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Original Article

Comparison of PAP test among high and non-high risk female

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ABSTRACT

A prospective study of pap smear in 100 high risk and equal number of non high risk female among total 1022 female Gynecological patients within a period of two and half months {Beginning of Sept. to middle of Nov. 1995} in Maternity Hospital, Thapathali is presented. There were 9 cases positive for dyskaryosis among high risk and 3 cases among the comparison group. All positive cases were at the age of 35 years and above. In 9 positive cases, 5 cases were in CIN I (55.55%) while 4 were in CIN II (44.44%). Similarly out of 3 positive cases in comparison group 1 was in CIN I category (33.33%) and 2 cases were in CIN II (66.66%). Relation of positive cases with low social class revealed 80% CIN I and 50% CIN II among high risk group where as 66.6% CIN II in comparison group. Analysis of risk factor in development of various grades Dyskaryosis revealed 60% of CIN I had high parity while 50% had CIN II. There are about 40% of CIN I and 75% CIN II among child birth < 19yrs, 60% smoker had CIN I where as 100%. Smoker had CIN II. 80% of CIN I gave history of excessive vaginal discharge where as 50% of CIN II had excessive vaginal discharge. 40% of CIN I was having injection Depo provera. Cases were also analyzed according to risk factor. Out of 9 positive cases among high-risk females 5 positive had parity more than 4 and 4 cases had less than 4. 5 positive cases were among less than 19 years of first childbirth, 4 among more than 19 years. 7 positive cases were smoker and 2 positive cases were non-smoker. 6 positive cases gave history of abnormal vaginal discharge and 3 positive cases had no abnormal vaginal discharge. Out of 9 positive cases 2 had history of injection Depo provera continuously for >5 years where as 7 were non users.

Key words: PAP Smear, High risk, Dyskaryosis, CIN,

Cancer of the cervix is the commonest cancer among women in developing countries even in Nepal. This study is being conducted in order to detect early cases of carcinoma cervix and to find out the precancerous condition like dyskaryosis in suspected case. The cervix being easily accessible smear can be taken from it and the early abnormal cellular changes [dyskaryosis / cervical intraepithelial neoplasis (CIN)], are recognized before they become cancerous. The changes in these cells are more common in patients who are identified as High Risk such as: patient with early onset of sexual intercourse, multiple sexual partners, low socio-economic status, cigarette smoker, high parity, excessive vaginal discharge, abnormal bleeding per vagina, post coital bleeding, long term hormonal contraceptive user.

In most of the instances CIN disappear and the cervix return completely to normal. In some cases CIN persist and does not progress to develop cancer. The frequency with which CIN progresses to invasive cancer has been the subject of considerable investigation. The time intervals during which one changes develop into other is quite variable and it is seen that some patients develop invasive cancer sooner. One of the data from Ferenezy suggested that when Pap smear shows CIN-I (early stage)- 15% of them will develop CIN-III within a period of 7 years, 50-60% will develop into microinvasive carcinoma from the development of CIN-III (late stage) within an interval of 14 years and 100% of them development of microinvasive carcinoma. In 40% of all diagnosed cases deaths usually occurs after 2-3 years (1).

Using the powerful statistical tool of relative risk analysis, investigators have been able to demonstrate an increased risk for the development of CIN in women with multiple sexual partners and early age of the onset of sexual activity (2). When compared with women with only one sexual partner, the risk of claimed CIN-III was increased eight fold among women with 3-5 sexual partners and if they have more than 6 partners the risk increased to 14.2 fold.

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In patient who first experienced intercourse at the age of 20 years and younger, the relative risk of CIN-III was 2.5 times greater than that of women who began sexual activity at 21 or older. More recently smoking have been reported to increase the risk of cervical neoplasia. Lyon et al in a careful case control study of 217 women with cervical carcinoma in situ found a relative risk of 3.0 for cigarette smoking after controlling for other socio-economic and sexual risk factors (3). In a similar study in England, Harris et al reported a 3-4 fold increased risk of CIN among women who smoked 20or more cigarettes a day.

Prospective studies by Stern et al in Los Angeles have suggested an increased risk of progression of cervical dyskaryosis among women using hormonal contraceptives (4). This has been supported by work of Meiseles et al (5). Among French Canadian and Harris et al who found the significance of hormonal contraceptive persisted in English women even after correction for number of sexual partners, age at first intercourse and other risk factors (2).

Strong association of CIN with parity had been established. Prevalence recorded is 0.8% with zero parity to 1.4% with para seven and more.
Recent evidence points to a casual link between some of the precursors lesion of cervical cancer and specific papilloma virus. The DNA of these viruses if found in majority of the cases.

Methodology
It is a prospective cross sectional study. Study is conducted in Gynae OPD, Maternity Hospital, Thapathali, Kathmandu. The women with Gynaecological problem attending the clinic of the hospital were selected for the study. Specially designed interview questionnaire was developed and pretested. This study started from middle of Bhadra to end of Kartik 2052 (beginning of Sept. to middle of Nov. 1995). According to protocol cases were collected two days in a week i.e. Monday and Thursday. Total 1022 cases attended clinic over a period of 20 days of study in 10 weeks period. 397 (38.86%) cases were the high-risk group among them. Average 20 patients attended clinic in a day of study. First 4-6 cases which fulfilled the inclusion criteria were interviewed, examined, Pap smear taken and forms were filled. An equal number of remaining cases with exclusion criteria like prolapse uterus, fibroid uterus, bleeding P.V and P.I.D were also examined.

The technique used in this study for screening is Pap smear. A wooden spatula was used for scraping the transformation zone. The sample was spread evenly with the circular motion unto the glass slide covering about 1/3rd to half of the slide. Smear was fixed in 95% ethyl alcohol for 15 minutes. Once fixed, the slides were dried and then are transferred to pathology department at the end of clinic. Smear was stained in the pathology department with papanicolou stain.

The results of Pap smear were entered weekly in a register manually. Interim analysis was carried out after the completion of fourth clinic. Thus data entry and interim analysis was continued all long the study period. This was done manually and an attempt has been made to estimate the prevalence of dyskaryosis in high risk as well as in comparison group of cases.

Results
Out of 100 slides. Nine showed dyskaryotic cells making the prevalence rate of 9% in high-risk group. In the slide taken from comparison group only 3% were positive for dysakaryotic cells. In the 9 positive cases, 5 cases were in CIN-I (55.55%), while 4 were in CIN-II (44.44%). Similarly out of 100 comparison group, 3 cases showed positive smear, 1 was in CIN-I category (33.33%) and 2 cases in CIN-II. (66.66%).

During microscopic study of 100 smear of high-risk group, 13 smears showed monilial infection, 3 smears showed trichomonas vaginalis and 62 showed inflammatory cells. Out of 9 positive smear, 2 smear showed monilial infection and 3 smear showed trichomonas vaginalis.

Relation of Positive cases with Age

Age	No. of patient		No. of positive cases	
	High Risk	Comparison	High Risk	Comparison
15-19	5			
20-24	11			
25-29	14			
30-34	10			
35-39	26	61	2	2
40-44	17	27	2	1
45-49	17	12	5	0
Total	100	100	9	3

Positive cases were found at age of 35 and over.

Table 1: Relation of Positive cases with Social Class

Social Class	High Risk		Comparison	
	Patient	Positive cases	Patient	Positive cases
High	7	0	2	0
Medium	45	3	53	1
Low	48	6	45	2
Total	100	9	100	3

Low socio-economic status has the definite effect on the development of dyskaryosis. (5,6,7)

Table 2: Relation of Social Class with CIN

High Risk		Low Socio-Eco. Status		Comparison	
Cases	CIN			Cases	CIN
1	I	0		1	I
2	I	0	x	2	II
3	I	0	x	3	II
4	I				
5	I	0			
6	II				
7	II	0			
8	II				
9	II	0			

80% of CIN I in high risk group were from low socio-economic status and
50% CIN II in high-risk group were from low socio-economic status.
66.6% of CIN II in comparison group from low socio economic status.

Table 3: Relation of Risk Factor with CIN

Cases	CIN	Risk Factor					
		Para >4	Child Birth<19	Smoker	P.C.T	E.V.D	Hormonal Contraceptive
1	I		x	0		#	@
2	I	*		0		#	
3	I	*	x			#	@
4	I					#	
5	I	*		0			
6	II		x	0			
7	II		x	0			
8	II	*		0		#	
9	II	*	x	0		#	

High parity : 60% of CIN had high parity while only 50% had CIN II.
Child Birth in <19 years: These are about 40% of CIN I and 75% of CIN II.
Smoker: 60% smoker had CIN I where as 100% smoker had CIN II
Excessive Vaginal Discharge(EVD) : 80% of CIN I gave history of EVD where as 50% of CIN II had EVD.
Hormonal Contraception : 40% of CIN I was having Injection Depo provera

Table 4: Grading of Dyskaryosis with Age

Age	High Risk		Comparison	
	CIN-I	CIN-II	CIN-I	CIN-II
35-39	2		1	
40-44	1	1		2
45-49	1	4		
Total	4	5	1	2

Late stage of dyskaryosis is found in advanced age.

Table 5: Parity and Dyskaryosis

Parity	No. of High Risk	No. of positive cases
<4	39	4(10.25%)
>4	21	5(23.81%)
Total	60	9

More positive cases were found with parity more than 4. (8,9)

Table 6: Relation of Positive cases with Age of 1st Childbirth

Age in Years	No. of High Risk	No. of positive cases
<19	50	5(10%)
>19	10	4(40%)
Total	60	9

More percentage of positive cases were found in the women having 1st childbirth in less more than 19years.

Table 7: Smoking and Dyskaryosis

Habit	No. of High Risk	No. of positive cases
Smoker	31	7(22.58%)
Non Smoker	29	2(6.90%)
Total	60	9

Positive cases are found more in smoker. (10, 11, 12)

Table 8: Vaginal Discharge and Dyskaryosis

Vaginal Discharge	No. of High Risk	No. of positive cases
Present	25	6(24%)
Absent	35	3(8.57%)
Total	60	9

More % positive cases are associated with excessive vaginal discharge. (13, 14, 15)

Table 9: Hormonal Contraception and Dyskaryosis

Contraceptives	No. of High Risk	No. of positive cases
O.C	4	0
Depo provera	5	2(40%)
Non Users	51	7(13.73%)
Total	60	9

Only two positive cases were having Injection Depo provera and 7 positive cases were non-user of hormonal contraception.

Discussion and Conclusion

The results of this study clearly demonstrate the correlation between risk factor and cervical cellular dyskaryosis. Only age factor 35 years and above was considered in non high-risk patient and some dyskaryosis was found.

In this study the prevalence of CIN is 9% in high-risk population and 3% in comparison group. The prevalence of CIN is three times more in high-risk group in contrast to comparison group. This is also suggested by many literatures which showed 2.5 –3 fold high prevalence of CIN in high-risk group.

In Brazil, extensive screening program was done between 1970 and 1985, where 981,000 women were examined. 1% showed Dyskaryosis and 0.15% cervical carcinoma.

Analysis of age factor shows definite relation of dyskaryosis with age. Nine positive cases in high-risk population and 3 in comparison group were found over the age of 35 years. Maximum numbers of positive cases were at the age group 45-49. Higher grade of dyskaryosis was found in advance age. Literature also suggests that incidence rises rapidly from age 20 to reach a plateau at about 40-50 years of age.

After evaluation of the results, risk factors like smoking, excessive vaginal discharge and low economic status had shown the strong association with dyskaryosis. (16, 17)

Socio economic status has always been playing an epidemiological factor in the development of dyskaryosis. In this study more positive cases in high risk as well as in control are found to be in the patient from low socio-economical status.

Screening programme in Sao Paulo showed the relation with CIN with high parity. The prevalence being 1.3% with parity 4-6. Adadevoh S.W. in his study has shown the relation of CIN with parity more than 5. Similarly Becker T/M/ showed an increased risk of 3.9 fold with more than 2 vaginal deliveries.

Risks are closely related to the sexual habit. Early sexual experience and multiple partners are related to high risk of cervical cancer. Data of this study shows more positive cases between 20-24 years of marriage. This study also shows large group of high risk population get married at an earlier age i.e. less than

19 years. This rising trend of early childbirth contributes in the development of dyskaryosis.

This study is also directed to correlate the association of CIN and smoking. CIN is more prevalent among smokers. Literature has proved this risk is around 2.5 times in the smoker. Tobacco related substances had been isolated in the cervical fluid of smoker. Likely mechanism of action could be to act as a co-carcinogen to an earlier viral infection.

Excessive symptomatic discharge plays a role in contributing the development of CIN is also proved to be the risk factor in the present study. Trichomoniasis and CIN has been correlated in few literatures. This study also shows two positive cases associated with monilial infection and three cases with trichomoniasis. The relation of Human papilloma virus and CIN could not be studied in the present study due to lack of facility.

In the present study 100 non high-risk cases were studied with the pap smear. This comparison group shows 3% positive case of CIN. Prevalence of dyskaryosis among the non high risk can be explained by the fact that age which is considered in this study had some role in the development process. As all the positive cases were above 35 years in high risk as well as in comparison group indicating that age factor to be more vulnerable.

This study goes to support the hypothesis that the pick up rate of CIN in screening high-risk women would be high. However, in spite of not having high risk factors in women at and above the age of 35 years should also be screened. The later group also had percentage of higher grade of dyskaryosis.

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