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Original Research Article

Comparison between imprint cytology and frozen sections in intraoperative consultation of ovarian tumours

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ABSTRACT

Background: The ovaries frequently are the site for various primary tumors. Correct intraoperative diagnosis is crucial. The application of imprint cytology is very useful where frozen section facility is not available. The present study is a comparison of imprint cytology and frozen section during intraoperative consultation for various types of benign and malignant ovarian neoplasms in different age groups.
Methods: Seventy-six cases of ovarian tumors were examined using both imprint cytology and frozen section and evaluated, taking histopathological report as gold standard. The histopathological diagnoses consisted of benign (54), borderline (9), and malignant (13). The malignant tumors consisted of various types including serous carcinoma, mucinous carcinoma, endometrioid carcinoma, clear cell carcinoma and carcinoid.
Results: All 54 benign cases were accurately diagnosed as benign by imprint cytology. With frozen section 53 cases were correctly diagnosed as benign but one case was over diagnosed as borderline. Among 13 malignant cases 11 (84.6%) were correctly diagnosed with both techniques. Borderline tumors were not able to be diagnosed with imprint smear, 3 out of 9 cases were correctly diagnosed with frozen section.
Conclusion: When compared with frozen section, imprint cytology is a simple, inexpensive and useful diagnostic tool in intraoperative diagnosis of benign and malignant ovarian tumors. Imprint smear is not useful in borderline tumors where only frozen section is useful. Imprint cytology can be used as an adjunct to frozen section for better diagnosis.

Keywords: Imprint cytology, Frozen section, Intraoperative consultation, Ovarian tumours

INTRODUCTION

A precise evaluation of the gross morphology along with tumor markers is important for the intraoperative consultation of ovarian tumours.[1] The histological diagnosis of frozen sections of large ovarian tumors is difficult because of the limited number of tumor samples studied. Using imprint cytology, samples are obtained from wide areas of tumors and is useful for the intraoperative consultation of ovarian tumors. Thus, the combined use of both imprint cytology and histological diagnosis of frozen sections gave an accuracy rate of 90% compared to 84% and 74% of either method used separately, and in a short time.[2] Cytological evaluation by imprint smears should be considered an important complementary tool to get a correct diagnosis during the intraoperative consultation.[3] In the present study, comparison of imprint cytology and frozen sections in the intraoperative consultation of ovarian tumors were performed using the final histopathology as gold standard and the useful aspects of cytology were clearly defined.

METHODS

Among the patients undergoing surgery for an ovarian tumor between July 2018 and December 2019, at, Believers Church Medical College and Hospital, Thiruvalla, Kerala. Samples from 76 patients, who had both imprint cytology and histological diagnoses of frozen sections were selected. Samples for imprint cytology were obtained from multiple areas of the ovarian mass presenting with different gross morphology of solid, cystic and necrotic areas. Papanicolaou staining was done for these samples. Samples for frozen sections were taken from a few areas of the tumors which are likely site of maximum disease and processed in a conventional manner to produce frozen sections, and the tissue sections were stained with haematoxylin-eosin (HE). Surgical resection tissues fixed in 10% formalin were routinely processed for light microscopy, and the histological diagnosis of the tissue sections was made by HE staining. The histological diagnosis of an ovarian tumour was established according to a newly published World Health Organization (WHO) classification.[4]

The histological diagnoses of the surgical resections were divided into a benign group (54 cases), a borderline group (9 cases), and a malignant group (13 cases). The benign group consisted of benign cyst with torsion (1 case), fibro-thecoma (2 cases), mucinous cystadenoma (15 cases), mature teratoma (3 cases), struma ovarii (3 cases), endometriotic cyst (11 cases), serous cystadenoma (13 case), and corpus luteal cyst (2 cases). The cases belonging to the malignant group were diagnosed as various types of carcinoma, including serous carcinoma (4 cases), mucinous carcinoma (3 cases), endometrioid carcinoma (3 cases), clear cell carcinoma (2 cases), and carcinoid well differentiated neuroendocrine tumor (1 case). Based on the histological diagnosis, the accuracy of intraoperative imprint cytology was evaluated, and the accuracy of imprint cytology and frozen sections was compared. The present study is a retrospective study. The operating gynecologist obtained written informed consent for performing the cytological and histological examinations from all patients. The informed consent form and procedures were approved by the Research ethics committee of Believer's Church Medical College Hospital.

Frequency, percentage, mean and standard deviation are calculated using Statistical Package for Social Sciences (SPSS) Version 21. Figures prepared using Microsoft PowerPoint. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy calculated manually.

RESULTS

From the 76 participant's samples studied, benignity was diagnosed entirely by imprint cytology and frozen tissue section. But one benign case was reported as borderline in frozen section. Age of the participants were ranging from 13 years to 86 years, with mean 51.18 and standard deviation 12.81. Among the 76, one was unmarried (13 years) who presented with torsion ovary with gangrene. The malignancy was diagnosed in 11 out of 13 cases by imprint cytology and frozen section. Endometrioid carcinoma was reported as endometriotic cyst in imprint cytology and as endometriosis tumor of low malignant potential in frozen due to stratification of lining epithelium and mild nuclear atypia. Rare case of malignant carcinoid well differentiated neuroendocrine tumor was reported as granulosa cell tumor in both imprint and frozen section (table 1). For the borderline group, the diagnostic accuracy of imprint cytology was zero (0/9) compared with that of frozen sections (3/9) (table 1). In the 4 cases with serous borderline tumors, an accurate diagnosis was not achieved by imprint cytology (table 2), with under-diagnoses in all 4 cases as benign. But with frozen section, 2 out of 4 was correctly diagnosed and 2 underdiagnosed. In 5 cases with mucinous borderline tumors, an accurate diagnosis was not achieved by imprint cytology (table 2), with under-diagnoses in all 5 cases as benign. But with frozen section, 1 out of 5 was correctly diagnosed and 4 under diagnosed as benign. The diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of imprint cytology verses frozen section, imprint cytology versus histopathology and frozen section versus histopathology are displayed in table 3. Concerning the diagnosis of the different types of carcinoma, serous carcinoma, mucinous carcinoma and clear cell carcinoma were diagnosed entirely with the same accuracy using imprint cytology and frozen sections. In endometrioid carcinoma, the diagnostic accuracy of imprint and frozen sections was same (2/3), it was reported as endometriotic cyst in imprint and endometriosis tumor of low malignant potential in frozen section. In one rare case of carcinoid, well differentiated neuroendocrine tumor it was wrongly diagnosed as granulosa cell tumor in both imprint and frozen section. For the overall accuracy of the diagnoses of the above-mentioned carcinomas by imprint cytology and frozen sections was almost same.

DISCUSSION

Imprint cytology in intraoperative consultation of ovarian epithelial tumors, Nagai et al. examined the imprint cytology of 354 specimens, and reported that the accuracy of intraoperative imprint cytology was 87.1% for benign, 30% for borderline, and 83.6% for malignant tumours.[5] Nagai et al reported that, imprint cytology was useful for the diagnosis of malignancy based on the operating characteristic curves. In a similar study by Khunamornpong et al., they examined the scrape cytology of 131 cases of ovarian tumors, and their accuracy was 95% for benign, 47% for borderline, and 98% for malignant tumours.[6] Toshiharu Matsumoto et al., examined 55 cases of ovarian tumors by both imprint and frozen section. Overall accuracy including benign, borderline, and malignant groups were 90.9% for imprint cytology and 96.3% for frozen section.[7] Our results are similar to the above-mentioned studies; benign lesions

were accurately diagnosed by imprint cytology and frozen sections in intraoperative consultation. Malignant lesions were diagnosed with same accuracy of 84.6% in both techniques. The intraoperative accuracy of the imprint cytology in diagnosing the borderline tumors were zero in our study, which is similar to other studies.

Table 1: Intraoperative accuracy of imprint cytology and frozen sections in 76 cases (benign, borderline and malignant tumours) diagnosed by surgical resection tissues.

Group (Number of cases)	Diagnosis of imprint cytology (Number of cases)	Histological diagnosis of frozen sections (Number of cases)
Benignity (54 cases)	Benignity (54 cases)	Benignity (53 cases)
		Borderline (1 case)
Borderline (9 cases)	Benignity (9 cases)	Benignity (6cases)
	Borderline (0 case)	Borderline (3cases)
Malignancy (13 cases)	Benignity (2 cases)	Benignity (1case)
	Malignancy (11cases)	Borderline (1case)
		Malignancy (11 cases)

Table 2: Comparison among diagnosis of intraoperative imprint cytology, intraoperative frozen sections, and surgical resection tissues in 76 cases of ovarian tumours.

Case No.	Diagnosis of imprint cytology	Histological diagnosis of frozen section	Histological diagnosis of surgical resections
B1	Benign cyst	Benign cyst with torsion	***Benign cyst with torsion***
			n, % (1, 1.3%)
B2	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B3	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B4	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B5	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B6	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B7	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B8	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B9	Benign Cystic lesion	Endometriotic cyst	Endometriotic cyst
B10	Haemorrhagic benign cyst	Endometriotic cyst	Endometriotic cyst
B11	Haemorrhagic benign cyst	Endometriotic cyst	Endometriotic cyst
B12	Haemorrhagic benign cyst	Endometriotic cyst	***Endometriotic cyst***
			n, % (11,14.47%)
B13	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B14	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B15	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B16	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B17	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B18	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B19	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B20	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B21	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
Case No.	**Diagnosis of imprint cytology**	**Histological diagnosis of frozen section**	**Histological diagnosis of surgical resections**
B22	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B23	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B24	Benign serous cyst	Serous cystadenoma	Serous cystadenoma
B25	Benign serous cyst	Serous cystadenoma	***Serous cystadenoma***
			n, % (13,17.10%)
B26	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B27	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B28	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B29	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma

Continued.

Case No.	Diagnosis of imprint cytology	Histological diagnosis of frozen section	Histological diagnosis of surgical resections
B30	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B31	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B32	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B33	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B34	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B35	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B36	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B37	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B38	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B39	Mucinous cystadenoma	Mucinous cystadenoma	Mucinous cystadenoma
B40	Mucinous cystadenoma	Mucinous cystadenoma	***Mucinous cystadenoma***
			n, % (15,19.73%)
B41	Corpusluteal cyst	Corpusluteal cyst	Corpusluteal cyst
B42	Corpusluteal cyst	Corpusluteal cyst	***Corpusluteal cyst***
			n, % (2,2.6%)
B43	Benign serous tumor	Serous cystadenofibroma	Serous cystadenofibroma
B44	Benign serous tumor	Serous cystadenofibroma	Serous cystadenofibroma
B45	Benign serous tumor	Serous cystadenofibroma	Serous cystadenofibroma
B46	Benign serous tumor	Serous cystadenofibroma	***Serous cystadenofibroma***
			n, % (4,5.26%)
B47	Teratoma	Teratoma	Mature cystic teratoma
B48	Teratoma	Teratoma	Mature cystic teratoma
B49	Teratoma	Teratoma	***Mature cystic teratoma***
			n, % (3,3.9%)
B50	Teratoma	Teratoma with hemorrhage	Struma ovarii
B51	teratoma	teratoma	Struma ovarii
B52	teratoma	Teratoma with thyroid tissue	***Struma ovarii***
			n, % (3,3.9%)
B53	Fibroma	Fibroma	Fibrothecoma
B54	Fibroma	Fibroma	***Fibrothecoma***
			n, % (2,2.6%)
BOR1	Benign mucinous	Borderline Mucinous	Mucinous borderline tumour
BOR2	Benign mucinous	Benign mucinous	Mucinous borderline tumour
Case No.	**Diagnosis of imprint cytology**	**Histological diagnosis of frozen section**	**Histological diagnosis of surgical resections**
BOR3	Benign mucinous	Benign mucinous	Mucinous borderline tumour
BOR4	Benign mucinous	Benign mucinous	Mucinous borderline tumour
BOR5	Benign mucinous	Benign mucinous	***Mucinous borderline tumour***
			n, % (5,6.57%)
BOR6	Benign serous cyst	Borderline serous cyst	Serous borderline tumour
BOR7	Benign serous cyst	Borderline serous cyst	Serous borderline tumour
BOR8	Benign serous cyst	Benign serous cyst	Serous borderline tumour
BOR9	Benign serous cyst	Benign serous cyst	***Serous borderline tumour***
			n, % (4,5.26%)
M1	Endometriotic cyst	Endometriosis tumour of low malignant potential	Endometrioid carcinoma
M2	adenocarcinoma	adenocarcinoma	Endometrioid carcinoma
M3	adenocarcinoma	adenocarcinoma	***Endometrioid carcinoma***
			n, % (3,3.9%)
M4	Serous carcinoma	Serous carcinoma	Serous carcinoma
M5	Serous carcinoma	Serous carcinoma	Serous carcinoma
M6	Serous carcinoma	Serous carcinoma	Serous carcinoma
M7	Serous carcinoma	Serous carcinoma	***Serous carcinoma***
			n, % (4,5.26%)
M8	Mucinous carcinoma	Mucinous carcinoma	Mucinous carcinoma
M9	Mucinous carcinoma	Mucinous carcinoma	Mucinous carcinoma

Continued.

Case No.	Diagnosis of imprint cytology	Histological diagnosis of frozen section	Histological diagnosis of surgical resections
M10	mucinous carcinoma	Mucinous carcinoma	***Mucinous carcinoma***
			n, % (3,3.9%)
M11	Clear cell carcinoma	Malignant epithelial neoplasm	Clear cell carcinoma
M12	Clear cell carcinoma	Malignant epithelial neoplasm	***Clear cell carcinoma***
			n, % (2,2.6%)
M13	Granulosa cell tumour	Granulosa cell tumour	***Carcinoid, well differentiated neuroendocrine tumour***
			n, % (1,1.3%)

Table 3: Sensitivity, Specificity, positive predictive value (PPV), negative predictive value and diagnostics accuracy.

	Benign	Borderline	Malignant
Imprint versus frozen			
Sensitivity	100	0	100
Specificity	64.7	100	100
PPV	90.5	UD	100
NPV	100	91.9	100
Diagnostic accuracy	91.9	91.9	100
Imprint versus histopathology			
Sensitivity	100	0	84.6
Specificity	50	100	100
PPV	82.5	UD	100
NPV	100	87.8	96.8
Diagnostic accuracy	85.1	87.8	97.3
Frozen versus histopathology			
Sensitivity	98.1	33.33	84.6
Specificity	72.7	95.5	100
PPV	89.8	50	100
NPV	94.1	91.4	96.9
Diagnostic accuracy	90.8	88.2	97.4

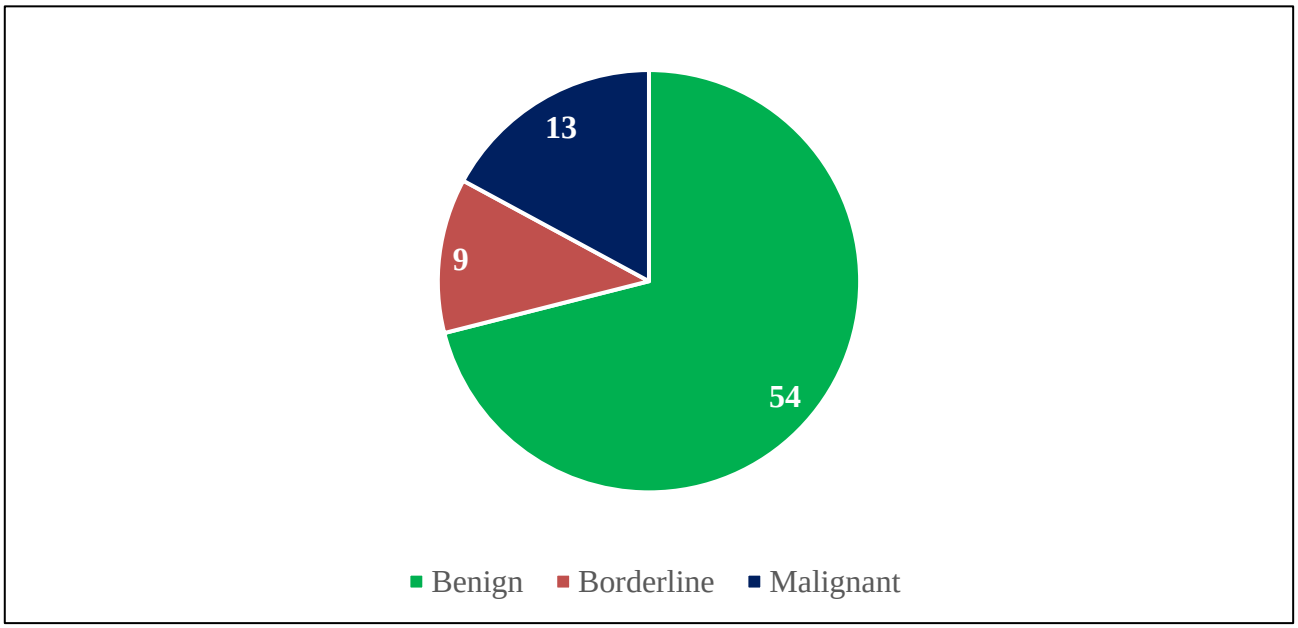

Figure 1: Distribution of cases according to histopathology using pie chart.

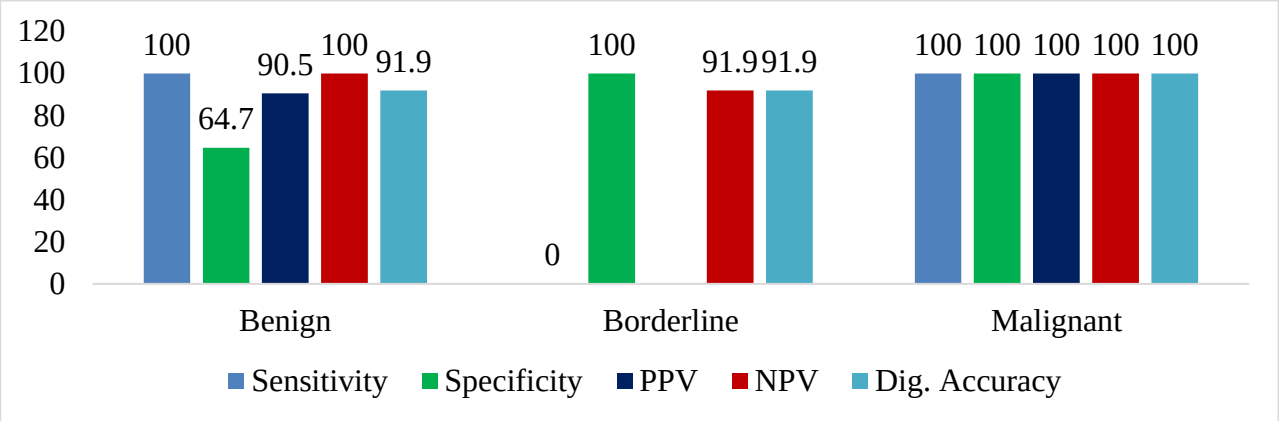

Figure 2: Sensitivity, Specificity, positive predictive value (PPV), negative predictive value and diagnostics accuracy (Imprint Versus Frozen).

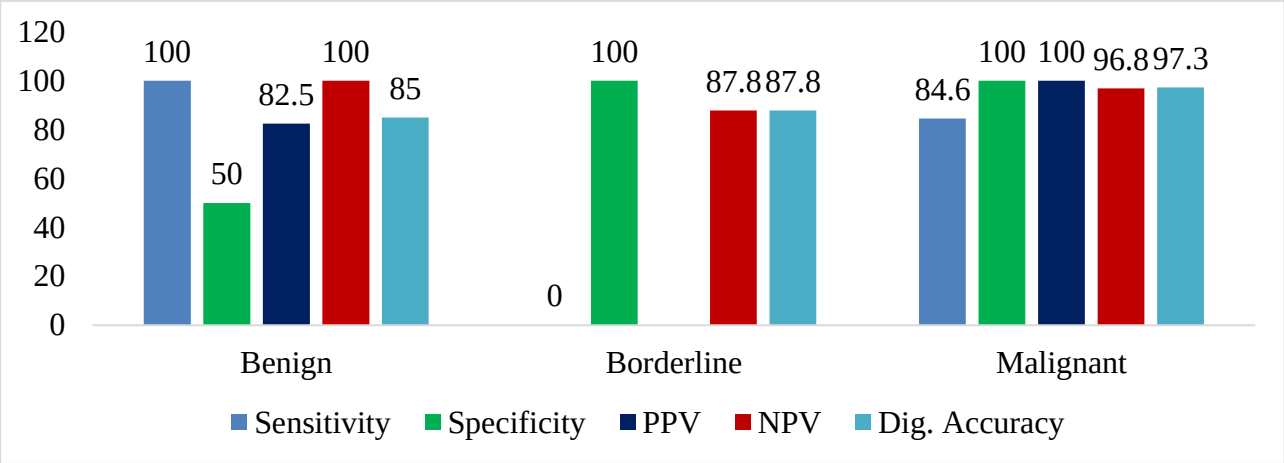

Figure 2: Sensitivity, Specificity, positive predictive value (PPV), negative predictive value and diagnostics accuracy (Imprint Versus Histopathology).

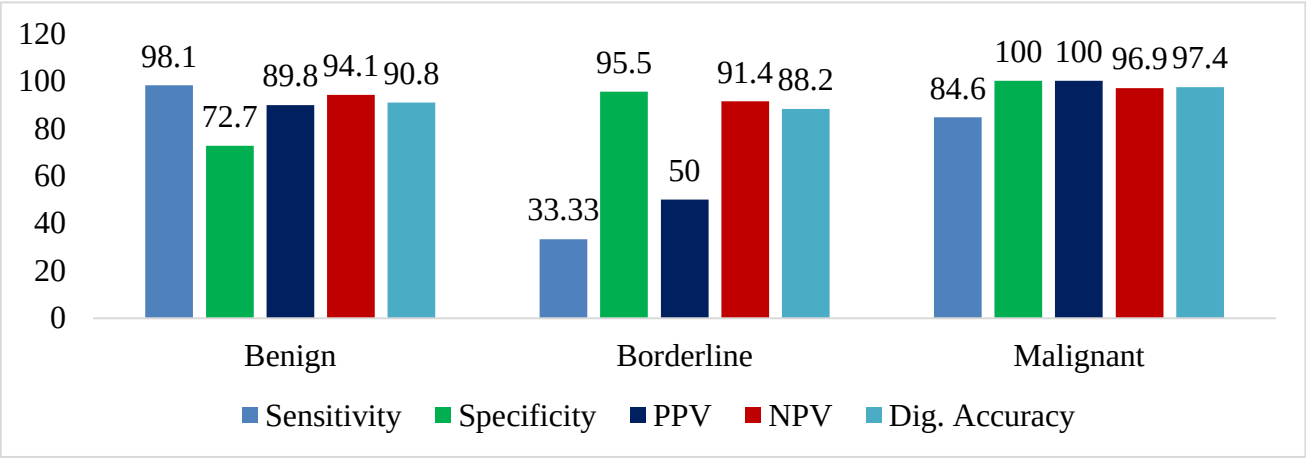

Figure 3: Sensitivity, Specificity, positive predictive value (PPV), negative predictive value and diagnostics accuracy (Frozen Versus Histopathology).

Kushima et al suggested that borderline tumors could be more accurately diagnosed by intraoperative cytology when the borderline areas are a main component of the tumor. Due to the admixture of benign and borderline areas in the tumor, and the evaluation of stromal invasion not possible by cytology, the intraoperative diagnosis of borderline tumors by cytology is difficult.[7] A comparative study of intraoperative cytology and frozen sections was

performed by Michael et al. in 63 cases and reported that cytology was slightly better than frozen sections.[8] But in our present study, the histological diagnosis of frozen sections was slightly better than that of cytology similar to the study by Toshiharu et al. Michael et al. used different methods to obtain cytological materials. He used a combination of imprint cytology, fine-needle aspiration cytology, and scrapes to get adequate material for cytology. FNAC and scrapes are superior to imprints in cytological study, and this may have led to their conclusion that cytology was better than frozen sections. The comparison of intraoperative cytology and frozen sections in our study indicates that imprint cytology is similar to the frozen sections in diagnosing the histological types of carcinoma, such as clear cell carcinoma, serous carcinoma and mucinous carcinoma. Overall, nearly 85% of malignant ovarian tumors are epithelial, which contributes to the superiority of imprint cytology for the diagnosis of these tumors especially in poor resource settings.

CONCLUSION

When compared with frozen section, Imprint cytology is a simple, inexpensive and useful diagnostic tool in intraoperative diagnosis of benign and malignant ovarian tumors. Imprint smear is not useful in borderline tumors where only frozen section is useful. Imprint cytology can be used as an adjunct to frozen section for better diagnosis.

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