



“PREVALENCE OF ABNORMAL CERVICAL CYTOLOGY IN ANTENATAL WOMEN BY LIQUID BASED CYTOLOGY IN A TERTIARY CARE HOSPITAL IN NORTH INDIA”

Obstetrics & Gynaecology

Dr. Ankita*

Senior Resident, Department of Obstetrics & Gynaecology, VMMC and Safarjang Hospital New Delhi. *Corresponding Author

Dr. Vijay Zutshi

Professor & Consultant, Department of Obstetrics & Gynaecology, VMMC and Safarjang Hospital New Delhi.

Dr. Mukul Singh

Professor & Consultant, Department of Pathology, VMMC and Safarjang Hospital New Delhi.

ABSTRACT

Background: This study aimed to know the prevalence of abnormal cervical cytology in pregnant women by liquid-based cytology (LBC). **Materials and Methods :** Cross sectional study done at a tertiary care hospital in between August 2017 to January 2019. Six hundred pregnant women attending the OPD at their first visit were enrolled and after taking consent, history and clinical examination, subjected to cervical cancer screening by LBC. **Result:** Out of 600 samples, 10 samples (1.67%) were unsatisfactory for evaluation due to low cellularity. Among 590 samples, only 2 reported as LSIL (Low grade squamous intraepithelial lesion) and 588 reported as NILM (Negative for intraepithelial lesion or malignancy). Inflammation of varying degree, mild, moderate and dense was reported in 58.65%, 24.92% and 16.44% respectively. Infection was reported in 3.73% and Candida. **Discussion:** prevalence of abnormal cervical cytology among pregnant women in region was low but screening for cancer cervix should be done for all pregnant women, adverse pregnancy outcomes like premature rupture of membranes, preterm birth and low birth weight.

KEYWORDS

Cervical cancer, India, Antenatal women

INTRODUCTION

Cervical cancer is a preventable disease. The organized screening programmes have brought down the incidence of cervical cancer in developed world. When there is no organized screening programme in place, antenatal visits can be utilized to screen women for cervical cancer. Antenatal period provides us the opportunity to do speculum examination in all women.

The majority of pregnancies occur between the ages of 18 and 35 years, corresponding to the age range associated with the greatest incidence of cervical intraepithelial neoplasia (CIN).^[3] It has been reported that even once in a life-time screening for cervical cancer can bring down the mortality due to invasive cancer by 30%.^[4]

Additional advantage of doing cytology in pregnancy is that it can detect genital infections like candida, trichomonas and bacterial vaginosis and treatment can be given and probably prevent adverse pregnancy outcomes like preterm birth and premature rupture of membranes.^[5,6]

The incidence of cervical cancer in pregnancy varies between 0.1 to 12 per 10,000 pregnancies and that of CIN varies between 1.30 to 2.70 per 1000 pregnancies.^[7,8] Conventional Pap smear (CPS) has been used by various authors to screen antenatal women in different parts of the world. Only two studies have been reported by using liquid based cytology to determine the prevalence of abnormal cervical cytology in antenatal women.^[9,10]

The aim of this study was to screen pregnant women by LBC and determine the prevalence of abnormal cervical cytology.

MATERIALS AND METHODS:

This cross-sectional study was conducted at a tertiary care hospital from August 2017 to January 2019 after institutional ethical approval and informed written consent from all the participants. Six hundred antenatal women attending the OPD at their first visit were screened for cervical cancer by LBC.

The inclusion criteria were pregnant women attending antenatal clinic irrespective of gravidity and parity at their first visit. The exclusion criteria were women who had Pap smear in past 3 years, active bleeding, leaking or discharge present on speculum examination, history of vaginal medication in past 48 hours, history of threatened abortion in present pregnancy and obvious growth over cervix.

Six hundred pregnant women at their first visit not later than 34 weeks were screened with LBC. All women underwent clinical assessment

and detailed history like age, residence, education, age at marriage, age at first intercourse, parity, period of gestation, smoking, history of pelvic inflammatory disease and use of IUCD was taken. Pap smear was taken by rovers cervix brush which was rotated 360 degrees in clockwise motion 5 times at external os. The rovers cervix brush was detached and put in liquid Pap solution in the bottle. The sample was sent for examination to department of pathology.

STATISTICAL ANALYSIS:

Based on previous study^[9], prevalence of abnormal cervical cytology in antenatal women was 3.4%. Taking this value as reference, the minimum required sample size of 561 was required with 1.5% margin of error and 5% level of significance.

The formula used was: $N \geq ((p(1-p))/(me/za)^2$

Where, z_a is value of z at two-sided alpha error of 5%, me is margin of error. p is prevalence rate.

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean \pm SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality is rejected then non parametric test was used.

Statistical tests were applied as follows-

1. Quantitative variables were compared using Unpaired t-test/Mann-Whitney Test (when the data sets were not normally distributed.) between the two groups.
2. Qualitative variables were correlated using Chi-Square test /Fisher's exact test.

A p value of <0.05 will be considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Type of Study:- Prospective Observational Cross sectional Study.

RESULTS:

Among the 600 screened women, mean age was 25.48 ± 2.55 years and 76% women belonged to urban areas (Table 1). All the women in the study could read and write in one language and 77.5% women had studied upto class 12. Around 6.2% screened women had some knowledge about cervical cancer screening but none had been screened previously. A statistically significant correlation (p value < 0.0001) was seen between level of education and knowledge about

cervical cancer screening (Table 2).

Maximum number of women (95%) had their first intercourse between the age of 21-25 years of age. We had 65.83% primigravida, 30.17% second gravida and 4% were third gravida (Table 1). Among multiparous women , mean age at first childbirth was 23.04±1.53 years. None of the screened women were smokers or had any history of sexually transmitted disease or pelvic inflammatory disease, habit of smoking or family history of any cancer. No women had used IUCD in the past.

Regarding period of gestation at which screening was done , 11.16%, 73.83%, 9.50% and 5.50% of women were of <12 week, 12-24 weeks, 25-28 weeks and 29-34 weeks of gestation respectively (Table 1) . The mean period of gestation was 18.36±6.56 weeks. The cervix appeared healthy in majority of women (85.33%). A statistically significant correlation (p value 0.013) was reported between abnormal cervical findings on speculum examination and prevalence of infection in the cytology report (Table 3).

Ten samples (1.67%) were unsatisfactory for evaluation due to low cellularity. Among rest 590 samples, only 2 reported as LSIL (Low grade squamous intraepithelial lesion) and 588 reported as NILM (Negative for intraepithelial lesion or malignancy) . Inflammation of varying degree, mild, moderate and dense was reported in 58.65%, 24.92% and 16.44% respectively. Infection was reported in 3.73% smears. Candida, Trichomonas and Gardnerella species were present in 2.71%, 0.51%, 0.51% respectively (Table 4).

DISCUSSION:

The incidence of cervical cancer in pregnancy varies between 0.1 to 12 per 10,000 pregnancies and that of CIN varies between 1.30 to 2.70 per 1000 pregnancies.^[7,8] There is enough evidence to suggest that cervical cancer screening coverage of 80% can reduce the incidence of the disease by 93%.^[9] It has been reported that even once in a lifetime screening for cervical cancer can bring down the mortality due to invasive cancer by 30%.^[4]

Opportunistic screening should be utilized in places where organized screening programmes are not in place, to reduce the burden of cervical cancer. Studies have shown that cervical cancer screening by cervical cytology during pregnancy increases the coverage . In our study 0.33% screened women showed abnormal cytology reports. Out of 590 samples which were satisfactory for evaluation, 588 reported NILM and only 2 cases of LSIL were detected. Various Indian studies^[11-16] where cervical cancer screening was done by CPS showed the prevalence of abnormal cytology in the range of 0-0.9% which is similar to our results. In a cross sectional study^[17] from western part of India a higher prevalence of 3% has been reported .The reason for this could be that mean age at marriage in this study was 17.7years , maximum women (46%) had their first intercourse below 20 years of age and most women were illiterate or had education till primary level. Studies from other parts of the world have also reported prevalence of abnormal cytology as 1.9%^[18], 0.9%^[19], 0.4%^[20] and 0.8%^[21] among antenatal women screened by CPS. There are only two studies reported from Thailand where LBC has been used to determine the prevalence of abnormal cervical cytology in antenatal women. Parkpinyo N et al.^[9] screened 655 pregnant women at their first antenatal visit by LBC and found the prevalence of abnormal cytology as 3.4% while Khaengkhar P et al.^[10] screened 143 pregnant women by LBC and found the prevalence of abnormal cervical cytology as 7%. The reported prevalence in these two studies is much higher than our results and other studies. This could be due to the fact that , in the study by Parkpinyo N et al.^[9] 9.4% of the women screened had their first intercourse at less than 16 years of age and 54.3% had multiple sexual partners . Khaengkhar P et al.^[10] reported that 38.9% of the women screened had their first intercourse between 16-19 years of age ,24.8% were smokers and 47% had 2-4 sexual partners.

Various risk factors like early age at marriage , repeated trauma due to coitus and multiple child birth predisposes cervix to persistent inflammation and risk for preinvasive lesions of the cervix. The mean age at marriage was 22.62±1.54 years in our study. Various other Indian studies^[22,23] have also reported the mean age of marriage as 23.4 years and 22 years respectively which is similar to our study. The prevalence of abnormal PAP in the above studies is also corroborating with our results. Shaheen R et al.^[17] in North western part of India reported mean age at marriage as 17.7 years resulting in a higher

prevalence of abnormal cervical cytology as 3%.

In our study, 6.2% women had knowledge about need for cervical cancer screening but none has been screened previously for cervical cancer . There was a statistically significant correlation (p value<0.0001) between level of education and knowledge about cervical cancer screening. This observation shows the lack of awareness among Indian women for the need of cervical cancer screening which is in agreement with studies of Rizwana S et al.^[17] and Pahwa S et al.^[13] where only 2% and 3% women had prior knowledge about cervical cancer screening. On the contrary, studies from Thailand and Turkey have shown that 34-84% of women had knowledge about the same, showing better awareness about cervical cancer screening in other parts of the world.^[9,10,20]

It is reported that as pregnancy advances cervix becomes hypertrophied due to hormonal influence and then it becomes difficult to take a satisfactory smear. Several studies^[22-25] have reported the prevalence of unsatisfactory smear by CPS ranging from 4.3% to 46.7% and that of LBC ranging from 1.7%-16.6%. The above studies have shown that prevalence of unsatisfactory smear by LBC is comparatively less as compared to CPS. The reason for this is that in LBC , RBCs, inflammatory cells and mucous are reduced and cells are distributed randomly throughout the slide and clear background obtained enhances sensitivity and quality. In our study, 10 samples (1.67%) were unsatisfactory for evaluation due to low cellularity. LBC was used in our study which probably would be advantageous in terms of taking sample which were satisfactory on report. In LBC, the brush used is soft and there is no need to use endocervical brush separately. None of our participants complained of any discomfort or spotting after the procedure. Out of 590 samples, only two (0.33%) reported LSIL. We did not find any correlation between period of gestation at screening and abnormal cytology report .

Unhealthy cervix is also a risk factor for cervical cancer. We found healthy cervix in 85.33%, ectopy in 7.83% and hypertrophy in 6.83% of the women . In our study, infection was reported in 3.73% and Candida, Trichomonas and Gardnerella species were present in 2.71% ,0.51% , 0.51% respectively, but none of these women had any complaints. A statistically significant correlation was seen between speculum findings of ectopy/ hypertrophy and infection in Pap smear report (p value 0.013) . Pahwa S et al.^[13] in their study screened 300 antenatal women by CPS and found that per speculum findings of unhealthy cervix was present in 35 women and 31 (18.45%) of these had abnormal smears. A statistically significant correlation (p value 0.0007) was reported between unhealthy cervix and abnormal Pap smear report which was similar to our results. Pregnancy increases the frequency of vaginal candida colonization, this is thought to be the consequence of increased levels of circulating estrogen and deposition of glycogen and other substrates in the vagina during pregnancy. The prevalence of infection reported by conventional Pap smear in pregnant women in Indian studies has been reported ranging from 4-5.33%. Studies^[9,10] done by LBC reported much higher prevalence of infection as 24.1% and 33.56% respectively. This might be due to the fact that 9.4% and 38.9% of the women screened by Parkpinyo N et al.^[9] had their first intercourse at < 16 years and 16-19 years of age respectively , 54.3% had multiple sexual partners and 24.8% were smokers. Similarly, 69% of the women screened by Khaengkhor^[10] et al had their coitarche between 16-19 years of age and 47% had 2 - 4 sexual partners. This shows that early age at coitarche and having multiple sexual partners may be associated with the higher prevalence of infection in antenatal women in these studies.

CLINICAL CHARACTERISTIC	NUMBER OF WOMEN	PERCENTAGE (%)
Age(in years)		
21-25	339	56.5
26-35	261	43.5
Residence		
Rural	144	24
Urban	456	76
Age at marriage (in years)		
21-25	569	94.83
26-30	31	5.17
Education		
Primary school	105	17.5
Secondary school	360	60
Graduate	135	22.5

Knowledge about screening		
Yes	37	6.2
No	563	93.8
Parity		
Primigravida	395	65.83
Multigravida	205	34.17
Period of gestation at screening		
<12 weeks	67	11.16
12-24 weeks	443	73.83
25-28 weeks	57	9.50
29-34 weeks	33	5.50

[Table -1]: Clinical parameters during history and physical examination of the women

Education	No. Of Women	Percentage (%)	Knowledge About Screening	P Value
1) 6th to 8 th class	105	17.50%	0	
2) 10th-12 th class	360	60.00%	0	<0.0001
3) Graduate	126	21.00%	35(94.5%)	
4) Postgraduate	9	1.50%	2(5.5%)	
Total	600	100.00%	37(100%)	

[Table -2]: Correlation between knowledge about cervical cancer screening and education of the women

	Speculum Examination			Total	P Value
	Ectopy	Healthy	Hypertrophied		
Infection					
No	43 (91.49%)	490 (97.22%)	36 (90.00%)	569 (96.28%)	0.013
Yes	4 (8.51%)	14 (2.78%)	4 (10.00%)	22 (3.72%)	
Total	47 (100.00%)	504 (100.00%)	40 (100.00%)	591 (100.00%)	

[Table -3]: Correlation between speculum examination of cervix and infection in LBC report

REPORT	NUMBER OF WOMEN	PERCENTAGE (%)
Satisfactory smear	590	98.33
Unsatisfactory smear	10	1.67
NILM	588	98
LSIL	2	0.33
INFLAMMATION		
Mild	346	58.65
Moderate	147	24.92
Dense	97	16.44
INFECTION		
Candida	16	2.71
Trichomonas	3	0.51
Gardnerella	3	0.51

[Table -4]: LBC report of the screened pregnant women

CONCLUSION:

Although the prevalence of abnormal cervical cytology among pregnant women in our region was low , but screening for cancer cervix should be done for all pregnant women. It gives us an opportunity to do speculum examination in them, to detect epithelial cell abnormalities, to look for any growth and pick up cervical cancer at an early stage. Added advantage of doing cervical cytology in pregnancy is that in some women infective organisms can be picked up and can be treated to minimize adverse pregnancy outcomes like premature rupture of membranes, preterm births and low birth weight.

REFERENCES:

1. Ferlay J, Soerjomataram I, Ervik M. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013.
2. Bray F, Ren JS, Masuyer E. Estimates of global cancer prevalence for 27 sites in the adult population in 2008. *Int J Cancer* 2013; 132(5):1133-45.5
3. Kaplan KJ, Dainty LA, Dolinsky B, Rose GS and Carlson J, McHale M ,Elkas JC. Prognosis and recurrence risk for patients with cervical squamous intraepithelial lesions diagnosed during pregnancy. *Cancer* 2004 Aug 25;102(4):228-232.
4. Juneja A, Murthy NS, Tuteja RK, Sardana S, Das DK. Reduction in the cumulative incidence rate of cervical cancer by one life time selective screening. *Neoplasma* 1997;44:272-4.
5. Herbert Kiss, Iris Holzer, Michael Hagmann, Peter Husslein ,Alex Farr .Recurrent asymptomatic vaginal colonization with *Candida albicans* is associated with impaired pregnancy outcomes. *Eurpoean Journal of Obstetrics and Gynecology and Reproductive Biology*. 2016;vol 206: p1-264, e1-e194.
6. Christine L Roberts, Charles S Algert, Kristen L Rickard and Jonathan Morris.

Treatment of vaginal candidiasis for the prevention of preterm birth : a systematic review and meta analysis. *Biomed Central Syst Rev* 2015; 4:31.

7. Al-Halal H, Kezouh A, Abenheim H. Incidence and obstetrical outcomes of cervical intraepithelial neoplasia and cervical cancers in pregnancy. A population based study on 8.8 million births. *2012. Arch GynecolObstet* 2013 Feb;287(2):245-50.
8. Takushi M, Moromizato H, Sakumoto K, Kanazawa K. Management of invasive Carcinoma of uterine cervix associated with pregnancy: outcomes of intentional delay in treatment. *Gynecol Oncol* 2002 Nov;87(2):185-189.
9. Parkpinyon N, Inthasorn P, Laiwejipithaya S, Punnarat T. Benefits of cervical cancer screening by liquid based cytology as part of Routine Antenatal Assessment. *Asian Pac J Cancer Prev*. 2016;17(9):4457-4461.
10. Khaengkhor P, Mairang K, Suwannarurk K, Thaweekul Y, Poomtavorn Y, Pattaraarchachai J et al . Prevalence of Abnormal cervical cytology by liquid based cytology in the Antenatal Care Clinic. *Thammasat University Hospital. J Med Assoc Thai* 2011; 94(2):152-158.
11. Manikkam B. Screening for cervical cancer during pregnancy. *Int. J. Community Med Public Health*. 2016 Sep ;3(9):2493-2498.
12. T. Radha Bai Prabhu, Velayudham D, Nethaji S, Singhal H, Venkatachalam R. Opportunistic cervical cancer screening in Pregnancy. *International Journal of Community Medicine and Public Health* 2016 Sep ; 3(9):2493-2498.
13. Pahwa S, Mahajan R, Nagpal M, Amanbeer . Expanding Horizon of Cervical Cancer screening by involving Antenatal patients. *JMSRC* 2016 ;4:14805-14813.
14. Himabindu P, Kanwal A, Vasudha. Pap smear in Antenatal women-Routine Screening in low resource setting. *IOSR- JDMS* 2015; 14:04-05.
15. Mishra V, Dorairajan G, Neelaiah S, Chinnakali P. Prevalence of abnormal Pap smear during pregnancy in a teaching hospital in South India. *Int J Reprod Contracept Obstet Gynecol* 2015 Oct; 4(5):1296-1299.
16. Singh P, Baghel V. Screening of pregnant women for cervical malignancies. *Int J Reprod Contracept Obstet Gynecol* 2013 Sep ;2(3):359-362.
17. Shaheen R, Paliwal S, Bakoliya A. Prevalence of abnormal Pap smear in pregnant women attending the antenatal clinic in Dr. S.N Medical college and attached hospitals, Jodhpur. *Indian Journal of Applied Research* 2017;7:69-71.
18. Jose Candido C, Xavier -Junior , Rozany M Duffloth , Diama B. do Vale ,Thalita A.Tavares et al . High grade squamous intraepithelial lesions in pregnant and non- pregnant women. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 2014;175: 103106.
19. Dinc A. Pap smear screening results for Turkish pregnant women. *Asian Pac J Cancer Prev* 2012; 13(11): 5835-5838.
20. Ngaojaruwong N, Vuthiwong C, Punnpuakdeekoon P, Thongsorn N. Prevalence of abnormal Papanicolaou smear in pregnant women at Phramongkutlao Hospital. *Thai Journal of Obstetrics and Gynaecology*, 2008 July; 16: 179-185.
21. Sueblinvong T, Suwannarurk K, Chanthasenanont A, Treetampinich C, Pongrojapw D. Prevalence and management of abnormal Pap smear in Antenatal care clinic at Thammasat University Hospital. *J Med Assoc Thai* 2005;88(2):133-7.
22. Baker JJ. Conventional and Liquid based Cervicovaginal cytology; a comparison study with clinical and histologic follow up. *Diagn Cytopathol*. 2002 Sep ;27(3):185-8.
23. Ranjana H, Sadhna S. Comparison of conventional pap smear versus liquid based cytology in a diagnostic centre of central Madhya Pradesh. *Indian J. Pathol. Oncol*. 2016;3(1):42.
24. Singh VB, Gupta N, Nijhawan R, Srinivasan R, Suri V, Rajwanshi A. Liquid-based cytology versus conventional cytology for evaluation of cervical Pap smears: Experience from the first 1000 split samples. *Indian J. Pathol. Microbiol*. 2015 Jan 1;58(1):17.
25. Shanmugapriya N, Devika P. Comparing the effectiveness of liquid based cytology with conventional PAP smear and colposcopy in screening for cervical cancer and it's correlation with histopathological examination: a prospective study. *Int. J. Reprod Contracept Obstet. Gynecol*. 2017 Nov 23;6(12):5336-40.