

## AGE AT MENARCHE AND RISK OF CANCER CERVIX

Vaishali V. Gawande\*, S.N. Wahab\*\*, S.P. Zodpey\*\*, N.D. Vasudeo\*\*\*

### ABSTRACT:

**Research Problem:** What is the role of early menarche as a risk factor in the outcome of cancer cervix?

**Objective:** To investigate the role of early menarche as a risk factor for cancer cervix.

**Study Design:** Hospital based, group matched, case control study.

**Setting:** Gynaecology Clinic, Govt. Medical College Hospital, Nagpur.

**Participants:** The study was carried out on 230 incident cases of cancer cervix confirmed by histopathology and equal number of controls selected from female patients admitted to the study hospital for conditions other than gynaecological cancers and showing pap smear within normal limits. The controls were group matched for 5 years class interval.

**Study Variable:** Age at menarche.

**Statistical Analysis:** Univariate analysis was done using Pearson's chi - square test and Odds Ratio while Adjusted Odds Ratio was calculated by using Unconditional Multiple Logistic Regression. Attributable and Population-Attributable Risk Proportion were also calculated.

**Result:** A significant trend was observed towards increasing cancer cervix risk with decreasing age at menarche. Study subjects who had menarche before 13 years of age were at a significantly higher risk of cancer cervix. Various statistical characteristics endorsed this findings.

**Conclusion:** The study identified a significant association of early menarche with cervical cancer.

**Recommendation:** Independent and interactive role of early menarche in the outcome of cancer cervix needs further exploration by conducting studies involving multiple factors and using multivariate analysis.

**Key Words:** Age at menarche, Cancer cervix, Risk factor.

### INTRODUCTION:

It is generally acknowledged that cancer cervix is a multifactorial disease<sup>1</sup>. A number of risk factors have been shown to be associated with the outcome of this condition<sup>1,2</sup>. The relative contribution of these hypothesised risk factors is variable from one

population group to another<sup>1,3</sup>. Moreover, incidence of cancer cervix is dependent on prevalence of risk factors in a particular population group<sup>4</sup>. Additionally, it is also recognized that there exists a variation in the strength of association of various risk factors and cervical cancer<sup>2</sup>. Age at menarche is such a controversial factor, that only a few studies have identified its significant contribution in the etiology of cervical cancer<sup>5,6</sup> and few studies have derecognized its role<sup>7,8</sup>. With this back ground and fortified by the fact that no such study, which assessed the age at menarche as a risk factor for cancer cervix, has been conducted in central India, this study was carried out to investigate this relationship by using case - control study design.

### MATERIAL AND METHOD:

The current hospital based grouped matched case control study was carried out at Gynaecology Clinic, Govt. Medical College Hospital, Nagpur during 1995-1996. A total of 230 incident cases of cancer cervix, confirmed by histo - pathology (Stage I onwards)<sup>9</sup> and admitted to study hospital were included in the current study. Equal number of controls were selected from female patients admitted to study hospital for conditions other than gynaecological cancers and showing pap smear within normal limits (Bethseda System)<sup>10</sup>. The controls were group matched (frequency matching) for 5 years class interval.

Interview technique was used as a tool of data collection, which included relevant details of risk factors i.e. age at menarche and further information about study subjects. Univariate analysis was carried out by estimating Odds Ratio (OR) and its 95% confidence interval (CI). Chi - square test was used as a test of proportion. To estimate Adjusted OR and its 95% CI, Unconditional Multiple Logistic Regression (MLR) analysis was carried out by using MULTLR statistical software package. Attributable Risk Proportion (ARP) and Population Attributable Risk Proportion (PARP) were also calculated<sup>11</sup>.

\* Resident, \*\*Assoc. Professor, \*\*\*Professor & Head,

Dept. of Preventive and Social Medicine, Govt. Medical College., Nagpur - 440009

**RESULT:**

Table - I shows the distribution of study subjects according to their age at menarche. It is evident from the table that majority of cases i.e. 82 (35.7%) attained menarche at 12 years of age, while 74 (32.2%) controls attained menarche at 14 years. Strikingly, it was observed that for both cases and controls the minimum and maximum age at menarche was 10 years and 17 years respectively. It can be seen from this table that there was a significant trend towards increasing risk of cancer cervix with decreasing age at menarche ( $\chi^2$  trend = 12.36, df = 4, p = 0.00044).

For the purpose of dichotomize analysis, early menarche was defined as attaining menarche below the age of 13 years. Table - II shows statistical characteristics of early menarche as a risk factor for cancer cervix. The mean age at menarche for cases and controls was estimated to be 13.1 and 13.5 years respectively. On comparison, study subjects who had menarche before 13 years of age were at a significantly higher risk of cancer cervix. ARP was estimated to be 0.43 and PARP was calculated to be 0.16. Thus about 43% of cancer cervix in women with early menarche may be attributed in part to early menarche. However, 16% of all cancer cervix in the target population may be attributed in part to early menarche.

**DISCUSSION:**

In the present study, the observed mean age at menarche for cases was estimated to be 13.1 years. This finding is consistent with the earlier studies<sup>6</sup>. Although the role of early menarche in the outcome of cancer cervix is recognized to be controversial<sup>5-8</sup>, this study endorsed its significant contribution in the cancer cervix aetiology. Estimates of chi-square, chi-square trend, crude & adjusted OR, ARP and PARP confirmed its significant association with cervical cancer. Earlier investigators also recognized this significant association<sup>5,6</sup>. But there are also a few studies which did not approve this relationship<sup>7,8</sup>.

It has been already stressed that early menarche may not be an independent risk factor for cervical cancer, however, it may initiate a cycle of events involving other more important risk factors, thereby increasing the risk of cervical cancer. Early menarche may be a factor in Indian context, which leads to early marriage, and subsequently early coital exposure, which may again culminate in early pregnancy and thereby

resulting into early childbirth<sup>6</sup>. Moreover, early marriage may be responsible for long duration of married life and multiparity. Role of early marriage, early coitus, early pregnancy, early childbirth, long duration of married life and multiparity in the cervical cancer aetiology has been well documented. Hence, it can be stated that early menarche may act through interactions and interdependence of these risk factors. This could be a reason for its significant contribution in the cancer cervix outcome identified in this study.

The present study used a case - referent study design for the assessment of relationship between cancer cervix and age at menarche. This design, which is a retrospective one, is susceptible to biases<sup>11</sup>. Although all sincere efforts were made to minimize or eliminate the role of various biases during planning and analysis stage, appearance of certain biases like recall bias can not be ruled out. Considering the fact that even if it would have appeared, it would have been distributed equally in both case and control groups, thereby minimizing its effect on the estimation of a risk.

In conclusion, this case - referent study identified a significant association of early menarche with risk of cervical cancer. However, its independent and interactive role in the cancer cervix needs further studies to be conducted involving multiple factors and using multivariate analysis.

**TABLE - I****DISTRIBUTION OF STUDY SUBJECTS  
ACCORDING TO THEIR AGE AT MENARCHE**

Age at menarche (years)	Cases No. (%)	Controls No. (%)
≤ 11	16 (06.9)	14 (06.1)
12	82 (35.7)	44 (19.1)
13	42 (18.3)	48 (20.9)
14	56 (24.3)	74 (32.2)
≥ 15	34 (14.8)	50 (21.7)
<b>Total</b>	<b>230 (100)</b>	<b>230 (100)</b>

TABLE - II

**STATISTICAL CHARACTERISTICS OF EARLY  
MENARCHE AS A RISK FACTOR FOR  
CANCER CERVIX**

Statistical Characteristics	Estimates
Mean age at menarche (years)	
Cases	13.1
Controls	13.5
Chi - square value (df = 1)	15.51
P value for chi -square	0.0000817
Crude OR (95% CI)	2.2(1.46 - 3.30)
Adjusted OR (95% CI)	1.74 (1.10 - 2.75)
ARP (95% CI)	0.43(0.09 - 0.64)
PARP (95% CI)	0.16 (0.03 - 0.31)

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