

Evaluation of Intraoperative Cytology in Ovarian Tumours

¹Dr Kumudini Sardar, ²Dr Jitendra Singh, ³Dr Sarita Tirkey

¹Junior Resident, Department Of Obstetrics & Gynaecology, Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand.

²Senior Resident, Department Of Laboratory Medicine, Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand

³Associate Professor, Department Of Obstetrics & Gynaecology, Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand

Abstract :

Background: ovarian neoplasms is a heterogenous group of benign and malignant tumours of epithelial, stromal and germ cell origin. Ovarian cancer is the second most common of all genital cancers and accounts for 10-15 % of all gynaecological cancers in developing countries. Most of the ovarian tumours cannot be easily distinguished from one another on the basis of their clinical or gross characteristics alone. Therefore cytological interpretation of the ovarian neoplasms is both interesting and challenging. Imprint cytology is a rapid cheap and simple procedure to study the cytology of tissues.

Material and methods: The present study “ evaluation of intraoperative cytology in ovarian tumours “ was carried out in the Department of Obstetrics and Gynaecology in collaboration with the department of Pathology, RIMS, Ranchi, in the period between May 2013 to October 2014. Sample size were 100.

Results : out of 100 cases, 61 were benign ovarian tumours, 32 were malignant and 7 were borderline type. 72% were epithelial, 22% were germ cell, 4% were sex cord stromal and 2 % were metastatic. Sensitivity and specificity of the present study is 92.42% and 91.18% respectively.

Conclusion: intraoperative cytology is extremely useful and provides a simple, rapid and inexpensive adjunctive technique for intraoperative consultation of ovarian lesion in the low resource setup.

Keywords : ovarian tumour, imprint cytology,

I. Introduction

Ovarian tumour is not a single entity, but a complex wide spectrum of neoplasms involving a variety of histological tissues ranging from epithelial tissues, connective tissues, specialised hormone-secreting cells to germinal and embryonic cells. Ovarian cancer is the second most common of all genital cancers and accounts for 10-15 % of all gynaecological cancers in developing countries.[1] 70% of the women diagnosed with ovarian carcinoma have advanced disease at the time of diagnosis.[2] the ovarian tissue are constantly in a dynamic state. The complex anatomy of ovary and its peculiar physiology, the constant cyclical changes from puberty to menopause give numbers of cell, each of which is capable of giving rise to complex varieties of tumours.[3]. Most of the ovarian tumours cannot be easily distinguished from one another on the basis of their clinical or gross characteristics alone. Therefore cytological interpretation of the ovarian neoplasms is both interesting and challenging.[4] Cytology has been underutilised as a modality for primary diagnosis of ovarian cancer. This has been mainly due to accuracy of imaging techniques like ultrasonography, CT scan in detecting malignancy and omental or peritoneal deposits.[5] Fine needle aspiration cytology in the preoperative investigation of ovarian tumours has been discouraged from the safety point of view due to possibility of needle tract seeding and dissemination.[6,7] In such situation, intraoperative imprint cytology will provide rapid diagnosis. In a young woman, this will avoid unnecessary removal of contralateral ovary and help in preservation of fertility.

II. Objective

Diagnostic accuracy, sensitivity & specificity of imprint cytology in the intraoperative diagnosis of the ovarian tumours and to compare it with histopathology.

III. Materials and methods

This was observational study done on 132 patients with ovarian tumours of varied age groups attending outpatient department and emergency room, department of Obstetrics and gynaecology, RIMS, Ranchi during the study period of may 2013 to October 2014. Out of these, 20 were excluded and 12 cases were lost due to non compliance. Hence total of 100 patients who underwent laparotomy at RIMS, Ranchi were recruited for the study.

Inclusion criteria: all women diagnosed ovarian tumours irrespective of age, parity.

Exclusion criteria Patients who underwent cytoreductive surgery before.,Patients having morbid medical conditions, Patients with coagulopathy.,Patients presenting with acute emergency eg. Torsion The study was approved by institutional ethical committee(IEC) , RIMS, Ranchi. Written consent was taken from all the patients in the study. Detailed clinical history, clinical examination and investigations were recorded for each patient included in the study. Evaluation needs: for effective intraoperative and onsite pathological consultation, proper collection, preparation, staining as well as interpretation and diagnosis of the various cellular specimens is required.

Smear preparation: imprint/touch smear

After thorough examination of specimen, smear prepared by the gentle touch of resected specimens with minimal trauma to the cells. 4 slides were prepared.

Fixation and staining of smears

2 of wet smear were fixed with 95% ethanol and 2 were air dried. Ethanol fixed smear stained with rapid papanicolaou stains. The air dried smears were stained with Leishman – Giemsa stain(LG stain)

Procedure for histopathology

Tissue processing and section cutting:

Fixation: done with 10% formalin

Dehydration: done in ascending grade of isopropyl alcohol.

Clearing: done with xylene

Impregnation : carried out with the help of wax

Embedding and blocking: embedding was done with help of wax and blocking was done in L blocks(Leukhart's block)

Section cutting : 4-5 mm thick section were taken with the help of rotatory microtome.

Routine staining: the processed tissue section were then subjected to routine staining by Hematoxylin and Eosin stain.

Results: nucleus : stained blue; cytoplasm : stained pink.

IV. Results

The present work “ **evaluation of intraoperative cytology in ovarian tumours** “ was carried out on 100 surgical ovarian specimens of patients who underwent oophorectomy or Total abdominal hysterectomy with bilateral salpingo-oophorectomy as per indications. The cytosmear was evaluated for the following parameters:

1. Cellularity
2. Arrangement of epithelial cells
3. Cellular features of malignancy
4. Necrosis
5. Background

Based on the cytomorphology , lesions were classified as benign or malignant neoplasms. The diagnostic accuracy was reviewed after histopathological diagnosis was made. Fig no.1 & table no.1 : shows the case distribution of various types of ovarian tumours in this study. Out of 100 cases studied, (61/100 cases; 61%) were benign tumours; (32/100 cases; 32%) were malignant and (7/100cases; 7%) were borderline type.

Fig no. 1

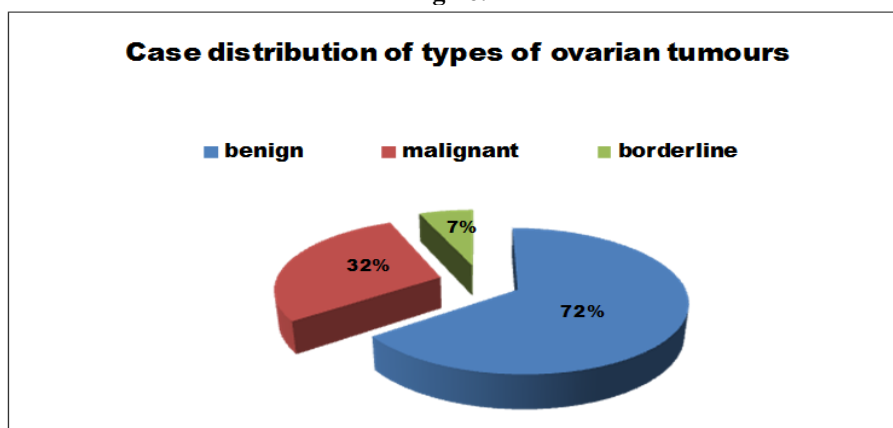


Table no. 1: Distribution of type of ovarian tumours (n=100)

Types of tumour	No. of cases
Benign	61
Malignant	32
Borderline	7

Fig no.2 & table no.2 : shows the case distribution of various histological types of ovarian tumours in this study. Out of 100 cases; 72 cases(72%) were of epithelial type, of which 45(45%) cases were serous type and 27(27%) cases were of mucinous type. Germ cell tumours comprises of 22(22%)cases. Sex cord stromal tumours & metastatic tumours constitutes 4% and 2% respectively.

Fig NO. 2

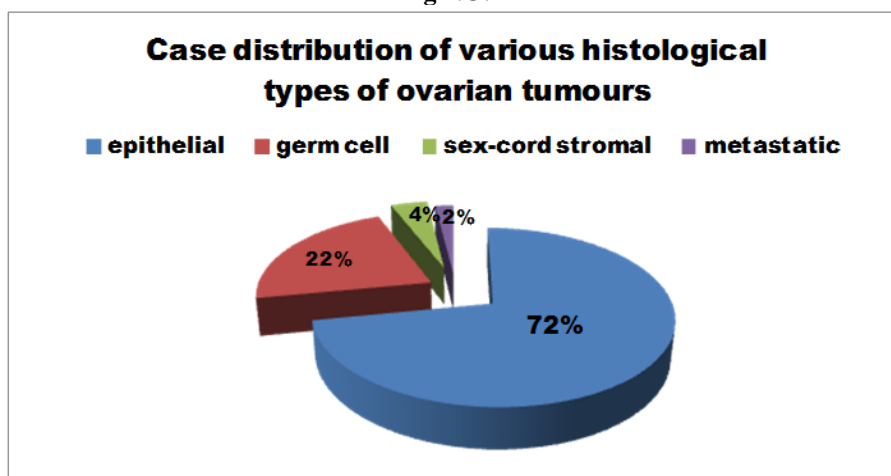


Table no. 2: Case distribution of histological type of ovarian tumours(n=100)

Histological type	No. of cases
Epithelial	72
Germ cell	22
Sex cord stromal	4
Metastatic	2

Table below : Age group to morphological types of tumours

Morphological types	Age in groups (years)				Total
	0-20	21-40	41-60	>60	
Epithelial tumours					
serous	1	22	21	2	26
Benign	1	14	9	0	24
Borderline	0	4	1	0	5
Malignant	0	4	11	2	17
Mucinous	5	12	8	1	26
Benign	4	8	5	1	18
Borderline	0	2	0	0	2
Malignant	1	2	3	0	6
Germ cell tumours	8	13	1	0	22
Dermoid benign	2	12	1	0	15
Dermoid malignant	1	0	0	0	1
Dysgerminoma	5	0	0	0	5
Yolk sac tumours	0	1	0	0	1
Sex- cord stromal tumours	0	0	3	1	4
Fibroma	0	0	2	0	2
Granulosa cell tumour	0	0	1	1	2
Metastatic adenocarcinoma	0	1	1	0	2
	14	48	34	4	100

Out of 100 cases studied, majority of patients; 48 cases(48%) belonged to the age group of 21-40 years, followed by 34 cases (34%) in the age group of 41-60 years. Highest number of benign tumours (34 cases; 34%) was prevalent in age group of 21-40 years. Highest number of malignant tumours ,15 cases(15%) was prevalent in age group of 41-60 years, followed by 8 cases(8%) & 7 cases(7%) in age group of 41-60years and 0-20 years respectively.

The most common malignant tumour is serous cystadenocarcinoma (17 cases;17/32;~53%). Maximum number of malignant germ cell tumours (6 cases) belong to 0-20 years; comprising of 5 cases of dysgerminoma & 1 case of immature teratoma. Ovarian tumours in the age group >60 years was least prevalent (4 cases;4%) comprising of 2 cases of serous cystadenocarcinoma,1 case of mucinous cystadenoma & 1 case of granulosa cell tumour. Maximum number of Borderline tumours was prevalent in age group of 21-40 years (6 cases;6%). 3 cases of Sex cord stromal tumours was observed in age group of 41-60 years. 2 cases of Metastatic adenocarcinoma was observed in age group of 21-40years and 41-60 years ;one in each group.

Fig no. 3

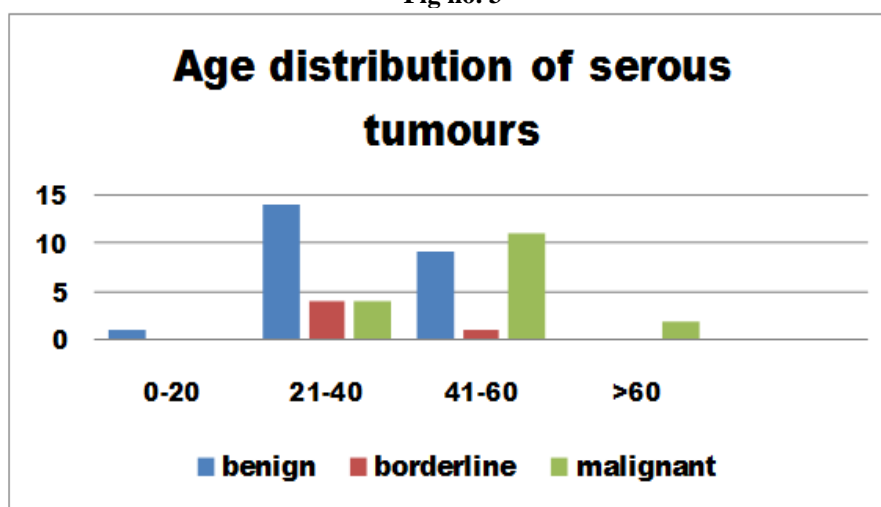


Table No. 3: Age distributions of serous tumours

	0-20yrs	21-40yrs	41-60yrs	>60yrs
Benign	1	14	9	0
Borderline	0	4	1	0
Malignant	0	4	11	2

Fig. no.-3& table no.3: Maximum cases of Serous cystadenoma 14 cases found in age group of 21-40 years. Maximum cases of serous cystadenocarcinoma 11 cases found in age group of 41-60 years.

Fig no. 4

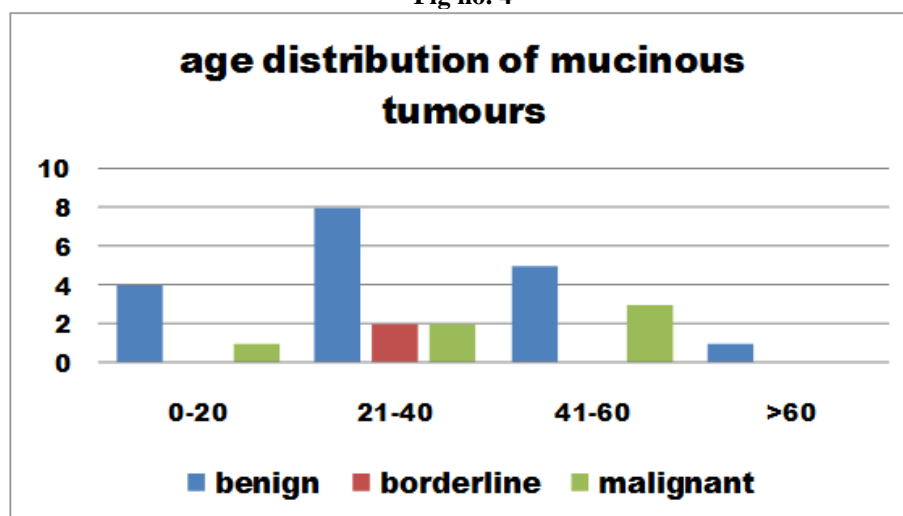


Table no. 4 : Age distribution of mucinous tumours

	0-20 yrs	21-40yrs	41-60yrs	>60 yrs
Benign	4	8	5	1
Borderline	0	2	0	0
Malignant	1	2	3	0

Fig. no.4 & table no.4: Maximum cases of mucinous cystadenoma 8 cases found in age group of 21-40 years. Maximum cases of mucinous cystadenocarcinoma 3 cases found in age group of 41-60 years.

Fig no. 5

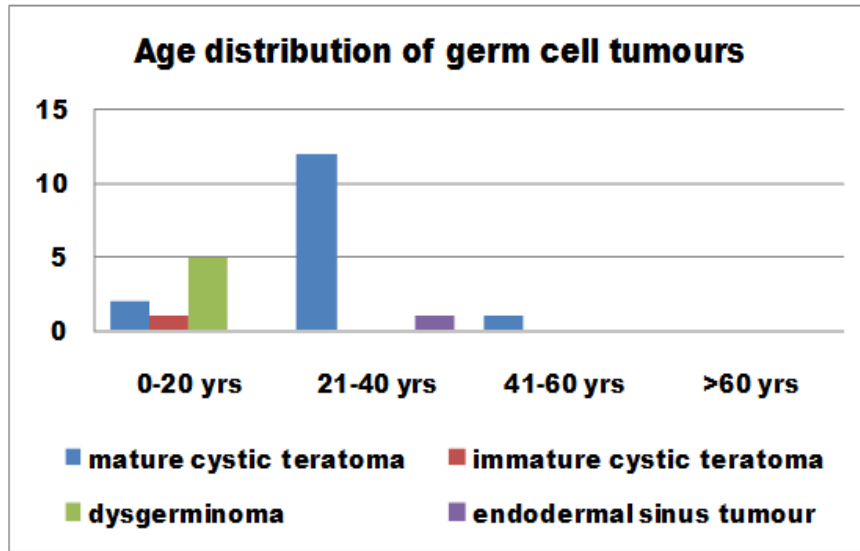


Table no. 5

	0-20 yrs	21-40 yrs	41-60 yrs	>60 yrs
Mature cystic teratoma	2	12	1	0
Immature cystic teratoma	1	0	0	0
Dysgerminoma	5	0	0	0
Endodermal sinus tumour	0	1	0	0

Fig. no.5 & table no. 5 shows mature cystic teratoma is the most common tumour in germ cell category (15 cases; 15/22; ~68%) mostly seen in the age group of 21-40 years. Most common malignant germ cell tumour is Dysgerminoma (5 cases ; 5/22; ~ 23%) all occurring in the age group of 0-20 years. In my study 1 case each of immature cystic teratoma and endodermal sinus tumour were found.

Fig no.- 6

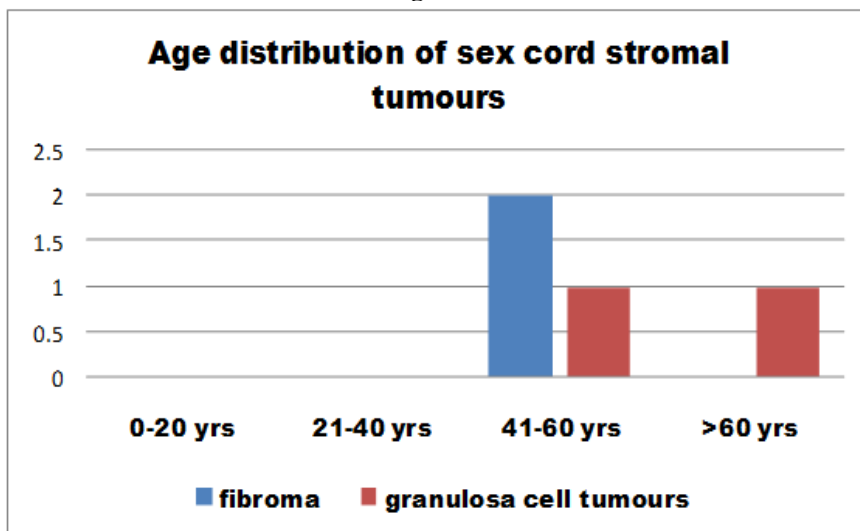


Table no. 6 : Age distribution of sex- cord stromal tumourrs

	0-20 yrs	21-40 yrs	41-60 yrs	>60 yrs
Fibroma	0	0	2	0
Granulosa cell tumour	0	0	1	1

Fig. no.6 & table no.6 shows 2 cases each of Fibroma and Granulosa cell were found. They were found in age group of 41-60 & >60 years.

Fig no. 7

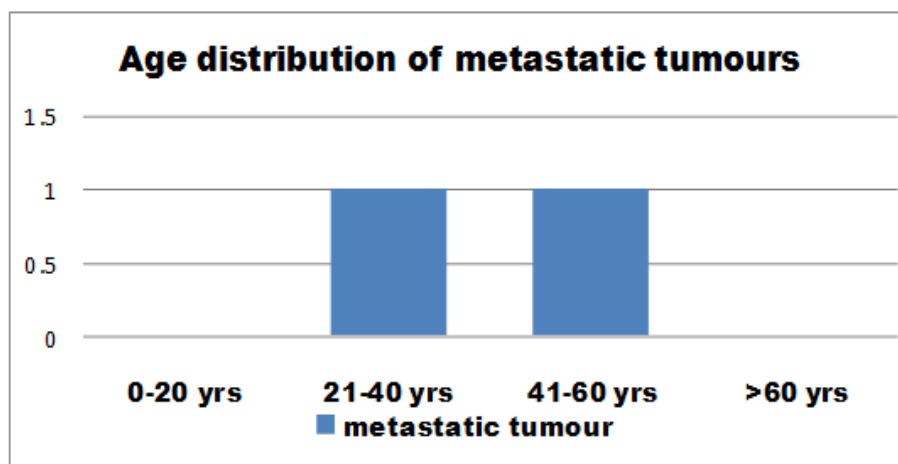


Table no . 7: Age distribution of metastatic tumours

	0-20 yrs	21-40 yrs	41-60 yrs	>60 yrs
Metastatic adenocarcinoma	0	1	1	0

Fig No. 7 & table no. 7 shows 2 cases of metastatic adenocarcinoma found occurring in the age group of 21-40 yrs, 41-60 yrs one in each group.

Table no. 8 Cytohistological correlation

Imprint intraoperative cytology	number	histopathology	Number
Epithelial tumours			
Benign			
Serous cystadenoma	26	Serous cystadenoma	24
		Borderline serous cystadenoma	2
Mucinous cystadenoma	18	Mucinous cystadenoma	18
Malignant			
Serous cystadenocarcinoma	20	Serous cystadenocarcinoma	17
		Borderline serous cystadenoma	3
Mucinous cystadenocarcinoma	8	Mucinous cystadenocarcinoma	6
	8	Borderline mucinous cystadenoma	2
Non epithelial tumours			
Benign			
Mature cystic teratoma	15	Mature cystic teratoma	15
Fibroma	2	Fibroma	2
Solid teratoma	1	Immature teratoma	1
Granulosa cell tumour	2	Granulosa cell tumour	2
Malignant			
Endodermal sinus tumour	1	Endodermal sinus tumour	1
Dysgerminoma	5	Dysgerminoma	5
Metastatic adenocarcinoma	2	Metastatic adenocarcinoma	2

Table no. 8 : shows cytohistological correlation of ovarian tumours. Considering hisopathology as agold standard in the diagnosis of ovarian tumours. It was observed that out of 100 cases, 92 cases were accurately diagnosed by imprint cytology. Overall diagnostic accuracy of the given study is 92%. Out of 64 benign cases as diagnosed by imprint cytology, 61 cases were concordant with histopathology and 3 cases were

discordant. The diagnostic accuracy of imprint cytology for benign tumours is (61/64; 95.31%) . out of 36 cases, 31 were concordant with histopathology and 5 cases were discordant. The diagnostic accuracy of imprint cytology for malignant tumours is(31/36; 86.1%).

Statistical Analysis

		HISTOPATHOLOGY	
		Benign	Malignant
IMPRINT CYTOLOGY	Benign	61(True Positive)	3(False Positive)
	Malignant	5(False Negative)	31(True Negative)

Sensitivity: true positive/(true positive+false negative) x 100: 92.42%

Specificity: true negative/(true negative+ false positive) x 100: 91.18%

Sensitivity and specificity of the present study is 92.42% and 91.18% respectively.

V. Discussion

Ovarian cancer is the second most common of all genital cancers and accounts for 10-15% of all gynaecological cancers in developing countries. About 80% of all ovarian tumours are benign and occurs mostly in young women between 25 and 40 years of age. The importance lies in distinguishing benign and malignant tumours of ovary in the reproductive age group where the conservation of other ovary is important. In the areas of the world where access to rapid histological diagnosis is limited or non-existent, intraoperative cytology is probably the only means of obtaining a rapid intraoperative diagnosis. Since the imprint technique is simple, rapid, cost effective it can be utilised to provide a rapid intraoperative diagnosis in set ups where frozen section facilities are not available. Advantages of cytological examination over frozen section is the avoidance of artifacts produced by freezing and sectioning techniques of frozen section resulting in good nuclear and cytoplasmic details. Mair et al(1990)[8] Geza et al (2002)[9]studies supported the same views. Imprint cytology has been widely used in intraoperative diagnosis of various tumours. But its use in intraoperative diagnosis in ovarian tumours has not been widely recognised. Relative incidence of ovarian tumours in various studies tabulated below

	Benign (%)	Malignant (%)	Borderline(%)
Ramchandran et al[10]	68.9		
Kar et al[11]	61.19	38.8	
Stewart et al[12]	56.2	35.1	8.7
Marinas et al[13]	57.7	34.6	7.7
Present study	61	32	7

In the present study , serous cystadenoma was the most common of all ovarian tumours(24%)similar incidence were reported by, Saxena et al(1980)[14], Verma et al(1981)[15], Kooning et al(1989)[16], Tyagi et al(1967)[17],Kar et al(2005). It was more common in age group 21-40 years. Benign mucinous tumours were predominant in age group 21-40 years. In the present study , 2 cases of serous cystadenoma and 3 cases of serous cystadenocarcinoma were later diagnosed as borderline serous tumour by histopathology. This was because of the evidence like: absence of complex branching, nuclear pleomorphism and hyperchromasia in imprint cytology, the overall morphology of cells closely resembles that of a benign serous tumour. And also , it was extremely difficult to separate epithelial tumours of low malignant potential from well differentiated carcinomas .Imprint cytology showed diagnostic accuracy of 100 %in germ cell tumours , sex cord stromal tumours and metastatic adenocarcinoma.

Diagnostic accuracy of imprint cytology in various studies is tabulated below.

	Diagnostic accuracy(%)
Suen KC et al (1978)[18]	93.8
Moran et al(1993)[19]	96.4
Kar et al (2005)	89.55
Mathur et al (2007)	90-95
Shalinee et al (2009)[20]	92
Stewart et al (2011)	97.8
Present study	92

Sensitivity & specificity of cytodiagnosis of ovarian tumours by various authors documented below

	Sensitivity	Specificity
Kjellgren et al (1971)[21]	90	85
Nandji et al(1979)[22]	96.4	92.9
Ganjei et al(1996)[23]	91.4	100

Roy et al(2003)[24]	75	100
Kar et al(2005)	93	92
Nazoora Khan et al (2009)[25]	94.2	100
Choudhury et al(2011)[26]	80	100
Present study	92.42	91.18

Majority of ovarian tumours seen in reproductive age group 21-40 years (48 cases) followed by 34 cases occurring in the age group 41-60 years. Overall sensitivity and specificity of the intraoperative imprint cytology was 92.42% and 91.18% respectively. In the present study, sensitivity and specificity of imprint cytology is similar. It was observed there is some drawback regarding imprint smears. They are not reliable for providing the depth of infiltration of the tumours. The inability to detect the non invasive growth and difficulties in distinguishing nuclear atypia seen in borderline malignancy from frank invasive carcinoma results in false positive carcinoma reporting. Thus this study has once again reflected that the role of histopathology for the diagnosis of ovarian tumours, as it is still the gold standard for the diagnosis of the ovarian tumours, but imprint cytology is a very important cost-effective tool for intraoperative diagnosis .

VI. Conclusion

Intraoperative cytology is extremely useful and provides a simple , rapid and inexpensive adjunctive technique for intraoperative consultation of ovarian lesion. It can act as a good complement to histopathology and can be of benefit for rapid preliminary diagnosis and surgical management planning especially in young women.

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Rapid Pap Kit



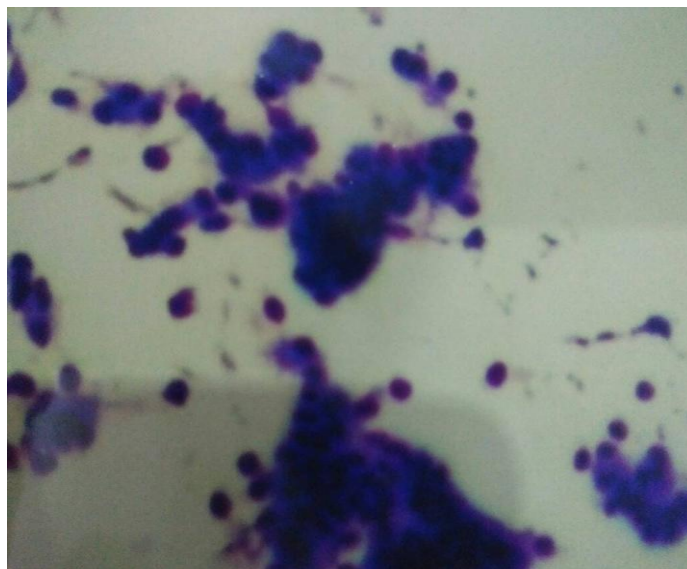
Technique Of Imprint Smear



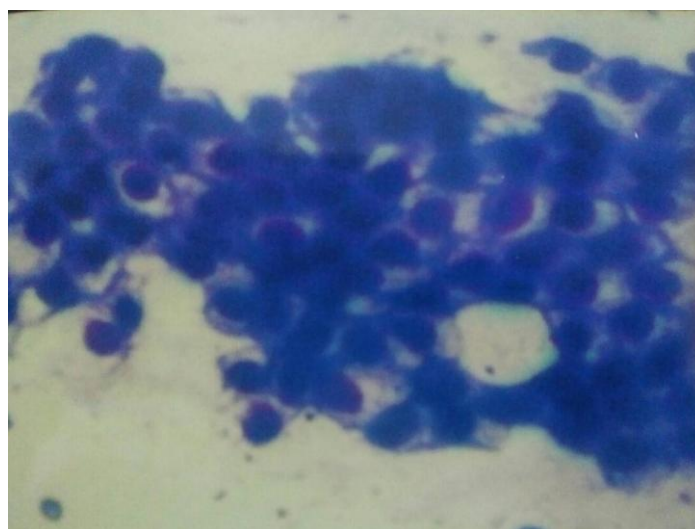
Big solid ovarian tumour during surgery



Bilateral Malignant Solid Ovarian Tumour



Touch Imprint Of Serous Cystadenoma



Touch Imprint Of Mucinous Cystadenoma