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# Comparative risk assessment of age and parity in cervical carcinogenesis

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**OBJECTIVE(S):** To find which of the two risk factors - age and parity, play dominant role in cervical carcinogenesis

**METHOD(S):** Detailed information regarding age and parity has been available in 12,456 women registered for cervical cytology between January 1992 and May 2005 at our gynecological out patient department. Critical analysis was carried out in these women categorizing them into two groups viz., women of different age groups with varying parity and women of different parity groups with varying age.

**RESULTS:** The incidence of squamous intraepithelial lesion (SIL) in the present series was 10.5% (1314 /12456) while squamous cell carcinoma was 0.8% (109 /12456). The incidence of SIL and carcinoma cervix showed progressive rise with increasing age and parity. The detailed analysis of the two groups defined above revealed SIL incidence rising with increasing parity in nearly all age groups and with increasing age in nearly all parity groups but the corresponding figures were much higher in women of high age and high parity. The SIL rate was found to be maximum in women of high age with high parity. Similar trend was also seen in case of carcinoma cervix.

**CONCLUSION(S)** : Women of high age with high parity are at very high risk of developing carcinoma cervix and this may be due to cumulative effect of both these risk factors. Hence women of this category need special attention for mandatory cytological screening.

**Key words :** age, parity, squamous intraepithelial lesion, carcinoma cervix.

## Introduction

Though the etiology of carcinoma cervix is multifactorial, age and parity play a predominant role in the process of malignant transformation which extends for over 5 years. It will be quite interesting to find out which of these two factors - age and parity-highly influences cervical carcinogenesis or combination of both has a greater impact. At our hospital routine cytological screening is in progress in women attending gynecological out patient department and we have 12,456 women registered between January 1992 and May 2005 of whom detailed information regarding age and parity is available. We investigated the differential role of these two risk factors by analyzing the incidence of squamous intraepithelial lesion (SIL) and carcinoma cervix in different age groups with varying parity and in different parity groups with varying age.

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## Methods

The present study relates to 12,456 women on whom cervical cytology was done between January 1992 and May 2005 and a detailed information regarding their age and parity was available. These women were from the low and middle socio-economic classes and visited the hospital for treatment of gynecological ailments. In each case a scrape smear was collected from the squamocolumnar junction of the cervix and stained by Papanicalaou technique. The cytopathological changes observed in cervical smears were classified according to Bethesda System of reporting cervical cytological diagnosis [1]. According to the study protocol,

cervical biopsy was taken in all high squamous intraepithelial lesions (HSIL) and carcinoma cervix cases.

Where P1 is the percentage observed in the study group and P in the control group (n=1374). The P value was ascertained on the findings of the Z value. If the Z value was <1.96, the difference was not significant (P>0.05). If the Z value was >1.96 the difference was significant (P<0.05). If the Z value was >2.58, the difference was highly significant (P<0.01).

**Results**

Cytological evaluation of the cervical smears in 12,456 women revealed following cytopathologies –

| | | |
|---|---|---|
| I. | Squamous intraepithelial lesions (SIL) | 1314 (10.5%) |
| Ia | Low grade squamous intraepithelial lesions (LSIL) | 1112 (8.9%) |
| Ia-1 | Mild dysplasia | 969 (7.8%) |
| Ia-2 | Condyloma (HPV) | 143 (1.1%) |
| Ib | High grade squamous intraepithelial lesions (HSIL) | 202 (1.6%) |
| Ib-1 | Moderate dysplasia | 173 (1.4%) |
| Ib-2 | Severe dysplasia | 29 (0.2%) |
| II | Invasive squamous cell carcinoma | 109 (0.8%) |

The incidence of SIL in the present series was 10.5% (1314/124/56) while that of cervical malignancy 0.8% (109/124/54). Incidence of SIL and squamous cell carcinoma in different age groups is shown in Table 1. Incidence of SIL showed progressive rise with increasing age rising from 5.8% in younger women below 20 years to 12.4% in women beyond 40 years of age. The difference was statistically highly significant (P<0.01). Incidence of invasive squamous cell carcinoma also showed rise with progressive age but no case of malignancy was encountered in young women below 20 years.

The incidence of cytopathologies in the cervix in different parity groups is shown in Table 2. The SIL incidence showed progressive rise from 7.2% in nulliparas to 11.2% in paras ≥ 3. This difference was statistically highly significant (P<0.01). However, the difference in SIL rate between nulliparas and para 1 and 2 was insignificant (P>1.01). The incidence of squamous cell carcinoma also showed a rising trend with increasing parity. It was maximum in those with parity ≥ 3 or more. No case of malignancy was observed in nulliparous women.

For purpose of detailed analysis, the 12,456 women were categorized into two groups - (a) women of different age groups with varying parity and (b) women of different parity groups with varying age. The incidence of SIL and squamous cell carcinoma in different age groups with increasing parity is shown in Table 3. In women upto 20 years of age, the SIL incidence of 4.4% observed in nulliparas rose to 9.9% in multiparas and the difference was statistically highly significant (P<0.01). However, in women between 21-30 years of age, the rise was found to be insignificant (P>0.01), but in women beyond 30 years, the rise was highly significant (P <0.01). It is worth pointing out here that corresponding SIL incidences were much higher in older women beyond 40 years of age. As regards carcinoma cervix, no case was seen in young women of ≤ 20 years. However, five cases of carcinoma cervix were seen in women between 21-30 years of age but only with parity ≥ 2. In women 31-40 years of age, fluctuating trend was seen in the incidence of carcinoma cervix but in older women beyond 40 years, a definite progressive increase in the incidence was observed rising from 1.2% in women with single parity to 2.1% in multiparous women and the difference was statistically highly significant (P<0.01).

These figures reveal that both high age and high parity appear to be major contributory factors in the occurrence of cervical cytopathologies.

The incidences of SIL and carcinoma cervix were also investigated in different parity groups with varying age (Table 4). The SIL rate showed fluctuating trend in nulliparous women and in women with single parity but in multiparous women, the incidence showed progressive rise with increasing age and the difference was highly significant (P<0.01). It is emphasized here that the corresponding figures of SIL were much higher in women with parity ≥3. As regards carcinoma cervix, no case was seen in nulliparous women but in women with parity 1, a definite rise in the incidence of carcinoma cervix was seen with increasing age and the difference was highly significant (P<0.01).

**Table 1. Incidence of SIL and cancer cervix in different age groups.**

| Age (year) | Number of cases | Squamous intraepithelial lesion Number (Percentage) | Carcinoma cervix Number(Percentage) |
|---|---|---|---|
| ≤ 20 | 241 | 14 (5.8%) | Nil |
| 21-30 | 3529 | 331 (9.3%) | 5 (0.1%) |
| 31-40 | 4347 | 428 (9.8%) | 18 (0.4%) |
| ≥ 41 | 4339 | 541 (12.4%) | 86 (1.9%) |

**Table 2. Incidence of SIL and cancer cervix in different parity groups.**

| Age (year) | Number of cases | Squamous intraepithelial lesion Number (Percentage) | Carcinoma cervix Number(Percentage) |
|---|---|---|---|
| 0 | 289 | 21 (7.2%) | Nil |
| 1 | 835 | 66 (7.9%) | 2 (0.2%) |
| 2 | 2289 | 212 (9.2%) | 8 (0.3%) |
| > 3 | 9043 | 1015 (11.2%) | 99 (1.1%) |

**Table 3. Incidence of squamous intraepithelial lesion and cancer cervix in different parities of particular age groups.**

| Age (Years) | | Nulliparous | Parity 1 Number | Parity 2 Number | Parity ≥ 3 Number |
|---|---|---|---|---|---|
| ≤ 20 | n=241 | n=45 | n=85 | n=77 | n=34 |
| | SIL | 2 (4.4%) | 5 (5.8%) | 4 (5.1%) | 3 (8.8%) |
| | Carcinoma cervix | - | - | - | - |
| 21-30 | (n=3524) | n=143 | n=494 | n=1112 | n=1780 |
| | SIL | 13 (9.1%) | 43 (8.7%) | 101 (891%) | 174 (9.7%) |
| | Carcinoma cervix | - | - | 1 (0.08%) | 4 (0.2%) |
| 31-40 | (n=4347) | n=66 | n=167 | n=745 | n=3369 |
| | SIL | 3 (4.3%) | 11 (6.5%) | 63 (8.4%) | 351 (10.4%) |
| | Carcinoma cervix | - | 1 (0.5%) | 2( 0.2%) | 15 (0.4%) |
| ≥ 41 | (n=4339) | n=35 | n=81 | n=355 | 3860 |
| | SIL | 3 (8.3%) | 7 (7.8%) | 34 (12.3%) | 487 (12.6%) |
| | Carcinoma cervix | - 1(1.2%) | 5 (1.4%) | 80 (2.1%) | |

Figure in brackets represent percentages SIL - squamous intraepithelial lesion

**Table 4. Incidence of SIL and cancer cervix in different ages of particular parity group.**

| Parity | | Age (years) ≤ 20 | 30-35 | 31-40 | ≥ 41 |
|---|---|---|---|---|---|
| 0(289 case) | n=289 | n=45 | n=143 | n=66 | n=35 |
| | SIL | 2 (4.4%) | 13 (9.1%) | 3 (4.5%) | 3 (8.3%) |
| | Carcinoma cervix | Nil | Nil | Nil | Nil |
| | n=835 | n=85 | n=494 | n=157 | n=89 |
| | SIL | 5 (5.8%) | 43 (8.7%) | 11 (6.3%) | 7 (7.8%) |
| | Carcinoma cervix | Nil | - | 1 (0.5%) | 1 (1.1%) |
| | n=2289 | n=77 | n=1112 | n=745 | n=355 |
| | SIL | 4 (5.1%) | 101 (9.1%) | 63 (8.4%) | 44 (12.3%) |
| | Carcinoma cervix | Nil | 1 (0.08%) | 2 (0.2%) | 5 (1.1%) |
| ≥3 (9043 cases) | n=9043 | n=34 | n=1780 | n=3369 | n=3860 |
| | SIL | 3 (8.8%) | 174 (9.7%) | 351 (10.4%) | 487 (12.6%) |
| | Carcinoma cervix | Nil | 4 (0.2%) | 15 (0.4%) | 80 (2.1%) |

Number in brackets represent percentages SIL - squamous intraepithelial lesion

## Discussion

In the present series, the incidence of SIL and carcinoma cervix showed progressive rise with increasing age and parity and was maximum in women of age above 40 years and parity ≥3. In an earlier study in India, Iyer and Shah [2] (1981) found cervical dysplasia more commonly after the age of 30 years. This in all probability appears to be related to the prolonged sexual activity as marriage at an early age is very common in India. Caslaneda - Iniquez and Toledo [3], have also emphasized sexual activity at an early age as a potential risk factor for cervical premalignancies. In a recent UK National study on cervical cancer Green et al [4] have found that risk of squamous cell carcinoma was strongly related independently to the age at the first intercourse. They have also noticed that risk of cervical cancer was associated with high parity and the risk increased with early age at the first birth. In an Australian study emphasizing rurality factor, Dietsch et al[5] have found that risk of cervical cancer increases in women above the age of 50 years but CIN peaks in the 20-24 age group.

High parity has also been considered a great predisposing factor in the process of cervical carcinogenesis. Our findings obtain substantial support from earlier Indian study which noticed that the incidence of dysplasia increased with parity[6]. Caslanedo-Iniquez et al[3] have also stressed the number of pregnancies as a risk factor for developing cervical dysplasia.

The aim of the present investigation was to delineate which of these two risk factors - age or parity-plays a major role in the development of SIL and carcinoma cervix. Detailed analysis carried out in women of different age group with varying parity and in women of different parities with varying age group revealed progressive rise in SIL and carcinoma cervix in nearly all age groups with increasing parity and in all parity groups with increasing age. But interestingly, the corresponding figures as regards incidence of SIL and cervical cancer were much higher in women of higher age above 40 years and in those with high parity of 3. Moreover, the incidences of both SIL and carcinoma cervix were much higher in women of high age with high parity. Thus it can be stated that while high age and high parity individually play major role as risk factors in development of cervical cancer cumulative impact of both these predisposing factors may pose greater risk for the onset of premalignant transformation in the cervix and later for the development of squamous cell carcinoma. Hence though women of high age irrespective of parity and women of high parity irrespective of age should be considered as high risk for developing SIL and carcinoma cervix, when women of high age with high parity are encountered they should be presumed to be at great risk for development of carcinoma cervix and hence be provided special attention for immediate mandatory cytological evaluation to rule out any abnormal cytopathological changes originating in the cervix. The women of this category should not be left alone at any cost.

Lulla et al [7] considered age at marriage, years of married life, parity, genital infection, use of intrauterine contraceptive device and vitamin A deficiency to be significant risk factors but emphasized that risk factors should be considered collectively and devised a scoring system for the purpose.

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