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Original Article

Pathology Section

Pap Smear Evaluation through Opportunistic Screening Programme in Tertiary Care Hospitals and Rural Mangalore

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ABSTRACT

Introduction: Pap smear cytology enables the cytopathologist to detect and evaluate the degree of cellular alterations present in uterine cervical lesions. Cytopathological analysis of these smears has stood out amongst other tests because of its simplicity and low cost, which are essential characteristics of methods applicable to mass screening programmes.

Aim: Opportunistic screening by using Pap smear examination from the uterine cervix of women attending out reach camps and outpatient department employing the Bethesda System 2014.

To detect genital infections and epithelial cell abnormalities in symptomatic and asymptomatic women. Also to correlate the cytology of the lesions with histopathology, wherever available.

Materials and Methods: Opportunistic screening programme has the advantage to screen women who attend outpatient department and outreach camps. The study included 3255 Pap smears of women received from the outpatient departments of AJ Institute of Medical Sciences and Research Centre, Mangalore, KMC Hospital, Mangalore and various outreach camps and private consultants of rural Mangalore, Karnataka over a period of three years. The smears were stained by Modified Papanicolaou stain and analyzed using the Bethesda system criteria (2014). Histopathological correlation was done wherever available.

Results: Out of a total of 3255 pap smears, 626 (19.23%) were unsatisfactory, 2532 (77.78%) were Negative for Intraepithelial Lesion or Malignancy (NILM) and 97 (2.98%) showed epithelial cell abnormalities of which 23 (23.7%) showed malignancy.

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Pap smear cytology in the study were 80.49%, 92.23% , 67.35%, 95.96% and 90.28% respectively.

Conclusion: Cervical smear cytology assists in the early detection of precancerous lesions of the cervix thereby down staging cervical neoplasias and also helps in the diagnosis of specific infections of the female genital tract.

Keywords: Cancer screening, Cervical cytology, Histopathology

INTRODUCTION

Cancer of the cervix is the second most common cause of death from cancer among females [1]. Contrary to other malignancies, carcinoma cervix is readily preventable when effective programmes are conducted to detect and treat the precursor lesions [2]. The role of cervical cytology in checking the incidence of cervical carcinoma is well established and cancer control programmes have enabled some developing countries to achieve up to 80% reduction in the incidence and mortality from cervical cancer. Pap smear cytology enables one to detect and evaluate the degree of cellular alterations present in uterine cervical lesions. Due to the simplicity and cost effectiveness, which are the essential characteristics of methods applicable to mass screening programmes, cytopathological analysis of these smears has stood out amongst other tests [3]. Cervical cancer screening is based on the assumption that early detection may allow early treatment. However, in developing countries, the high burden of cervical cancer is largely due to the deficiency of effective screening programmes [4]. Therefore, in most of the cases opportunistic screening of cervical cancer becomes necessary. The Bethesda system for reporting the cervical cytology was developed as a uniform standardized system of terminology that would provide clear guidance for clinical management.

Thus, this study was conducted with the objective of opportunistic screening by using Pap smear examination from the uterine cervix of women attending outreach camps and outpatient department employing the Bethesda System 2014.

MATERIALS AND METHODS

This was a retrospective study of conventional pap smears of women received from the outpatient departments of AJ Institute of Medical Sciences and Research Centre, Mangalore, KMC Hospital, Mangalore, India and various outreach camps and private consultants of rural Mangalore in South Canara district of Karnataka state over a period of three years from January 2013 to January 2016. Pap smears of all women of reproductive age group and elderly women who attended the outpatient departments and camps were included in the study. Pap smears taken from post hysterectomy patients, already known cases of carcinoma cervix and pregnant women were excluded from the study. Pap smears were obtained from the transformation zone with the help of the Ayre's spatula. The material was immediately smeared on a clean labeled glass slide. The glass slide was dipped in Coplin jar with isopropyl alcohol and fixed for 20-30 minutes.The smears were stained by modified Papanicolaou stain and analysed using the Bethesda system criteria (2014) [5]. A total of 3255 pap smears, were studied. Histopathological correlation was done wherever available.

RESULTS

Out of a total of 3255 pap smears 626 (19.23%) were unsatisfactory, 2532 (77.78%) were negative for intraepithelial lesion or malignancy (NILM) and 97 (2.98%) showed epithelial cell abnormalities of which 23 (23.7%) showed malignancy. The bulk of the unsatisfactory smears was due to the absence of endocervical cells. The distribution of smears as per Bethesda System is shown in [Table/Fig-1,2a-e,3a-c].

Histopathological correlation was available in 247 (7.59%) of the total 3255 smears and 53 (54.64%) cases of a total of 97 cases with epithelial cell abnormality. The histopathological correlation is shown in [Table/Fig-4].

All six adenocarcinomas on cytology had histopathological correlation available.

Case 1: showed metastatic carcinoma from ovary and histopathological correlation showed metastatic serous cystadenocarcinoma from ovary to cervix.

Case 2: showed trophoblastic giant cells on cytology and gestational trophoblastic disease on histopathological correlation.

Case 3: which was adenocarcinoma on cytology, showed metastatic adenocarcinoma from rectum to cervix on histopathological correlation.

Case 4: was mucin secreting adenocarcinoma metastasis on cytology which showed squamous cell carcinoma on histopathological sections.

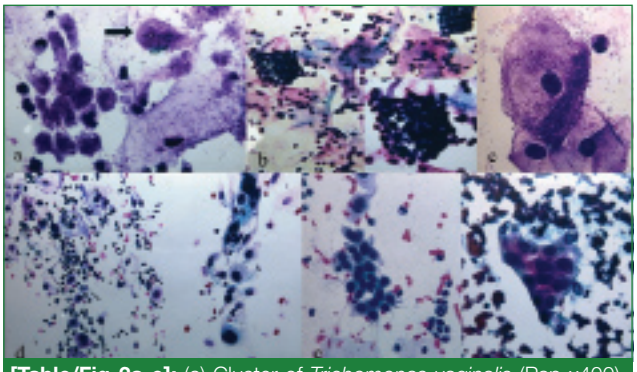
Case 5: which showed adenocarcinoma on cytology turned out to be endometrial carcinoma on histopathology.

Case 6: showed adenocarcinoma on cytology and it turned out to be endocervical adenocarcinoma on histopathology.

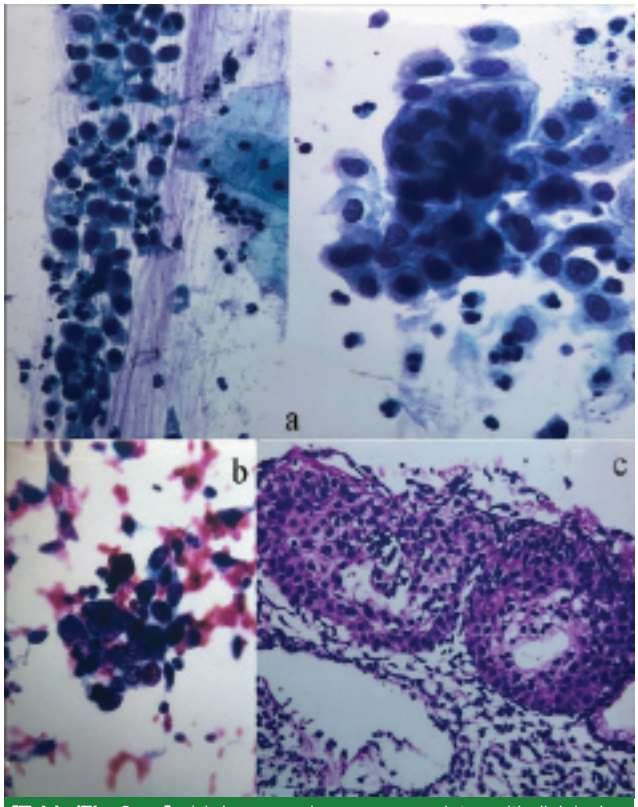
Exfoliation of endometrial cells in women aged ≥ 40 years

	Diagnosis	No. of cases	Percentage (%)
I	**Negative for Intraepithelial Lesion or Malignancy (NILM)**		
1.	**Non Neoplastic Findings**		
	1a. Normal	1060	41.86
	1b. Reactive cellular changes associated with inflammation	637	25.15
	1c. Atrophic	67	2.64
	1d. Follicular	1	0.03
	1e. Other non neoplastic changes	375	14.81
2.	**Organisms**	267	10.54
	i. *Candida*	42	1.29
	ii. *Trichomonas vaginalis* [Table/Fig-2a,b]	13	0.51
	iii. Bacterial vaginosis [Table/Fig-2c]	21	8.33
	iv. Actinomyces	1	0.03
	Total	2532	100
II	**Epithelial Cell Abnormality**		
3.	**Squamous Cell**		
	Atypical Squamous Cells of Undetermined Significance (ASC-US) [Table/Fig-2d]	35	36.08
	Low-grade Squamous Intraepithelial Lesion (LSIL) [Table/Fig-3a]	14	14.43
	High-Grade Squamous Intraepithelial Lesion (HSIL) [Table/Fig-3b]	15	15.46
	Squamous Cell Carcinoma (SCC)	17	17.52
4.	**Glandular Cell**		
	Atypical Glandular Cells (AGC) [Table/Fig-2e]	10	10.31
	Adenocarcinoma	6	6.18
	Total	97	100

[Table/Fig-1]: Distribution of smears as per Bethesda System (2014).



[Table/Fig-2a-e]: (a) Cluster of *Trichomonas vaginalis* (Pap x400). Pear shaped organism (black arrow) with sickle shaped nucleus (Pap x1000); (b) Pus balls seen in *Trichomonas vaginalis*- numerous neutrophils over the surface of squamous epithelium (Pap x400); (c) A typical clue cell covered by dense layer of organisms seen in a bacterial vaginosis smear (Pap x400); (d) Atypical squamous cells of undetermined significance (Pap x400); (e) Atypical glandular cells (Papx400).

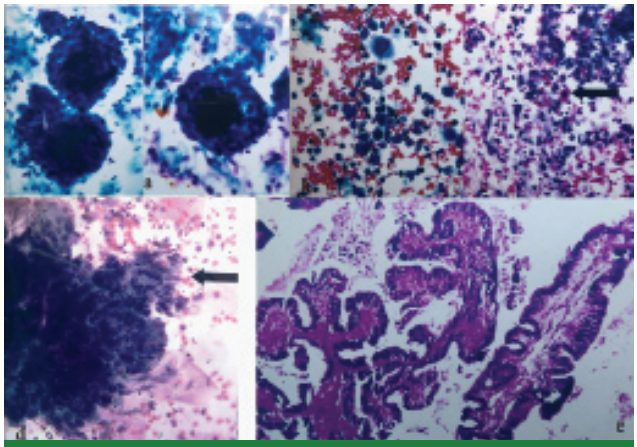


[Table/Fig-3a-c]: (a) Low grade squamous intraepithelial lesion (Pap x400); (b) High grade squamous intraepithelial lesion (Pap x400): (c) Histopathology section of the same showing squamous cell carcinoma in situ (H&E x400).

were seen in 4 smears in the form of exodus [Table/Fig-5a]. Two smears were normal, one smear was inflammatory and one was reparative smear.

On histopathology primary cervical carcinomas seen were of three types: nine non-keratinizing large cell squamous cell carcinomas [Table/Fig-5b], three keratinizing large cell squamous cell carcinomas [Table/Fig-5c] and one endocervical adenocarcinoma [Table/Fig-5d,e].

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Pap smear cytology in the study were 80.49%, 92.23%, 67.35%, 95.96% and 90.28% respectively.



[Table/Fig-5a-e]: (a) Exodus (Papx400); (b) Non keratinizing large cell squamous cell carcinoma (Papx400); (c) Keratinizing large cell squamous cell carcinoma (Papx200); (d) Endocervical adenocarcinoma showing characteristic nuclear feathering (Papx400); (e) Histopathology section of the same (H&E x400).

DISCUSSION

The percentage of unsatisfactory smears in the present study is 19.23% in comparison to study by Bamanikar et al., (5.71%) [1]. The bulk of the unsatisfactory smears were due to the absence of endocervical cells. The reason could be unskilled hand or ascent of transformation zone in elderly women.

A comparative analysis of smears diagnosed as NILM between the present study and a study by Malik et al., is shown in [Table/Fig-6] [6].

A comparison between the histopathological correlation of ASC-US was done between the present study and a study conducted by Guerrine and the results were comparable, except that no CIN- 2,3 was observed in the present study [7].

In this study, 14 LSIL smears were reported of which four had

Cytodiagnosis	No.	Histopathology study available	NILM	CIN-1	CIN-2,3	SCC	Adenocarcinoma
Unsatisfactory	626	63	59	2	1	-	1
NILM	2532	135	131	1	1	2	-
ASC-US	35	20	14	6	-	-	-
AGC	10	7	5	-	-	1	1
LSIL	14	4	1	2	1	-	-
HSIL	15	6	-	-	3 [Table/Fig-3c]	3	-
SCC	17	10	-	-	1	9	-
Adenocarcinoma	6	6	-	-	-	1	5
Total	3255	247					

[Table/Fig-4]: Histopathological correlation of cytologically diagnosed smears.

Findings	Malik et al., [6] (2001)		Present study	
	No.	%	No.	%
Non specific inflammation	26	17.69	637	25.15
Atrophic cervicitis	2	1.36	67	2.64
Follicular cervicitis	-	-	1	0.03
Trichomonas vaginalis	1	0.68	13	0.51
Candida species	4	2.72	42	1.29
Shift in vaginal flora	6	4.08	211	8.33
Actinomyces	-	-	1	0.03

[Table/Fig-6]: Comparative analysis of smears diagnosed as NILM.

histopathological correlation and 75% of the cases turned out to be CIN-1 and CIN- 2 and 3. This was compared with a study by Atla BL et al., wherein 91% of the cases turned out to be CIN 1 and CIN 2 [8].

One HSIL diagnosis was missed in cytology smear. Joshi et al., in their study experienced such cases, where pap smears were negative and histopathology showed CIN 1, 2, 3 and SCC [9]. Approximately two-third of the conventional Pap test false negatives are due to limitation of sampling and slide preparation [10]. In the present study sampling error could be the possible cause.

In the present study 50% of AGC showed chronic cervicitis. According to Bonfiglio and Erozan there can be many conditions which may lead to a diagnosis of AGC, especially of endocervical type [11]. This can be due to usage of endocervical brush (where abundant normal cells are seen in clusters), reparative/inflammatory changes (radiation, IUCD, trauma etc.,), tubal metaplasia, endometrial cells and microglandular hyperplasia. These can give a false high nuclear to cytoplasmic ratio mimicking AGC.

In the present study, on histopathological correlation, nine cases showed non-keratinizing large cell squamous cell carcinoma, three cases showed keratinizing large cell squamous cell carcinoma and one showed endocervical adenocarcinoma. Tengli MB et al., had discussed the incidence of various types of squamous cell carcinoma in their study and the results were comparable [12].

According to a dataset which included screening histories of 3305 women with invasive cervical cancer diagnosed since 1990 between 20 and 69 years of age, 641 (19%) were adenocarcinomas [13]. In the present study one case of endocervical adenocarcinoma was reported out of twenty three cervical cancers (4.34%).

Joste NE et al., studied the non correlating Pap tests and cervical biopsies [14]. They have discussed several factors:

(1) A dysplasia diagnosed on Pap test may resolve without treatment and no longer be present on a women's cervix.

(2) Squamous atypia may have been overdiagnosed as a dysplasia on the Pap test.

(3) The dysplasia may not be identified and sampled at the time of colposcopy.

(4) The abnormal cells in the Pap test may not have originated from the cervix, possibly transferred from elsewhere in the genital tract.

(5) The dysplasia may not be apparent on the resulting slide because of inadequate sectioning of the paraffin block.

In the study by Joste NE et al., 111 cervical biopsies (9.86%) did not correlate with the Pap test (1,126 smears) [14]. In the present study 6.48% cervical biopsies did not correlate with the Pap test.

The present study is compared with the study by Chhabra Y et al. The results of the two studies are comparable, except for the predictive value of positive test which is 67.35% in the present study and 92.8% in the study by Chhabra Y et al., [Table/Fig-7] [15]. The difference is due to the inclusion of the categories atypical squamous cells and atypical glandular cells (The Bethesda System 2014) in the present study. Mostafa MG et al., found accuracy rate of 48% [16]. High accuracy was seen in the present study due to the study being done in a tertiary care hospital and being an opportunistic screening programme.

Screening Parameters	Chhabra et al.,[15] (2003)	Present study
Sensitivity	81%	80.49%
Specificity	95%	92.23%
Positive Predictive Value	92.8%	67.35%
Negative Predictive value	86.6%	95.96%
Accuracy	88%	90.28%

[Table/Fig-7]: Comparison of the screening parameters.

LIMITATION

There are certain important limitations of this study. The idea of screening in Indian population is still at a nascent stage. The socio-economic factors could not be explored in detail since it was a screening study. Eventual outcome could not be evaluated since all patients could not be followed-up. Use of liquid based cytology could have improved the results.

CONCLUSION

In our study it has been observed during rural screening programmes, that the women folk to a great extent were aware of genital hygiene despite their poor economic status. The occurrence of *Trichomonas Vaginalis* infection was at the lowest in this part of the country. Intraepithelial lesions and malignancy (2.98%) were very low in rural areas of Mangalore. Cervical smear cytology assists in the early detection of precancerous lesions of the cervix thereby downstaging cervical neoplasias and also helps in the diagnosis of specific infections of the female genital tract which is clinically very significant.The Bethesda System 2014 for reporting cytology is found to be very useful as it mentions clearly regarding specimen adequacy, provides

an effective communication interface among cytologist and clinician for patient evaluation wherever needed.

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