selected.

In conclusion, the 2006 ASCCP consensus guidelines made significant changes to the recommendations for colposcopic evaluation in the adolescent and pregnant populations. Overall, recommendations are for less aggressive management of those with low-grade cytology. Although compliance is a concern among these populations, this study confirms that the rate of squamous cell carcinoma is exceedingly low in these populations. Practitioners can be reassured that compliance with these new guidelines will not result in

missed diagnoses of CIN2/3 and/or carcinoma. In addition, these data support the most recent recommendations by ACOG in December 2009 for initiation of cervical cancer screening at age 21, which is a logical incremental step in the evolution of cervical cancer screening.

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Table 1

Adolescent referrals before and after institution of the 2006 ASCCP guidelines.

	Before N=1398(%)	After N=113 (%)	P Value
Cytology			
ASCUS	406 (29)	6 (5.3)	.0001
LSIL	530 (37.9)	40 (35.4)	.616
HSIL	121 (8.6)	42 (37.2)	.0001
ASC-H	55 (3.9)	23 (20.4)	.0001
Pathology			
Normal	578 (41.3)	18 (15.9)	.0001
CIN I	211 (15.1)	20 (17.7)	.496
CIN II	125 (8.9)	31 (27.4)	.0001
CIN III	117 (8.4)	12 (10.6)	.291
SCC	0 (0)	0 (0)	N/A

Table 2

Pregnant patient referrals before and after implementation of the 2006 ASCCP guidelines.

	Before	After	P Value
	N=958 (%)	N=168 (%)	
Cytology			
ASCUS	284 (29.6)	15 (8.9)	.0001
LSIL	370 (38.6)	22 (13.1)	.0001
HSIL	121 (12.6)	73 (43.5)	.0001
ASC-H	51 (5.3)	53 (31.5)	.0001
Pathology			
Normal	739 (73.1)	47 (28.0)	.0001
CIN I	78 (8.1)	28 (16.7)	.001
CIN II	52 (5.4)	17 (10.1)	.03
CIN III	47 (4.9)	20 (11.1)	.0001
SCC	1 (.06)	0 (0)	.32