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Article

Screening accuracy of PAP and VIA in terms of Colposcopy guided cervical biopsy: A comparative study

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A B S T R A C T

Approximately 80% of cervical cancer occurs in developing countries of which India contributes about 20-30% of the global burden. WHO considers cervical cancer as a preventable disease because it can be diagnosed in its precancerous phase. Cytology and VIA for screening and colposcopy for directed biopsy jointly may achieve accuracy of approximately 90% to 99%. An observational cross sectional comparative study was performed to find accuracy of screening protocols of exfoliative cervical cell cytology and visual inspection under acetic acid in terms of the diagnostic test of Colposcopy guided biopsy on 300 symptomatic women of age 18-60 years over the period of one year. Both PAP and VIA positivity increased with age, increasing parity, gynaecological symptoms. PAP and VIA positive results co related with Colposcopy directed biopsy histopatholgy reports in a statistically significant proportion. VIA can screen out a large number of women suspected to have cervical cancer in an easy method done in OPD in naked eye and does not require any meticulous microscopic examination with a high degree of sensitivity and high false positivity but on the other hand PAP was less sensitive but more specific test when both combined with Colposcopy guided biopsy. The associations between distribution of women who were Pap +ve and histology +ve as well as VIA and histo +ve were statistically significant.

I. INTRODUCTION

Cervical cancer is the second most common cancer after the cancer breast and 5th deadliest cancer in women worldwide. The worldwide incidence of cervical cancer is approximately 510,000 new cases annually with approximately 288,000 deaths worldwide. But the Indian statistics differ from the world statistics. Approximately 80% of cervical cancer occurs in developing countries of which India contributes about 20-30% of the global burden (Suraiya, 1994). In India it is the most common cancer among the women and is the leading cause of cancer deaths in Indian women. It kills around 73,000 women in India every year accounting to 1/3rd of global cervical cancer deaths. India has approximately 365.71 million women above 15 years of age who are at the risk of developing cervical cancer. The current estimates indicate approximately 132,000 new cases diagnosed and 74,000 deaths annually in India. Indian women face 2.5% cumulative life time risk and 1.4% cumulative death risk from cervical cancer.

Cervical cancer is the cancer arising from cervix due to abnormal growth of cells that have the ability to invade other parts of the body. The symptoms may be abnormal vaginal bleeding, pelvic pain, or bleeding during sexual intercourse. CIN is the term used for the precancerous lesions of the cervical cancer. It emphasizes on the spectrum of abnormalities in these lesions and to help standardize treatment (DeMay, 2007). It classifies mild dysplasia as CIN1, moderate dysplasia as CIN2 and severe dysplasia as CIS and CIN3.

WHO considers cervical cancer as a preventable disease. This is because it can be diagnosed in its precancerous phase and almost curable when diagnosed in its pre-invasive stage (CIN). Therefore, considerable efforts have been given into detecting and treating in its pre-invasive stage all over the world. Precancerous lesions occur more commonly in women less than 40 years of age which provide opportunity for screening and early detection of cervical cancer. In most developed countries, screening programs for early detection for preclinical cervical cancer have proven to be very useful and have contributed to improved results of treatment. The 5 years survival rate of cervical cancer when detected at earliest stage is 92% and the combined 5 years survival rate for all stages is 72%.

In all developed countries and in some developing countries, PAP smear test has become a routine procedure for every gynecological patient for detecting CIN and cervical cancer. PAP smear remains the most commonly used screening method for early detection of cervical cancer. It was introduced by George Papanicolaou into clinical practice in 1940 (Papanicolaou, 1940). Colposcopy is a medical diagnostic procedure to examine an illuminated, magnified view of cervix, vagina and vulva which provides an enlarged view of the area allowing distinguish normal from abnormal visually appearing cervical transformation zone (TZ) or squamocolumnar junction (SCJ) which turns white after the application of acetic acid or have an abnormal vascular pattern and take directed biopsy for histopathology. Colposcopy was developed in 1925 by the German physician Hans Hinselmann with the help from HelmitWirths (Chase et al, 2009).

It was stated in Krutzen and Ratnam that Colposcopy guided biopsy complements cytology and when combined with selective biopsy of the worst affected area allows a high level of diagnostic accuracy of 90.7% and 95% respectively (Khutzen and Sherwood, 1997 ; Ratnam et al 1999). Using cytology for screening and colposcopy for directing biopsy, a joint accuracy of approximately 90% to 99% can be achieved.

II. METHODS

This study was conducted over 1 year from 01.10.2018 to 30.09. 2019. It was an observational cross sectional comparative study to find accuracy of screening protocols of exfoliative cervical cell cytology and visual inspection under acetic acid in terms of the diagnostic test of Colposcopy guided biopsy. Our study population was symptomatic women of age 18-60 years willing to participate in this study. Symptomatic woman attending Gynae OPD of Burdwan Medical College

and Hospital (BMCH) with vaginal bleeding after intercourse, between periods and/or after menopause, menstrual bleeding that was heavier and lasted longer than usual, watery and/or vaginal discharge that might be heavy with or without foul odour and pelvic pain or pain during intercourse were included and pregnant women, women with diagnosed cervical cancer, women undergone hysterectomy and unwilling patients excluded from the study. About 6-8 samples per week were taken and sample size was 300 symptomatic women.

The result of PAP smear were classified under two categories, negative for intralesional malignancy (NILM, including inflammatory smear) and malignancy, divided into high grade squamous intraepithelial lesion (HSIL), low grade squamous intraepithelial lesion (LSIL) and atypical squamous cells of undetermined significance (ASCUS). The patient was then subjected to colposcopic examination in the same visit. VIA was performed applying 3% acetic acid to the cervix specially in the squamocolumar junction (SCJ) or transformation zone (TZ) to visually inspect the areas which turned white after the application of acetic acid or had an abnormal vascular pattern was considered for biopsy. The colposcopically directed biopsy was taken from all examined patients, by punch biopsy forceps from the most advanced part of lesion. Biopsy fragments were sent to pathology department in a sterile container containing formalin.

Descriptive Statistics was used for demographic and other details and chis quare test, students' t test were performed using spss version 22 software and open epi statistical software. Data collected was entered into predesigned proforma sheet and analyzed using suitable statistical test. P value of <= 0.05 was taken as significant.

III. RESULT

Table 1. Relation between age and pap smear finding

		PAP General			Total	p Value	Significance
		Epithelial Cell Abnomality	Unsatisfactory	Normal			
Age	11-20	0(0)	0(0)	4(100)	4(100)	<0.001	Significant
	21-30	0(0)	2(2.04)	96(97.96)	98(100)		
	31-40	4(3.33)	4(3.33)	112(93.33)	120(100)		
	41-50	12(25)	0(0)	36(75)	48(100)		
	51-60	12(42.86)	0(0)	16(57.14)	28(100)		
	61-70	2(100)	0(0)	0(0)	2(100)		
Total		30(10)	6(2)	264(88)	300(100)		

Age	PAP abnormal	PAP normal
<=30	02	100
>=30	34	164

Table 2. Relation between age with VIA finding (data inside bracket is the percentage)

		Via			Total	p Value	Significance
		Acetowhite+	Growth Anterior Lip	Normal			
Age	11-20	0(0)	0(0)	4(100)	4(100)	<0.001	Significant
	21-30	46(46.94)	0(0)	52(53.06)	98(100)		
	31-40	30(25)	0(0)	90(75)	120(100)		
	41-50	14(29.17)	2(4.17)	32(66.67)	48(100)		
	51-60	16(57.14)	0(0)	12(42.86)	28(100)		
	61-70	2(100)	0(0)	0(0)	2(100)		
Total		108(36)	2(0.67)	190(63.33)	300(100)		

Age	VIA abnormal	VIA normal
<=30	46	56
>=30	64	134

Table 3. Relation between parity and PAP smear finding (data inside bracket is the percentage)

		Pap General			Total	p Value	Significance
		Epithelial Cell Abnomality	Unsatisfactory	Normal			
Parity	0-2	4(3.77)	2(1.89)	100(94.34)	106(100)	<0.001	Significant
	3-4	14(8.54)	4(2.44)	146(89.02)	164(100)		
	5-6	10(35.71)	0(0)	18(64.29)	28(100)		
	7 or more	2(100)	0(0)	0(0)	2(100)		
Total		30(10)	6(2)	264(88)	300(100)		

Parity	Pap abnormal	Pap normal
<=2	4	100
>=2	28	164

Table 4. Relation between parity with VIA finding (data inside bracket is the percentage)

		Via			Total	p Value	Significance
		Acetowhite+	Growth On Anterior Lip	Normal			
Parity	0-2	36(33.96)	0(0)	70(66.04)	106(100)	0.001	Significant
	3-4	60(36.59)	0(0)	104(63.41)	164(100)		
	5-6	10(35.71)	2(7.14)	16(57.14)	28(100)		
	7 or more	2(100)	0(0)	0(0)	2(100)		
Total		108(36)	2(0.67)	190(63.33)	300(100)		

Parity	VIA abnormal	VIA normal
<=2	36	70
>=2	74	120

Table 5. Distribution of women to show relation between chief complain and PAP smear positivity (data inside bracket is the percentage)

		Pap General			Total	p Value	Significance
		Epithelial Cell Abnormality	Unsatisfactory	Normal			
Symptoms	White discharge	20(9.17)	2(0.92)	196(89.91)	218(100)	<0.001	Significant
	Post coital bleeding	2(8.33)	2(8.33)	20(83.33)	24(100)		
	Post menopausal bleeding	6(60)	0(0)	4(40)	10(100)		
	Abdominal pain	2(8.33)	0(0)	22(91.67)	24(100)		
	Menstrual irregularity	0(0)	2(8.33)	22(91.67)	24(100)		
Total		30(10)	6(2)	264(88)	300(100)		

Table 6. Distribution of women to show relation between chief complain and VIA positivity (data inside bracket is the percentage)

		VIA			Total	p Value	Significance
		Acetowhite+	Growth Anterior Lip	Normal			
Symptoms	White discharge	78(35.78)	0(0)	140(64.22)	218(100)	<0.001	Significant
	Post coital bleeding	10(41.67)	0(0)	14(58.33)	24(100)		
	Post menopausal bleeding	2(20)	2(20)	6(60)	10(100)		
	Abdominal pain	8(33.33)	0(0)	16(66.67)	24(100)		
	Menstrual irregularity	10(41.67)	0(0)	14(58.33)	24(100)		

Total	108(36)	2(0.67)	190(63.33)	300(100)

Table 7. Distribution of women according to histology findings (n=98)

	Frequency	Valid Percent
Chronic Non-Specific Cervicitis	70	71.4%
CIN1	2	2.0%
CIN2	8	8.2%
CIN3	6	6.1%
SCC	12	12.2%
Total	98	100.0%

Table 8. Distribution of women who were Pap +ve and histology +ve (n=98)

		Pap General		Total	p Value	Significance
		Epithelial Cell Abnomality	Normal			
Histopathology	Normal	4(15.38)	66(91.67)	70(71.43)	<0.001	Significant
	Abnormal	22(84.62)	6(8.33)	28(28.57)		
Total		26(100)	72(100)	98(100)		

Histo / PAP	Normal	Abnormal	Total
Normal	66 (94.29%)	6 (21.43%)	72 (73.47%)
Abnormal	4 (5.71%)	22 (78.57%)	26 (26.53%)
Total	70 (100%)	28 (100%)	98 (100%)

Table 9. Distribution of women who were VIA +ve and histology +ve

		VIA			Total	p Value	Significance
		Acetowhite+	Growth Anterior Lip	Normal			
Histopathology	Normal	68(72.34)	0(0)	2(100)	70(71.43)	0.041	Significant
	Abnormal	26(27.66)	2(100)	0(0)	28(28.57)		
Total		94(100)	2(100)	2(100)	98(100)		

Histo / VIA	Normal	Abnormal	Total
Normal	2 (2.86%)	0 (0%)	2 (2.04%)

Abnormal	68 (97.14%)	28 (100%)	96 (97.96%)
Total	70 (100%)	28 (100%)	98 (100%)

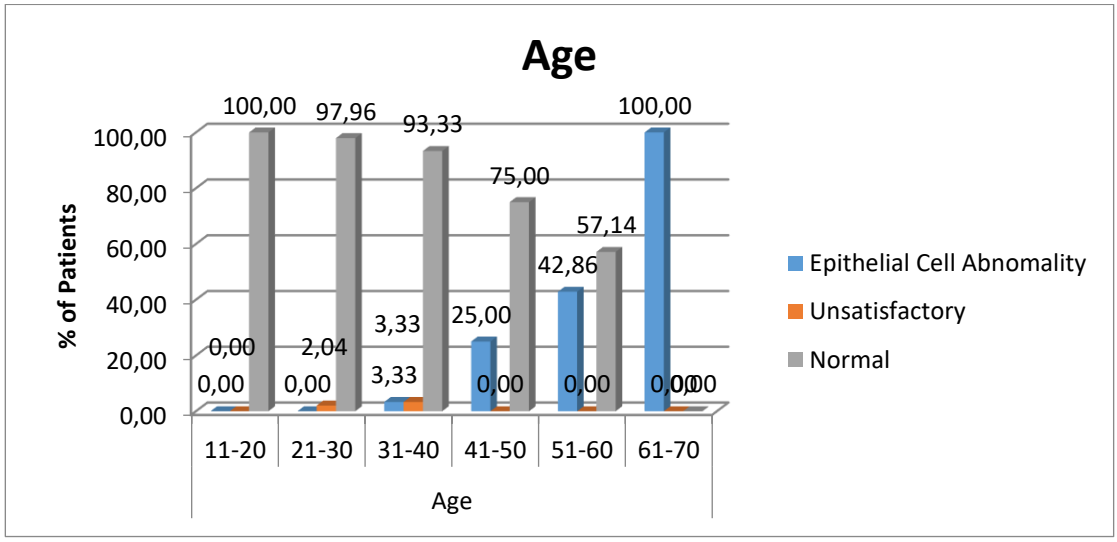

Figure 1: Relation between age and Pap smear finding

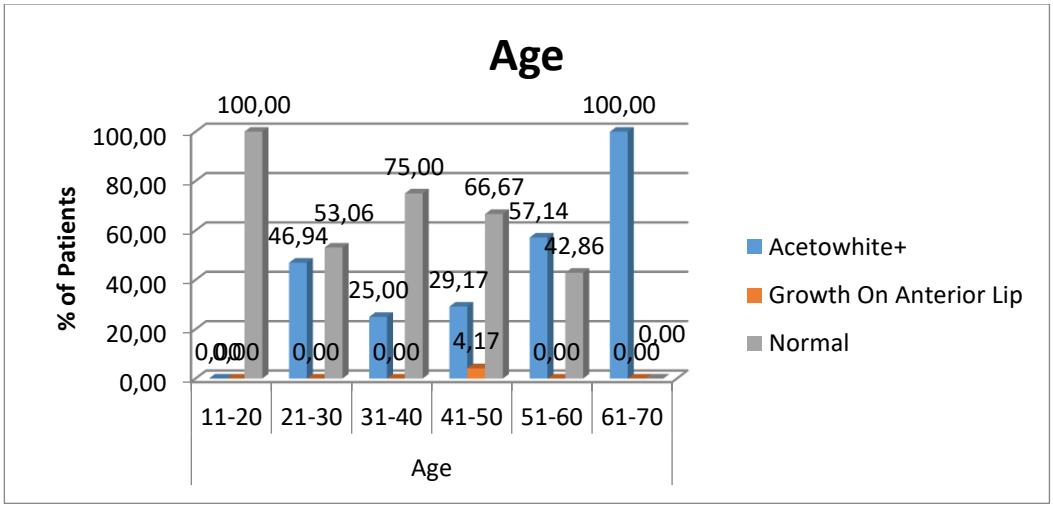

Figure 2: Relation between age with VIA finding

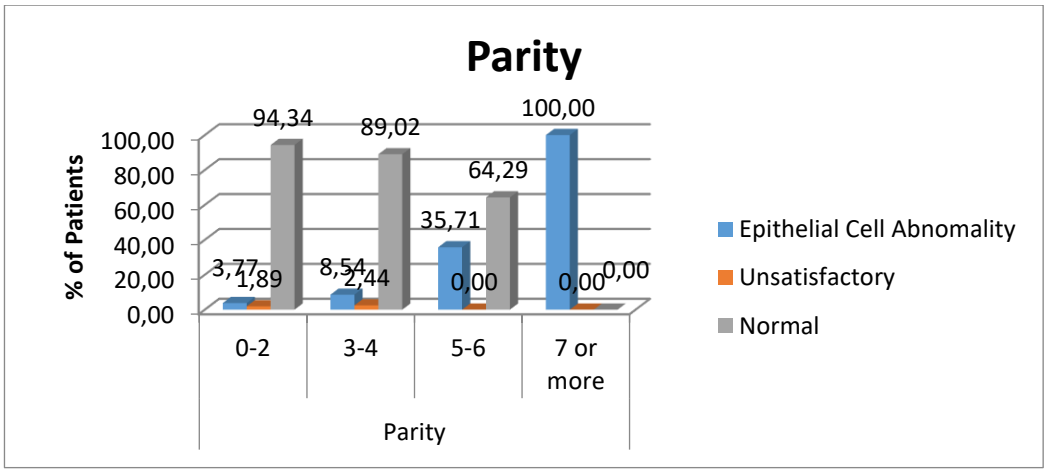

Figure 3: Relation between parity and Pap smear finding

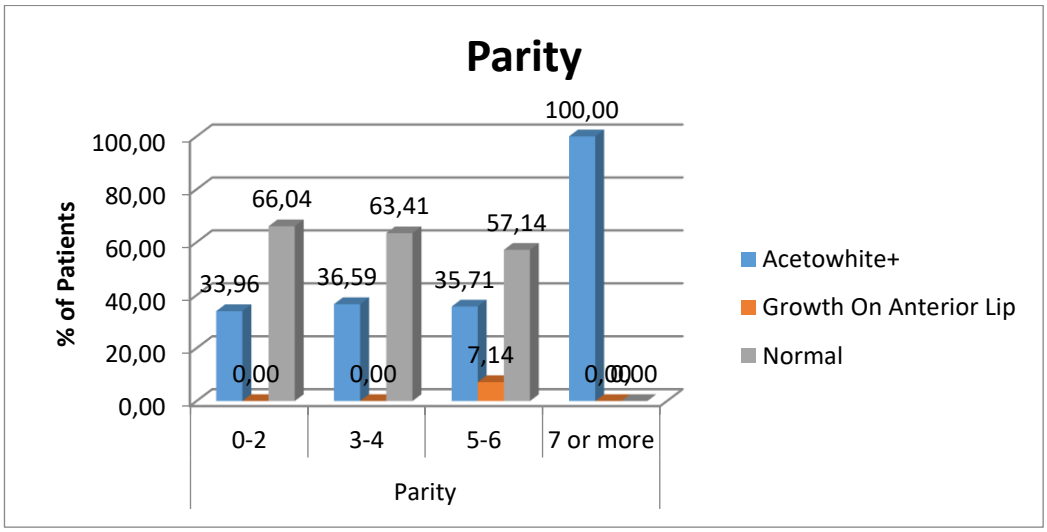

Figure 4: Relation between parity with VIA finding

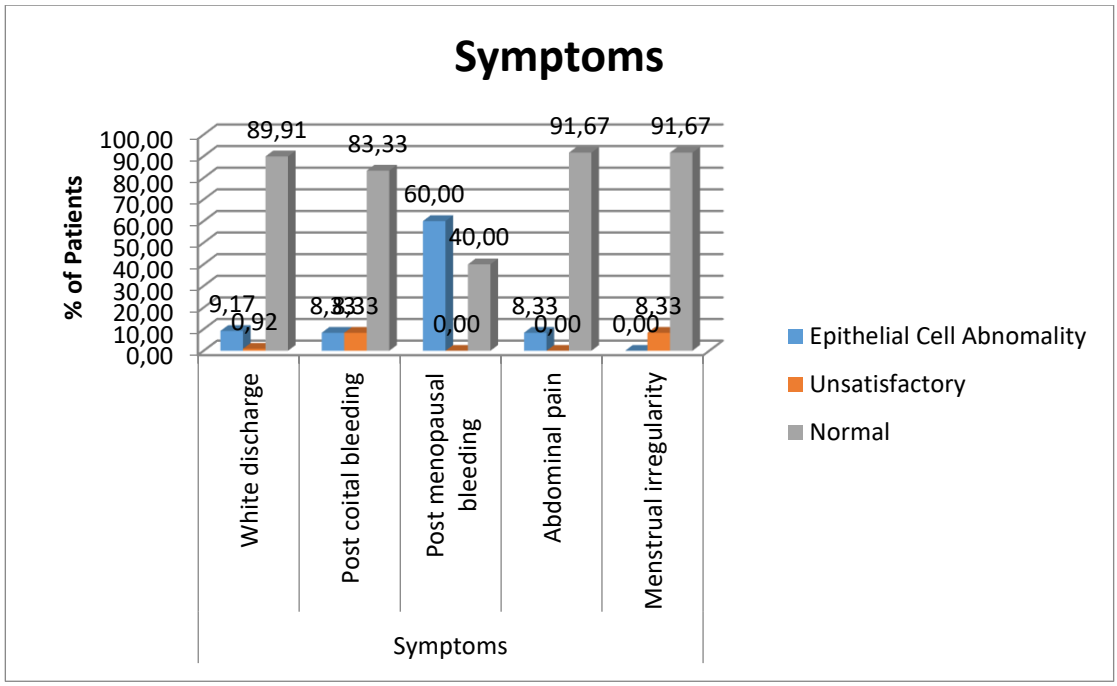

Figure 5: Relation between chief complain and Pap smear positivity

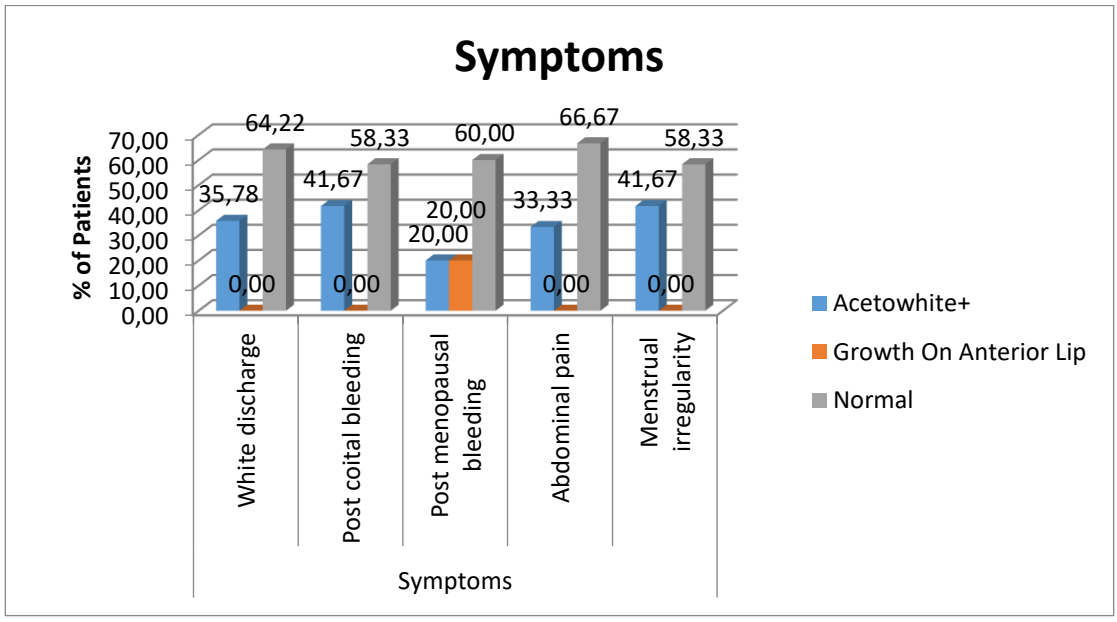

Figure 6: Relation between chief complain and VIA

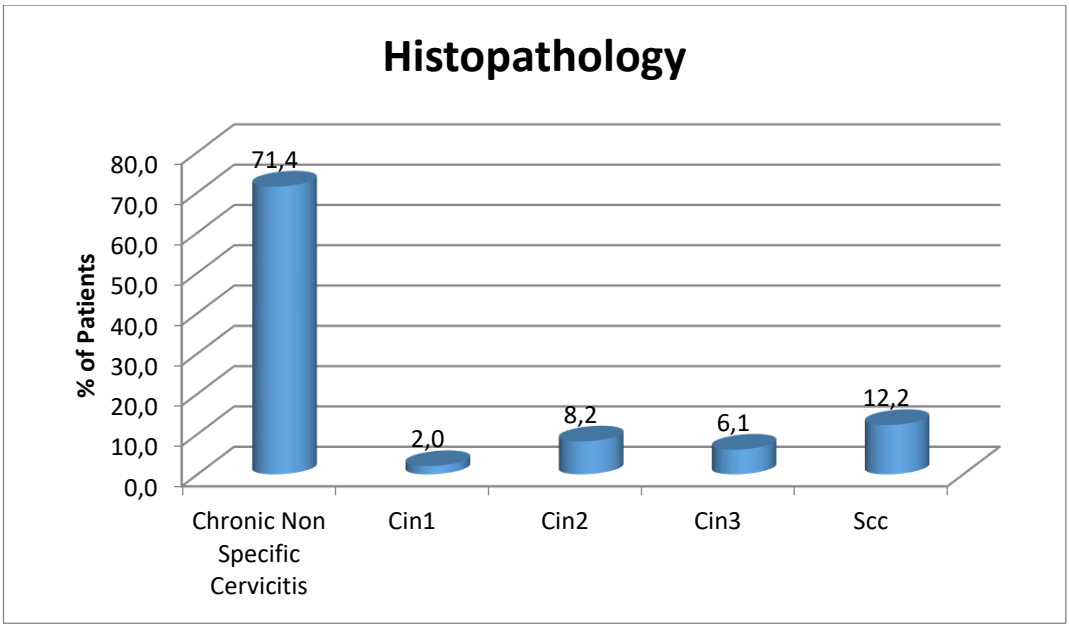

Figure 7: Distribution of women according to histology findings (n=98)

In this prospective and comparative study, conducted in the department of obstetrics and gynaecology of Bardhaman Medical College and Hospital, Burdwan from October, 2018 to September, 2020, 300 women were recruited, with complain of bleeding per vagina, post coital bleeding, white discharge or any abnormal finding on per speculum examination in the age group of 18 to 60 years.

We classified the PAP results of all patients into three broad categories for example epithelial cell abnormality, unsatisfactory & normal and distributed according to age subgroups. It was found that maximum epithelial abnormality was found in age group of 51 to 60 years, 42.86% (12 abnormalities out of 28 in this age group) followed by 25% in the age group of 41-50 years (12 abnormalities out of 48 in this age group) . Table1A also shows that PAP positively increases with increasing age which implies that chance of developing cervical cancer is more in higher age group for example we had only 2 patients in 61 to 70 years age range presenting with post-menopausal bleeding and both had epithelial cell abnormalities in their PAP smear, making it 100% positivity. Similarly, VIA positively is more with increasing age, though the difference with lower age group is small. There were 108 acetowhite lesion detected in VIA amounting to 36% positivity, among age groups, mostly in 51-60 years group, 57.14% (16 abnormalities out of 28 in this age group) followed by 29.17% in 41-50 years group (14 abnormalities out of 48 in this age group) (Table1B). Both PAP and VIA positivity increased with age and the association was statistically significant.

We found cervical epithelial cell abnormalities in 30 out of 300, mostly in parous women more than 5, 35.71% (10 abnormalities out of 28 in this age group) (Table 2A). Similarly, VIA positivity increases with high parity, 108 acetowhite lesions out of 300, 36.59% in parous women 3-4 and 35.71 in parous women of parity 5-6, which implies that increasing parity is a risk factor for cervical cancer (Table 2B). The association we found between PAP and VIA abnormality with increasing parity was statistically significant.

Cervical cell abnormality was found in 10% of symptomatic patients, mostly who presented with post-menopausal bleeding ie 6% (6 out of 10). 218 patients presented with white discharge per vagina of whom 20 cases were found to be epithelial cell abnormalities, 9.17%. Of 300 symptomatic patients, 108 was found to be acetowhite after applying acetic acid, ie 36%. Two out of all had growth in the anterior lip of cervix during speculum examination. These 2 patients

were in the subgroup of post menopausal bleeding. The relation between chief complain and PAP smear positivity as well as VIA positivity was statistically significant (Table 3A &3B).

Out of the 98 patients who underwent Colposcopy guided biopsy, most histopathologie were chronic non specific cervicitis, 71.4%. Frank carcinoma (SCC), CIN3, CIN2 and CIN1 were found to be 12.2%, 6.1% and 8.2% respectively (Table4A). Table 4B shows that the number of women who were both abnormal PAP (cervical epithelial cell abnormalities) and abnormal histopathology were 22, only m case were histologically negative among the PAP positives. This implies that PAP test is a highly specific test for screening cervical cancer. The association between distribution of women who were Pap +ve and histology +ve was statistically significant. Table 4C shows that large number of women was screened positive by VIA who did not have any cervical cancer as per histology finding. This implies that VIA is a non-specific test for screening cervical cancer. The association between distribution of women who were VIA +ve and histology +ve was statistically significant.

IV. DISCUSSION

In our cross-sectional study on 300 symptomatic women of 18 to 70 year age group attending the outpatient department during 2018–19, we have evaluated them with screening and diagnostic tests of cervical carcinoma. All these 300 women were screened for cervical cancer by two most commonly used methods, PAP smear and VIA and the confirmatory test was done by cervical biopsy and histopathology.

Among 300 women 30 were found to be PAP positive and 110 were found to be VIA positive. But only 28 women were confirmed to have cervical precancerous or cancerous lesion by histopathology. Hutchinson et al, 1992 showed that fewer than 20% of cells collected by PAP smears were transferred on to the slide and thus explained the high prevalence of true false-negative rate. They reported a higher percentage of cases of LSIL on liquid based cytology (10.6%) than conventional PAP smear (9.0%). Diaz-Rosario and KabawatI[6] reported increased detection of premalignant precursors on liquid-based cytology as compared to conventional smear. They found an increased percentage of cases of LSIL from 1.6% to 2.7% and of HSIL increased from 0.3% to 0.5%.

In our VIA study, acetowhite area was seen in 36% of cases. Our findings were consistent with the observations of Kenneth and Yao 2002, who had observed acetowhite areas in 30%, punctuations in 5.7% and mosaic pattern in 3.5%. A similar finding to Campion et a1 1986, who reported 100% of incidence of carcinoma in acetowhite areas.

In the IARC multicenter study done in India and Africa by Sankaranarayanan et al in 2004, which included 11 cross-sectional studies, the sensitivity of colposcopy and guided biopsy was in the ranges from 76.00% to 97.00% and the specificity was between 73.00% and 91.30%. Our results were consistent with that of the Panten et a1 in 1995 study at the University of Jimbanbe/ JHPIEGO cervical cancer project 1999, Denny et al. 2000 and Shankaranarayan et al in 2003 studies, which showed that combining colposcopy and guided biopsy with PAP smear markedly improved the performance as PAP screening test had high false-positive results and decreased specificity of . In our study, we tried to find out whether the combination of tests (i.e., PAP smear or VIA and Colposcopy guided biopsy) might improve the sensitivity of the screening tests. Our results showed that when the two tests were used in combination, the sensitivity was 100%, but this happened at the cost of increasing the percentage of false-positive and decreasing the specificity. VIA can screen out a large number of women suspected to have cervical cancer. This is an easy method and can be done in OPD. The result of VIA can be seen in naked eye and does not require any meticulous microscopic examination. There were many false positive results by VIA. On the other hand, PAP was less sensitive but more specific test. That means the false positive rates are less with PAP test and the ability to exclude the true negatives are more than VIA. In view of the results obtained in our study, it can be concluded that combination of VIA and PAP smear can accurately diagnose precancerous and cancerous lesions in majority of the cases. Some studies have advocated the usefulness of combination of PAP smear and speculoscopy (PAP

Sure). Sensitivity and specificity of PAP Sure was found to be 89.5% each (Twu Nae-fang et al, 2007).

V. CONCLUSION

Both PAP and VIA positivity increased with age and the association was statistically significant. The association we found between PAP and VIA abnormality with increasing parity was statistically significant. The relation between chief complain, white discharge per vagina and PAP smear positivity as well as VIA positivity was statistically significant. PAP test is a highly specific test for screening cervical cancer. The association between distribution of women who were Pap +ve and histology +ve was statistically significant. VIA is a non-specific test for screening cervical cancer.

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