

The Relationship between Age at Coitarche and Cervical Intraepithelial Changes Amongst Women Attending the Gynaecological Clinic at Jos UTH

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Abstract

The aim of the study was to determine the relationship between age at coitarche and cervical intraepithelial changes in Jos University Teaching Hospital. This was a cross-sectional study comprising 120 women with abnormal and 120 women with normal Pap smear results selected by systematic sampling after obtaining consent. Data were analysed with Epi-info 3.5.2 statistical software. Chi-square test compared categorical variables, Student's T-test compared means, while logistic regression was used to assess the interaction between independent and the leading independent variable. The level of statistical significance was <0.05 . Results show that the average age at coitarche of the study population was 19.7 years. Women with abnormal Pap smears had a lower mean age at coitarche (about 18 years) than those with normal Pap smears (about 21 years), and this was statistically significant ($P<0.001$). While ASC-US was the most frequent abnormality found (42.4%), HSIL was the least (4.2%). Women who attained coitarche at age less than 18 years were six times more likely to develop an abnormality. It was concluded that the age at coitarche was low and that having sexual debut at a much younger age is an independent risk factor for the development of squamous intraepithelial lesion.

Keywords

Age, Coitarche, Cervical Intraepithelial Changes

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1. Introduction

The development of cervical intraepithelial neoplasia is related to sexual behaviour leading to different consequences. Age at first sexual intercourse or age at coitarche is an essential indicator of exposure to the risk of sexually transmitted infection (STI) amongst other complications, during adolescence. The human papillomavirus (HPV) is now known as the most common sexually transmitted infection, with estimates of the prevalence of the disease ranging from 14% and 90%. [1, 2]

Cervical intraepithelial neoplasia (CIN), also commonly known as cervical dysplasia or squamous intraepithelial lesion (SIL) is an abnormal growth of squamous cells on the surface of the cervix. If left untreated, a small percentage of women with SIL will develop cervical squamous cell carcinoma. [3, 4] Several risk factors are related to the development and progression of SIL. Some of the common risk factors for the development of SIL include Human papillomavirus (HPV) infection with types-16 and type-18 implicated in most cases of cervical cancer, multiple sexual partners, early coitarche, tobacco smoking and combined oral

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contraceptive use and ethnicity. [5]

Squamous intraepithelial lesion is a precancerous change in the epithelium of the cervix. There are three categories of CIN/SIL. CIN 1 is considered to be low grade and reflects mild dysplastic modifications to the lower third of the epithelium. CIN 2 indicates a high-grade lesion and involves dysplasia limited to the basal two-thirds of the epithelium. CIN 3 is also high grade and is present when dysplasia encompasses from greater than two thirds to full thickness of the epithelium. [6, 7] HPV infection is most often transient, asymptomatic and self-limiting. The two most vital factors in determining whether the virus will lead to neoplasia are HPV subtype and persistence of the disease. Alterations in immune function also appear to increase the risk of neoplasia. Human papillomavirus infection and immune-compromised states as noted by low CD4⁺ counts are associated with a high frequency of SIL. [8]

In the United States of America, early age of coital debut has been shown to be associated with outcomes such as sexually transmitted infections, especially the human papillomavirus, decreased condom use and increased numbers of sexual partners. [9] There is a liberal attitude towards sexual relations in Sweden where education on sexuality/personal relationship has been part of the national school curriculum since 1956. Youth polyclinics tailored to the needs of adolescents from a network over the country to support young people in developing responsible sexual behaviour and to minimise reproductive health problem including sexually transmitted infections. Screening, free treatment and partner notification of sexually transmitted diseases has led to a reduction in case reports. [10] The association of squamous intraepithelial lesion with early first intercourse but not with the number of sexual partners bears greater similarity to findings from Latin America. [11] than the findings from North America. [12] Asia [13] or Europe. [14] Data from several parts of Nigeria point to increasing sexual activities among single adolescents and decreasing age of initiation of sexual activities among them; [15] Nigerian national demographic health survey found the mean age of first coitus to be over 16 years. [15] It has been found that women working in rural areas begin sexual activity almost three years earlier than those in urban areas (16.5 years and 19.2 years respectively). Women with more than secondary education wait nearly six years longer to initiate sexual activity than those with no education.

The median age at first sexual intercourse is 15.4 years in the North-West zone, compared with 20.4 years in the South-East zone of Nigeria. [15] The Pap smear is a screening tool for diagnosing pre-invasive disease, and even though it has an average false negative rate of approximately 10-20%, it is still considered a highly effective screening tool because of

the long latency of pre-invasive disease. Early age at first sexual intercourse has been associated with an increased risk of infection with high-risk human papillomavirus that in susceptible women is responsible for virtually all cases of invasive cervical cancer. [16, 17]

There are conflicting results that have been reported for an association between age at first sexual intercourse and seropositivity. Stone et al. reported that sexual debut before age 18 was associated with 2.5 times greater odds of HPV-16 seropositivity. [18] However, results from other studies did not support this association and hence, the development of squamous intraepithelial lesion and invasive cervical cancer. This study was carried out to find out the average age at coitarche amongst women attending the gynaecological clinic in Jos, the pattern of cervical intraepithelial abnormalities and to determine the relationship between age at sexual debut and the development of squamous intraepithelial lesion.

2. Materials and Methods

This was a cross-sectional study conducted at Jos University Teaching Hospital (JUTH), a 520-bed tertiary health institution located in Jos, the capital of Plateau State, in the north-central region of Nigeria. The hospital has an established Obstetrics and Gynaecology department where routine Pap smears are done on a daily basis, and which receives referrals from neighbouring States such as Bauchi, Gombe, Benue, Kogi, Nasarawa, Taraba, Adamawa, parts of Kaduna and Niger States.

The study population included women seen in the Gynaecological clinic that was asked to do a Pap smear and agreed to participate in the study. Approval for the study was obtained from the ethical committee of Jos University Teaching Hospital.

The sample size was determined by the formula: [19] $n = Z^2Pq/d^2$, where: n = sample size, Z = Standard normal deviate value of 95% (0.95) confidence interval read from standardized normal distribution table = 1.96, P = estimated prevalence in the target population on the basis of previous studies, expressed as fraction of 100% (7.7% [20]), q = complementary proportion = $1-p$, d = precision of degree of accuracy. The calculated sample size was 109.2, but a minimum sample size of 120 was recruited for the study to take care of study design defect (using an attrition rate of 10%). A similar sample size of 120 served as control.

Every third woman with abnormal Pap smear result was interviewed, as well as those with normal Pap smear results, after matching for age until the minimum sample size was reached.

The study was explained to all the subjects at the

Gynaecological clinic and a written consent obtained from them. The samples were taken and the smears made with the Nurses in the Oncology unit, who have been trained to proficiency in making Pap smears. The Histopathologists interpreted the findings in JUTH, and the results were reported using the Bethesda system of classification. Data collection was in collaboration with the Nurses, using questionnaires (self and interviewer-administered, as necessary) to interview women with abnormal Pap smear results, as well as those with normal results. The questionnaires were pretested first before used on the subjects.

Data analysis was conducted using the Epi-info 3.5.2 statistical software. Chi-square analysis was used for comparing proportions of categorical variables while the student's T-test was used for comparing means where applicable. A p-value less than 0.05 was taken as being significant. Bivariate analysis was performed for the estimation of the relationship. The interaction between independent variables and the leading independent variable were assessed using logistic regression.

3. Results

A total of 240 women made up of 120 cases (SIL), and 120 controls were studied, and these women were age matched. Their ages ranged between 21 and 72 years. The overall average age was about 42 years while the average age at coitarche was 19.7 years. Overall, age group 40-49 had the highest representation (almost 38%). Study subjects were mostly Christians (85%) and were married (82.9%). Over 49% had tertiary education, and 4.2% of all subjects were diabetic; 12.1% had histories of STDs, 4.6% were HIV positive and were all on anti-retroviral drugs (Tables 1 and 2).

Table 1. Background characteristics of study subjects (socio-demographic).

Characteristic	Frequency (n=240)	%
Age group		
<30	34	14.2
30-39	54	22.5
40-49	91	37.9
50-59	50	20.8
60+	11	4.6
Religion		
Christianity	204	85.0
Islam	36	15.0
Occupation		
Business	67	27.9
civil servant	50	20.8
Housewife	63	26.2
Professional	60	25.0
Education		

Characteristic	Frequency (n=240)	%
None	5	2.1
Primary	39	16.2
Secondary	78	32.5
Tertiary	102	42.5
Post-tertiary	16	6.7
Marital status		
Divorce	3	1.2
Married	199	82.9
Single	10	4.2
Widowed	28	11.7
Sexual debut		
<18	65	27.1
≥18	175	72.9
Sexual Partner		
Single	128	53.3
Multiple	112	46.7
Married as virgin		
Yes	128	53.3
No	106	44.2
Not married	6	2.5
Alcohol		
Yes	11	4.6
No	228	95.4
Cigarette		
Yes	2	0.8
No	237	99.2

Table 2. Background characteristics of study subjects (Clinical).

Characteristic	Frequency n=240	%
Hypertension		
Yes	26	10.8
No	214	89.2
Diabetes		
Yes	10	4.2
No	230	95.8
HIV		
Yes	11	4.6
No	229	95.4
STD		
Yes	29	12.1
No	211	87.9

Table 3 presents the mean and standard deviation (SD) of the baseline characteristics of the study subjects. The mean age of subjects was 42.3 years with a mean parity of about four children. The average age at menarche was 14.3 years while the mean age at coitarche was 19.7 years.

Table 3. Mean and SD of baseline characteristics of study subjects.

Characteristic	mean ± SD (n=240)
Age	42.29±10.22
Parity	3.93±2.61
Miscarriages	0.67±0.71
Menarche	14.32±1.51
Age at coitarche	19.72±3.72

As presented in Table 4, women with abnormal Pap smears had a lower mean age at coitarche (about 18 years) and

higher parity (5 children) than those with normal Pap smears (about 21 years) and (3 children) respectively and this was statistically significant ($P < 0.001$). The ages of the women,

their ages at menarche and number of miscarriages did not show any statistical difference between the normal and abnormal groups.

Table 4. Comparison of means of demographic indices of subjects with normal and abnormal Pap smear results.

Characteristic	Normal (mean ±)	Abnormal (mean ±)	t-test	p-value
Age	42.10 ± 10.27	42.48 ± 10.21	0.30	0.767
Parity	3.02 ± 2.23	5.03 ± 2.49	7.25	0.000
Miscarriages	0.61 ± 0.75	0.73 ± 0.67	1.36	0.174
Age at menarche	14.26 ± 1.66	14.38 ± 1.34	0.62	0.521
Age at coitarche	21.00 ± 3.90	18.43 ± 3.03	5.69	0.000

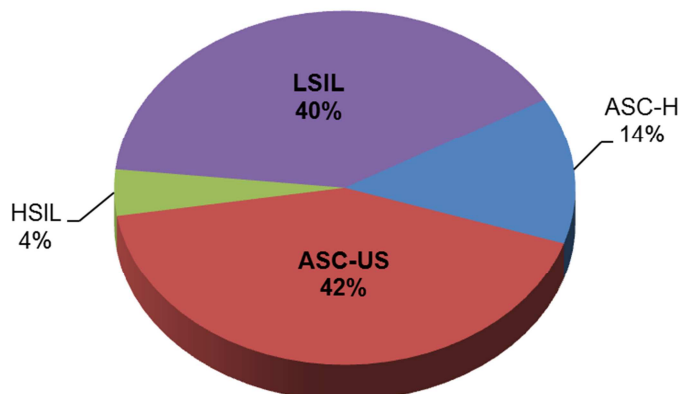


Figure 1. Pattern of abnormalities among women with abnormal Pap smears.

Figure 1 shows the pattern of Pap smear abnormalities. ASC-US and LSIL were present in an almost equal proportion of the cases, i.e. 42.4% and 40% respectively. ASC-H was found in 13.4% of the cases while HSIL was the least frequent abnormalities noted in the cases (4.2%).

undetermined significance, LSIL = Low grade squamous intraepithelial lesion, HSIL= High grade squamous intraepithelial lesion

Abbreviations: ASC-H =Atypical Squamous cells-cannot exclude HSIL, ASC-US =Atypical Squamous cells of

The pattern of Pap smear abnormalities concerning the demographic characteristics of the subjects, as represented in Table 5, showed that all subjects with HSIL in this study had had five or more children.

Table 5. Pattern of abnormalities by selected socio-demographic and clinical Characteristics.

Characteristic	ASC-H n=16(%)	ASC-US n=49(%)	LSIL n=48	HSIL n=5	TOTAL N=120
Lifetime Sexual partners					
Single	10(62.5)	27(55.1)	27(56.2)	4(80.0)	69(57.5)
Multiple	6(37.5)	22(44.9)	21(43.8)	1(20.0)	51(42.5)
Parity					
<5	6(37.4)	27(55.1)	22(45.9)	0(0)	56(46.7)
≥5	10(62.5)	22(44.9)	26(54.2)	5(100.0)	64(53.3)
Hypertensive					
Yes	3(18.8)	3(6.1)	3(6.2)	3(60.0)	12(10.0)
No	13(81.2)	46(93.9)	45(93.8)	2(40.0)	108(90.0)
Diabetic					
Yes	1(6.2)	2(4.1)	3(6.2)	2(40.0)	8(6.7)
No	15(93.8)	47(95.9)	45(93.8)	3(60.0)	112(93.3)
HIV					
Positive	1(6.2)	1(2.0)	3(6.2)	0(0)	5(4.2)
Negative	15(93.8)	48(98.0)	45(93.8)	5(100.0)	115(95.8)
STD History					
Yes	1(6.2)	3(6.1)	5(10.4)	0(0)	9(7.5)
No	15(93.8)	46(93.9)	43(89.6)	5(100.0)	111(92.5)

Figure 2 showed that 80% of subjects with HSIL had < 18 years of age at coitarche as opposed to 20% at coitarche age greater or equal to 18 years.

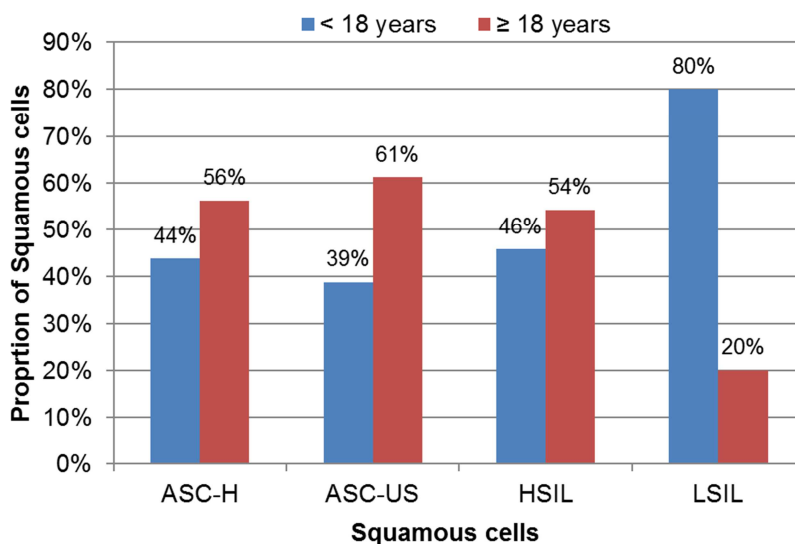


Figure 2. Pattern of abnormal Pap smears according to age at coitarche.

Abbreviations: ASC-H =Atypical Squamous cells-cannot exclude HSIL, ASC-US =Atypical Squamous cells of undetermined significance, LSIL = Low grade squamous intraepithelial lesion, HSIL= High grade squamous intraepithelial lesion

An equal proportion of subjects in both groups were hypertensive (10.8% each). Although there were more diabetics among those with abnormal Pap smears, this difference was not significant. Also, alcohol intake, smoking and the Presence of STD, HIV did not significantly influence the Pap smear result ($P>0.05$). This is presented in Table 6.

Table 6. Univariate analysis of some social and clinical characteristics of subjects with normal and abnormal Pap smear results.

Characteristic	Normal n=120(%)	Abnormal n=120(%)	P-value
Alcohol intake history			0.539
Yes	7(5.8)	4(3.4)	
No	113(94.2)	115(96.6)	
Smoking history			0.247
Yes	0(0.0)	2(0.8)	
No	120(100.0)	118(49.4)	
hypertension			1.000
Yes	13(50.0%)	13(50.0%)	
No	107(50.0%)	107(50.0%)	
Diabetes			0.102
Yes	2(14.3)	8(85.7)	
No	118(52.4)	112(47.6)	
HIV			1.000
Positive	6(5.0)	5(4.2)	
Negative	114(95.0)	115(95.8)	
STD			0.053
Yes	20(16.7)	9(7.5)	
No	100(83.3)	111(92.5)	

Table 7 shows the univariate analysis of demographic

characteristics of subjects with normal and abnormal Pap smear results. There was no statistically significant relationship between age group and number of sexual partners and having a normal or abnormal Pap smear result ($P>0.05$). However, the age at coitarche and parity significantly affected the Pap smear outcome ($P < 0.001$). Forty-three percent (43.0%) of subjects with abnormal Pap smear results compared to only 10.8% of those with normal result had sexual debut before 18 years.

Table 7. Univariate analysis of demographic characteristics of subjects with normal and abnormal Pap smear results.

Characteristics	Normal n=120(%)	Abnormal n=120(%)	P-value
Age group			0.970
<30	18(12.0)	16(13.3)	
30-39	27(22.5)	27(22.5)	
40-49	46(38.3)	45(37.5)	
50-59	23(19.2)	27(22.5)	
60+	6(5.0)	5(4.2)	
Sexual debut			<0.000
<18	13(10.8)	52(43.3)	
≥18	107(89.2)	68(56.7)	
Sexual Partner			0.244
Single	59(49.2)	69(57.5)	
Multiple	61(50.8)	51(42.5)	
Parity			< 0.001
<5	96(63.2)	56(36.8)	
≥5	24(27.3)	64(72.7)	

Figure 3 shows those women who attained coitarche before the age of 18 years recorded more abnormality in Pap smear (80%) than women who attained it at older ages (39%).

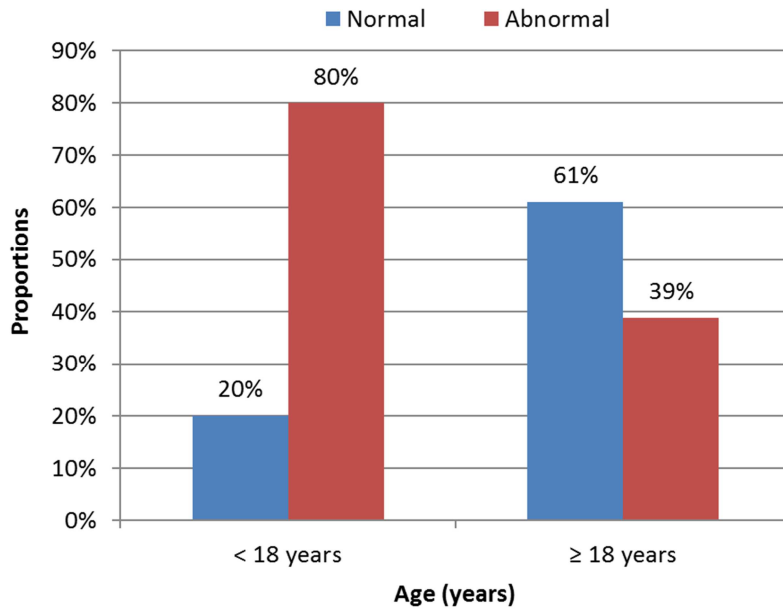


Figure 3. Pap smear result according to age at sexual debut.

After multivariate (logistic regression) analysis of the significant risk factors for abnormal Pap smear in this study the age at coitarche and parity of five or more were independent predictors of abnormalities of Pap smear result. Women who attained coitarche at age less than 18 years were six times more likely to develop an aberration than those who achieved it later.

Women with five children (grand multiparous) and more were about five times more likely to have defect than those with less than five children (Table 8).

Table 8. Multivariate analyses of risk factors of abnormal Pap smear.

Characteristic	Odds ratio	95%CI	p-value
Age at coitarche			
<18	6.3	3.2-12.4	0.000
≥18	1.0		
Parity			
≥5	4.6	2.6-8.1	0.000
<5	1.0		

4. Discussion

Squamous intraepithelial lesion (SIL) is a pre-malignant condition which could lead to the development of invasive cervical cancer, [3] which although preventable, remains a significant cause of morbidity and mortality, especially in developing countries. The HPV which predisposes to the development of SIL is acquired through sexual intercourse.

The result from this study showed that the mean age at coitarche for the entire study population in Jos was 19.7 years with a range of 12-35 years. This is comparable to reports of the Nigerian National Demographic Health Survey, which found the mean age of first coitus in women living in

urban areas to be 19.2 years. [15] This value found in Jos, in North-Central Nigeria comes between the mean age at coitarche of 15.4 years in the North-West zone and 20.4 years in the South-East zone of Nigeria. [15] This is in tandem with the pattern of other sexual and reproductive health indices across the different geopolitical zones in Nigeria, which have been attributed to the role of religion, culture and education.

It is also worthy of note that the mean age of first sexual intercourse among women with abnormal Pap smears in this study, was approximately 18 years compared to 21 years for those with normal results. A lower age at coitarche in women with abnormal Pap smear results compared with women having a typical finding in this study agrees with the widely documented suggestion that early age at coitarche is a risk factor for the development of cervical intraepithelial changes and cervical cancer. [21, 22] Similarly, a study carried out in Houston, USA suggested that age at first sexual intercourse less than or equal to 18 years carried a higher risk of developing SIL. [23]

One of the objectives of this study was to determine the pattern of abnormalities among women with abnormal Pap smears. About 42.4% of the abnormal results were ASCUS, 40% were LSIL, and 13.4% were ASC-H while 4.2% had HSIL. ASCUS was the most common abnormality in this study, corresponding with findings from studies in Saudi-Arabia, India and China, Belgium and USA where ASCUS was 60% [24], 59% [25], 73% [26], 59% [27] and 60% [28, 29] respectively, of all cervical epithelial abnormalities in Pap smear results. The result from this study also showed that HSIL was the least common abnormality (4.2%). In the studies in Saudi-Arabia, India and China; LSIL was the least common abnormality with 1.7%, 6% and 8.9% respectively.

This is different from the result of this study, where LSIL was 40% of the abnormal Pap smear result.

The finding of ASCUS as being the most common abnormality in this study and other studies cited above may be due to several factors that may be injurious to cervical epithelia, including minor infections and inflammation, which are common to women across ethnic and racial categories. The variable findings in the pattern of other groups of the squamous intraepithelial lesion in other studies may be due to the difference in the prevalence of HPV infection and the interplay of other risk factors like smoking, HIV and presence of STD. While it is well documented that these factors are associated with the development of squamous intraepithelial changes and then invasive cervical cancer, there was no significant association between smoking, HIV and STD and the development of abnormal cervical changes in this study.

Also, differences in the laboratory criteria for diagnosis and intrinsic differences in the nature of samples may have contributed to these variations. For example, while Atypical Glandular Cells of Undetermined Significance (AGUS) was included in computing the proportions of abnormalities in other studies, it was not included in this study.

Another objective of this study was to determine the relationship between age at coitarche and the development of cervical intraepithelial changes. In this study, 80% of the women with abnormal Pap smears had sexual debut before 18 years. The age at coitarche was shown to be significantly associated with the development of squamous intraepithelial lesion ($P < 0.001$). Also, the age at coitarche for those with abnormal results (18.4 years) was shown to be significantly lower than those with the normal result ($P < 0.001$). This agrees with a study by Mount and Papilla, which reported that the incidence of Pap smear with squamous intraepithelial lesion was higher in adolescence 10 to 19 years of age. [30, 31]

There are indications that such factors mediate the association between the age at coitarche and development of SIL as higher parity and number of lifetime sexual partners, this study did not show any significant relationship between having single and multiple sexual partners ($P > 0.05$). Although, higher parity significantly associate with SIL ($P < 0.001$) in this study, the significant association between age at coitarche and development of SIL was found to be independent of parity as shown by stepwise multiple regression analysis. Thus adding to existing literature that suggests a different role for parity at different points of carcinogenesis. [30]

This study also shows that women, whose age at coitarche was less than 18 years, were six times more likely to develop SIL compared to women who had their sexual debut after 18

years. It is also important to note that 80% of women with HSIL had sexual debut before 18 years, which may suggest that early sexual experience may well associate with higher grade lesions; however, large-scale studies will be required to validate this finding.

A limitation was the fact that the study was a tertiary hospital-based, and therefore, the result may not reflect the findings in the general population. The result would be more representative and epidemiologically significant if the study were multi-centred. SIL was determined using only cytology, without histologic confirmation. Only one (1) Pap smear result was used for each participant.

5. Conclusion

This study has shown that the age at coitarche is low in this part of the country and that having sexual debut at a much younger time of life is an independent risk factor for the development of squamous intraepithelial lesion. Also, ASC-US was found to be the most prevalent type of abnormality in this environment, followed by LSIL, ASC-H and HSIL.

Effort should be made to increase the age at coitarche in this environment, by female education and advocacy, as well as safer sex practices. All sexually active women should be encouraged to have routine Pap smears to detect those with the squamous intraepithelial lesion, and then institute appropriate management.

Author Contributions

NSM, HIS, SA, PHD and SSH participated in research design. All authors participated in the survey exercise and wrote and revised the manuscript. SA, PHD and SSH performed data analysis.

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Conflicts of Interest

The authors have no conflicts of interest.

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