

Abnormal cervical smears in adolescents: A ten-year comparative study of demographic criteria and management

M.M. Saleh, *Specialist Registrar*; A.A. Seoud, *Staff Grade*; M.S. Zaklama, *Consultant*

Department of Obstetrics and Gynaecology, Rochdale Infirmary, Whitehall Street, Rochdale, Lancashire (UK)

Summary

Objective: Comparison of the demographic criteria and management of adolescents and other age groups referred to a colposcopy clinic with abnormal smears. **Methods:** Retrospective study of newly referred cases to a colposcopy clinic in a UK district general hospital between 1996 and 2005. **Results:** Most of the sociodemographic and sexual factors associated with HPV infection and cervical cancer were more obvious among adolescents than older women. There was a comparable incidence of high-grade cervical lesions in the two groups. **Conclusions:** A policy is needed to deal with adolescents who are exposed to all the risk factors associated with the development of HPV infection and high-grade cervical lesions. This has become an important issue for discussion recently in the UK after raising the age of onset of cervical screening to 25.

Key words: Teenagers; Human papillomavirus; Cervical cytology; Cervical screening.

Introduction

Cervical cancer is still one of the common cancers in women worldwide [1]. The most common risk factors that have been associated with the development of cervical cancer and human papillomavirus (HPV) infection are: a woman's lifetime number of sexual partners, her age at commencement of sexual activity [2], and the number of sexual partners of the male partner [3]. Variables reflecting low socio-economic status, long-term use of oral contraceptives, smoking and high parity have been extensively studied but a valid association with cervical cancer was not established [4].

The incidence of abnormal smears among adolescents has been reported to be higher than in adult women [5]. Some investigators even showed that the prevalence of abnormal smears in young women was increasing worldwide [6]. Many behavioural factors, e.g., early age of first sexual intercourse [7], and biological factors, e.g., low immunity and vulnerability to HPV infection due to the rapid physiological changes of puberty [8] were thought to be related to this problem.

An understanding of the demographic criteria and risk factors in adolescents referred with abnormal cervical smears and a review of their management in comparison with other age groups are important for implementing a plan of care for these patients.

This study was planned to identify and compare the demographic criteria and the management of teenage patients referred with abnormal smears with those of other age groups and to analyse the current recommendations of the age of onset of cervical screening in UK.

Patients and Methods

This retrospective study was conducted on all the newly referred patients to a consultant colposcopy clinic at a UK district general hospital from 1996 to 2005. The total number of cases was 1,763. One hundred and fifty-five patients (8.79%) were teenagers (≤ 20 years). The rest of the group (1,608) had an age range between 21 and 83.

The details of each case were recorded manually on a proforma and then transferred to an electronic database. The electronic records were reviewed and extracted for the following information:

- Demographic criteria of the patient which included: age, age at first sexual intercourse, age at first smear, number of sexual partners, smoking, method of contraception and parity.
- Smear results (presenting cytological abnormality).
- Colposcopic findings and suspected diagnosis.
- Investigations performed, e.g., swabs, biopsies and their results.
- Histopathological findings.

Patients were divided into two groups according to age:

- Group A (≤ 20).
- Group B (> 20).

The two groups were compared as regards their demographic criteria and risk factors for development of cervical cancer, smear results, colposcopic findings, and histopathology results.

The data were analysed using a SPSS program, version 11.

Results

The demographic characteristics of the two groups of patients investigated in the current study are illustrated in Table [1]. Of the teenagers (group A) 36.8% had their first intercourse before the age of 16 compared to 15.5% in group B. All the patients in group A and 84.5% in group B were sexually active by the age of 20.

The percentage of adolescents who had multiple sexual partners (2-10) was higher than that of the other group (77.4% compared to 71.5%). On the other hand, the incidence of women with more than ten partners was higher in group B.

Table 1. — *Demographic criteria.*

	Group A (Total 155)		Group B (Total 1,608)	
	No.	%	No.	%
<i>Age at first intercourse</i>				
< 16	57	36.77%	249	15.49%
16- 20	98	63.23%	1,110	69.03%
> 20	—	—	192	11.49%
Not documented	—	—	57	3.54%
<i>No. of partners</i>				
1	20	18.71%	273	16.98%
2-10	120	77.42%	1,149	71.46%
> 10	6	3.87%	125	7.77%
Not documented	—	—	61	3.79%
<i>Smoking</i>				
Non smokers	57	36.77%	689	42.85%
Smokers	95	61.29%	796	49.5%
Previous smokers	3	1.94%	92	5.72%
Not documented	—	—	31	1.93%
<i>Contraception</i>				
None	35	22.58%	341	21.21%
Combined pills	85	54.84%	449	27.92%
Sheath	22	14.19%	138	8.58%
IUCD	1	0.65%	80	4.98%
♀ Sterilisation	—	—	193	12%
♂ Sterilisation	—	—	111	6.9%
Cap	—	—	5	0.31%
Others	12	7.74%	73	4.54%
Postmenopausal	—	—	194	12.06%
Not documented	—	—	24	1.49%
<i>Parity</i>				
0	90	58.06%	379	23.57%
1	56	36.13%	354	21.46%
> 1	7	4.52%	856	53.23%
Not documented	2	1.29%	28	1.74%

About 61% of the teenagers were smokers; the percentage dropped to 49.5% in those above the age of 20. Analysis of parity showed that 40.7% of group A had one or more children compared to 74.8% in group B. Variable methods of contraception were used by each group. Of the adolescents 54.8% used birth control pills; the percentage dropped to about 28% in the other group. Similar proportions in the two groups did not use any method of contraception.

Different types of vaginal and endocervical swabs were taken from 81.3% of group A and 69.8% of group B. The incidences of fungal, viral, protozoal and Chlamydia infections were higher in group A, whereas bacterial infections were more frequent in group B (Table 2).

Table 2. — *Swab results.*

Swab results	Group A		Group B	
	No.	%	No.	%
Normal	96	61.93%	812	50.49%
Fungal infection	10	6.45%	94	5.84%
Bacterial infection	7	4.52%	195	12.13%
Viral infection	1	0.65%	1	0.06%
Protozoal infection	5	3.22%	5	0.31%
Chlamydia	7	4.52%	16	0.99%
No swabs taken	29	18.71%	485	30.16%
Total	155		1,608	

All the patients in group A (except one) were referred with an abnormal smear result. Twenty percent of these patients had had their first smear before the age of 16. About 53% had a smear showing moderate or severe dyskaryosis. In group B none of the patients had had a smear before the age of 16 but 49.7% had their first smear between the ages of 16 and 20. Referral smear results suggestive of high-grade lesions were reported in 46.14% of cases in this group. Both groups had a similar percentage of borderline smears (9%). A minority of patients (1.2%) in group B presented with smears suggestive of invasive disease (Table 3).

Table 3. — *Referral smear results.*

Smear results	Group A		Group B	
	No.	%	No.	%
Normal	1	0.65%	24	1.49%
HPV	5	3.23%	—	—
Mild dyskaryosis	52	33.55%	467	29.04%
Moderate dyskaryosis	68	43.87%	477	29.66%
Severe dyskaryosis	14	9.03%	265	16.48%
Borderline changes	15	9.67%	145	9.02%
Invasive	—	—	20	1.24%
Infection	—	—	54	3.36%
Others	—	—	84	5.22%
Not documented	—	—	72	4.48%
Total	155		1,608	

HPV: Human papillomavirus; Others: Unsatisfactory.

Colposcopic examination supported the suspicion of a high-grade lesion in the majority of cases picked up by the smears in group A (79/82). It also proved that 14.8% of the cases in this group were normal. In group B it confirmed the presence of high-grade lesions in about 82% of cases suspected of having such lesions by smears (Table 4).

Table 4. — *Results of colposcopy examination.*

Colposcopy findings	Group A		Group B	
	No.	%	No.	%
Normal	23	14.84%	388	24.13%
Low grade	51	32.9%	357	22.2%
High grade	79	50.97%	593	36.88%
Microinvasive	—	—	15	0.93%
Invasive	—	—	11	0.68%
VAIN	—	—	3	0.19%
VIN	—	—	8	0.49%
Inconclusive	2	1.29%	173	10.76%
Not documented	—	—	60	3.73%
Total	155		1,608	

VAIN: Vaginal intraepithelial neoplasia; VIN: Vulval intraepithelial neoplasia.

Histopathological examination of biopsies or tissues removed during treatment (diathermy loop excision) showed high-grade lesions (CIN II & III) in 40.64% of the referred cases in group A, 25.4% of those with high-grade lesions (16/63) also had glandular involvement and one case had VAIN. In group B, the percentage of high-grade lesions shown by histology was 38.18%, and about 35.3% of them had glandular involvement. A very limited number of group B (< 0.1%) had microinvasive or invasive lesions (Table 5).

Table 5. — *Histopathology results.*

Histopathology results	Group A		Group B	
	No.	%	No.	%
Normal	7	4.51%	91	5.66%
Chronic cervicitis	29	18.71%	177	11.01%
HPV	17	10.97%	100	6.22%
CIN I	24	15.48%	191	11.88%
CIN I + glandular disease	—	—	7	0.44%
CIN II	26	16.77%	200	12.44%
CIN II + glandular disease	6	3.87%	36	2.24%
CIN III	20	12.9%	192	11.94%
CIN III + glandular disease	10	6.45%	181	11.26%
CIN III + VAIN	1	0.65%	5	0.3%
Microinvasive	—	—	3	0.19%
Invasive	—	—	12	0.75%
VAIN	—	—	5	0.3%
Unsatisfactory	1	0.65%	16	0.99%
Not documented	1	8.38%	104	6.47%
No treatment or biopsy	13	0.65%	288	17.91%

CIN: Cervical intraepithelial neoplasia.

Discussion

Many factors have been associated with the development of cervical intraepithelial neoplasia and invasive disease. Epidemiologic studies have shown that the risk of cervical cancer is increased among women who begin having sexual intercourse at an earlier age [2, 9, 10] and who have had greater number of sexual partners [11, 12]. The same factors have also been linked with HPV infection. The present study showed that a higher percentage of adolescents (group A) tend to have their first sexual contact before the age of 16 compared to the older group (group B). The tendency to have multiple sexual partners (2-10) was slightly higher in group A as well. If we put into consideration the average duration of sexual activity of each group, which is expected to be higher in group B, the finding would be more significant (Table 1).

There was no consensus on the effect of other risk factors, e.g., smoking, contraceptive pills, and parity on the development of cervical neoplasia. Controversy about the correlation between smoking and high-grade cervical lesions or cervical cancer was obvious. Some studies have shown the link [13] while others failed to find any association after adjusting for HPV infection [4, 14]. The same concept applies to the use of birth control pills which has been linked to the development of invasive cervical cancer by some authors [4, 15] while others failed to find this association [14, 16]. The percentage of the smokers and pill users in group (A) was higher than that in group (B) (Table 1). If we accepted these as risk factors, the findings would be significant. Current or previous pregnancy has been considered by some authors as a possible risk for HPV infection based on the hormonal effects of pregnancy on immune response shown from some *in vitro* studies [17]. The percentages of women with one or more children in the current study were higher in group B.

Chlamydia infection was suspected as a risk factor for cervical cancer [18]. Studies in Spain [19] and Nordic countries [1] showed that the presence of antibodies for

Chlamydia trachomatis after adjustment for HPV DNA were associated with a higher risk of developing CIN III and invasive cervical cancer. The indulging aetiology is not yet clear. The incidence of Chlamydia infection in our study was nearly four times higher among the adolescents compared with the older age group (Table 2). The above findings showed that most of the sociodemographic, sexual and obstetric factors traditionally associated with cervical cancer were detected in the two groups but they were more obvious among the adolescents (group A).

About 53% of the cases in group A and 46.14% in group B were referred with smears showing moderate or severe dyskaryosis. Colposcopic examination supported the presence of high-grade lesions in the majority of them (about 96% in group A and 80% in group B). Histology confirmed the diagnosis of high-grade lesions (CIN II and III) in 79.7% of these cases in group A with glandular involvement detected in 25.4% of them. In group B all the cases picked up as high-grade lesions by colposcopy were confirmed by histology, and the incidence of glandular involvement among them was 34.3%. The overall incidences of CIN II and CIN III in the two groups were comparable (Tables 3, 4, 5).

Dealing with abnormal smears in adolescents is usually a problem which has become more complicated recently in the UK after the implementation of the new national guidelines of the cervical screening programme which increased the age of onset of screening to 25 [20]. This means that the teenagers who start sexual activity before the age of 16 will be left exposed to the risks and unchecked for about ten years.

The rational behind raising the age of starting cervical screening is the rarity of cases of cervical cancer under the age of 25 [21] on one hand, and the high chance of transient HPV infection [22] and high percentage of low-grade disease which usually resolve spontaneously on the other hand [23]. In 2002, only 26 cases of cervical cancer were registered in this age group in the UK. In contrast, 55,000 women aged between 20 and 24 were reviewed with abnormal smears (borderline or worse) [20]. This view did not take into account the fact that the main aim of the cervical screening programme is the detection and treatment of precancerous lesions and not cervical cancer itself. A possible cause of the small number of cancer cases detected could be the large number of women in this age group (50,000) who were referred with abnormal smears and the treatment of high-grade lesions among them. Without knowing the number of high-grade lesions detected and treated in this group it is difficult to judge the efficacy of the screening programme among these patients.

A meta-analysis [24] of 15 studies dealing with the natural history of cervical squamous abnormalities showed that the risk of progression of borderline and low-grade abnormalities to invasive cervical cancer over 24 months was 1-2/1,000 and this risk increased to 23% in high-grade lesions. The present study demonstrated that the confirmed incidence of high grade lesions was nearly the same among the adolescents and the older

group. However, those under the age of 25 will not have a chance of diagnosis and treatment. With more teenagers tending to start their sexual life at an earlier age, and the current sexual behaviour of having unprotected sex and multiple partners, the risk is more likely to increase.

The new guidelines do not provide a solution for patients who might be at risk and/or develop high-grade lesions in their early teens (< 16 years old). Dealing with this problem could be either to lower the age of the first smear or to link that age to the age of first sexual intercourse. Perhaps we need to look into the current guidelines of the American Cancer Society [25] which recommend that screening be initiated within three years of the onset of vaginal intercourse but not later than the age of 21. These guidelines are based on studies which showed that there was little probability of a significant precancerous lesion being detected within the first three to five years after the onset of sexual activity. An important element of the plan of action should be sexual education and promotion of the practice of safe sex.

References

- [1] Koskela P., Anttila T., Bjorge T., Brunsvig A., Dillner J., Hakama M. *et al.*: "Chlamydia Trachomatis infection as a risk factor for invasive cervical cancer". *Int. J. Cancer*, 2000, 85, 35.
- [2] Ho G.Y.F., Bierman R., Beardsley L., Chang C.J., Burk R.D.: "Natural history of cervicovaginal papillomavirus infection in young women". *N. Engl. J. Med.*, 1998, 338, 423.
- [3] Burk R.D., Ho G.Y.F., Beardsley L., Lempa M., Peters M., Bierman R.: "Sexual behaviour and partner characteristics are the predominant risk factors for human papillomavirus infection in young women". *J. infect. Dis.*, 1996, 174, 679.
- [4] Bosch F.X., Munoz N., De Sanjose S., Izarzugaza I., Gill M., Viladiu P. *et al.*: "Risk factors of cervical cancer in Colombia and Spain". *Int. J. Cancer*, 1992, 52, 750.
- [5] Mount S.L., Papillo J.L.: "A study of 10,296 pediatric and adolescent Papanicolaou smear diagnoses in Northern New England". *Pediatrics*, 1999, 103, 539.
- [6] Mangan S.A., Legano L.A., Rosen C.M., McHugh M.T., Fierman A.H., Dreyer B.P. *et al.*: "Increased prevalence of abnormal Papanicolaou smears in urban adolescents". *Arch. Pediatr. Adolesc. Med.*, 1997, 151, 481.
- [7] Greenberg J., Magder L., Aral S.: "Age at first coitus: a marker for risky sexual behavior in women". *Sex Transm. Dis.*, 1992, 19, 331.
- [8] Moscicki A.B., Burt V.G., Kanowitz S., Darragh T., Shiboski S.: "The significance of squamous metaplasia in the development of low grade squamous intraepithelial lesions in young women". *Cancer*, 1999, 85, 1139.
- [9] Kotloff K.L., Wasserman S.S., Russ K., Shapiro S., Daniel R., Brown W. *et al.*: "Detection of genital human papillomavirus and associated cytological abnormalities among college women". *Sex Transm. Dis.*, 1998, 25, 243.
- [10] Franco E.L., Villa L.L., Sobrinho J.P., Prado J.M., Rousseau M.C., Déry M. *et al.*: "Epidemiology of acquisition and clearance of cervical human papillomavirus infection in women from a high-risk area for cervical cancer". *J. Infect. Dis.*, 1999, 180, 1415.
- [11] Baken L.A., Koutsky L.A., Kuypers J., Kosorok M.R., Lee S.K., Kiviat N.B. *et al.*: "Genital human papillomavirus infection among male and female sex partners: Prevalence and type specific concordance". *J. Infect. Dis.* 1995, 171, 429.
- [12] Kjaer S.K., Van den Brule A.J.C., Bock J.E., Poll P.A., Engholm G., Sherman M.E. *et al.*: "Determinants for genital human papillomavirus infection in 1000 randomly chosen young Danish women with normal Pap smear: Are there different risk profiles for oncogenic and non oncogenic HPV types?". *Cancer Epidemiol. Bio markers Prev.*, 1997, 6, 799.
- [13] Neglangel C., Munoz N., Bosch F.X., Limson G.M., Festin M.R., Deacon J. *et al.*: "Causes of cervical cancer in the Philippines: A case-control study". *J. Natl. Cancer Inst.*, 1998, 90, 43.
- [14] Olsen A.O., Gjoen K., Sauer T., Orstavik I., Naess O., Kierulf K., *et al.*: "Human papillomavirus and cervical intraepithelial neoplasia grade II-III: A population based case control study". *Int. J. Cancer*, 1995, 61, 312.
- [15] Invasive squamous-cell cervical carcinoma and combined oral contraceptives: Results from a multinational study. WHO collaborative study of neoplasia and steroid contraceptives. *Int. J. Cancer*, 1993, 55, 228.
- [16] Kjaer S.K., Van Den Brule A.J.C., Bock J.E., Poll P.A., Engholm G., Sherman M.E. *et al.*: "Human papillomavirus - the most significant risk determinant of cervical intraepithelial neoplasia". *Int. J. Cancer*, 1996, 65, 601.
- [17] Pater M.M., Hughes G.A., Hyslop D.E., Nakshatri H., Pater A.: "Glucocorticoid-dependant oncogenic transformation by type 16 but not type 11 human papillomavirus DNA". *Nature*, 1988, 335, 832.
- [18] Schachter J., Hill E.C., King E.B., Heilbron D.C., Ray R.M., Margolis A.J. *et al.*: "Chlamydia trachomatis and cervical neoplasia". *J. Amer. Med. Ass.*, 1982, 248, 2134.
- [19] De Sanjose S., Muñoz N., Bosch F.X., Reimann K., Pedersen N.S., Orfila J. *et al.*: "Sexually transmitted agents and cervical neoplasia in Colombia and Spain". *Int. J. Cancer*, 1994, 56, 358.
- [20] Colposcopy and programme management (2004) Guidelines for the NHS cervical screening programme. NHS CSP Publications No 2, Sheffield, 2004.
- [21] Sasieni P., Adams J.: "Effect of screening on cervical cancer mortality in England and Wales: analysis of trends with an age cohort model". *Br. Med. J.*, 1999, 318, 1244.
- [22] Adelstein A.M., Husain O.A.N., Spriggs A.I.: "Cancer of the cervix and screening". *Br. Med. J.*, 1981, 282, 564.
- [23] Collins S., Mazloomzadeh S., Winter H., Blomfield P., Bailey A., Young L.S. *et al.*: "High incidence of human papillomavirus infection in women during their first sexual relationship". *Br. J. Obstet. Gynaecol.*, 2002, 109, 96.
- [24] Melinkow J., Nuovo J., Willan A.R., Chan B.K.S., Howell L.P.: "Natural history of cervical squamous intraepithelial lesions: A meta-analysis". *Obstet. Gynecol.*, 1998, 92, 727.
- [25] Moscicki A.B.: "Cervical cytology screening in teens". *Curr. Womens Health Rep.*, 2003, 3, 433.

Address reprint requests to:
M.M. SALEH, M.D.
27 Clement Royds Street
Rochdale, Lancs OL12 6SG (UK)