Comparing Conventional Cytology Smear and Cell Block Techniques for Ovarian Cancer Diagnosis: A Prospective Observational Study

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ABSTRACT

Introduction: The cytological examination of ascitic fluid is widely recognised and well-documented for its importance in staging and prognosis of malignancy, and for providing information about inflammatory lesions. The Cell Block (CB) method offers improved architectural patterns and morphological features, aiding in the differentiation between reactive mesothelial cells and malignant cells, thus enhancing the efficacy of cyst diagnosis. Additionally, the CB technique finds applications in molecular biology and immunocytochemistry, making it advantageous for targeted therapy due to its ability to preserve cytological material.

Aim: To compare the accuracy of conventional cytology smear technique and CB from ascitic fluid with histopathology for diagnosing ovarian tumours.

Materials and Methods: A cross-sectional study was conducted in the Department of Pathology at Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India. A total of 45 patients with suspected ovarian tumours or presence of ascites were included. Biopsy samples were sent to the pathology laboratory for histological evaluation, while study samples were collected from the Department of Pathology between January 2021 and December 2022. Sample processing techniques, such as conventional cytology {including cytocentrifugation before Giemsa, Pap, and Haematoxylin and Eosin (H&E) staining} and thromboplastin-plasma technique for CB preparation, were employed. Evaluation parameters included comparing morphological features of frequently stained cytology smears and CB technique of ascitic fluid, along with their concordance with histopathological diagnosis. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) program for Windows, version 28.0.

Results: Among 45 patients, majority 24 (53.40%) of them belonged to 41-60 years of age group. It was noted that 24 (53.40%) patients had ascites, 11 patients (24.40%) had abdominal pain with ascites, and 10 (22.20%) had ovarian mass with ascites. Conventional cytology smear diagnoses revealed that 22 (48.9%) patients had infiltrates of serous cystadenocarcinoma. A significant correlation was found between the findings of the CB and Conventional Smear (CS) (p=0.0001), with a sensitivity of 94.12%, specificity of 100%, Positive Predictive Value (PPV) of 100%, Negative Predictive Value (NPV) of 85.71%, and a diagnostic accuracy of 95.65% for CB correlating with CS.

Conclusion: A combined strategy utilising stained cytology smears and the CB technique of ascitic fluid could be considered in the diagnostic approach for malignant ovarian tumours.

Keywords: Cystadenocarcinoma, Inflammatory lesions, Ovarian tumours, Serum-ascites-albumin gradient

INTRODUCTION

Ascites is a condition in which a large amount of fluid collects in the peritoneal cavity. Breast cancer, gastrointestinal malignancies, and gynaecological neoplasms (mainly ovarian and endometrial cancer) are the most frequent causes of malignant ascites. The most typical sign of ovarian cancer, which manifests at an advanced stage and has a dismal prognosis, is ascites [1,2]. Transudate fluid is created as a result of changes in hydrostatic pressure, while 90% of the ascitic fluids are transudates brought on by benign diseases such as congestive heart failure or liver cirrhosis. In contrast, exudate is a bodily fluid that ages out or is discharged from the tissue during inflamation and these are typically malignant (ovarian cancer) and have a cloudier fluid appearance than transudates, a higher cellular count, and a higher albumin level [3].

This differentiation is enhanced by the Serum-ascites albumin Gradient (SAAG). If the SAAG is >1.1, the values indicate a transudate caused by portal hypertension, cirrhosis, hepatic congestion, portal vein thrombosis, etc. If the SAAG is <1.1, the exudate is most likely of malignant etiology or caused by an infectious process in the peritoneum, nephrotic syndrome, and hypoalbuminemia from malnutrition. The pathogenesis of malignant ascites is assured to be multifactorial, with increased vascular permeability, lymphatic drainage obstruction, increased difference in hydraulic pressure, and reduced difference in oncotic pressure being the most important pathogenetic mechanisms [4]. The CB method can aid in diagnosing malignancies, staging lesions, and determining prognosis.

Ascites was detected as a sign of malignancy in 54% of the patients with peritoneal carcinomatosis [5]. The most significant pathogenetic processes for malignant ascites are increased vascular permeability, lymphatic drainage obstruction, an increase in the difference in hydrostatic pressure, and a decrease in the difference in oncotic pressure [6]. The presence of malignant ascites in secondary malignancies is a worse prognostic marker compared to ovarian carcinoma, and the survival period from the moment of detection is 7-13 weeks [7,8]. The CB method can aid in diagnosing malignancies, staging lesions, and determining prognosis. Cellular overlapping, delaying artifacts, suboptimal processing, preparative cut technique, and leaving behind useful material can lower the diagnostic yield in the Conventional Smear (CS) method. The residual material can be very useful in increasing the diagnostic yield with the CB method. This CB technique increases the sensitivity of detecting malignancies and can reduce false-positive interpretations. A recent method of CB preparation using a 10% alcohol-formalin combination as a fixative has shown to increase the cellularity and morphological details of cells.

It is a simple, reproducible, and cost-effective method that requires no extra material compared to other methods [9,10]. Despite numerous studies conducted worldwide involving a large number of patients with ovarian cancer, malignancy was not diagnosed by ascitic cytology in many cases [1,11]. Hence, the aim of the current study was to compare the accuracy of the conventional cytology smear technique and the CB method from ascitic fluid with histopathology for the diagnosis of ovarian tumours.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Pathology at Jawaharlal Nehru Medical College (JNMC), Wardha, Maharashtra, India, between January 2021 and December 2022. Informed consent was obtained from all patients before enrolling in the study. The study was approved by the Institutional Review Board and the Ethics Committee of DMIHER with reference number DMIMS (DU)/2020-21/9273.

Inclusion criteria: A total of 45 patients, who visited JNMC and were patients suspected of ovarian tumours or ascites based on clinical examination and ultrasonography were included in the study.

Exclusion criteria: All ovarian conditions with non neoplastic ovarian pathology were excluded from the study.

Sample size calculation: The sample size was calculated using the formula with a desired error margin. The formula used was:

$$n = \frac{\left(\frac{Zx}{2^2} * p(1-p)\right)}{d^2}$$

Where,

 $Z\alpha/2$ is the level of significance at 5% i.e., 95%

Confidence interval=1.96

p=Prevalence of ovarian cancer in Wardha district [12]

=4.4%=0.044

d=Desired error of margin is=6%=0.06

n=(1.962*0.044*(1-0.044))/(0.062)

n=44.88

=45 patients needed in the study

Study Procedure

Cytology smear technique: Sample processing techniques such as conventional cytology, which involved cytocentrifugation of the material before Giemsa, Pap, and H&E staining.

Cell Block (CB) method: The thromboplastin-plasma technique for CB was used. The obtained sample underwent centrifugation, and the supernatant was discarded. Two drops of plasma were added to the sediment and thoroughly mixed. Then, four drops of thromboplastin were added, and the mixture was stirred. The mixture was allowed to form a clot and settle for five minutes, after which the clot was transferred to a filter paper soaked in formalin fixative. The sediment was placed onto a labeled tissue cassette after carefully wrapping it in filter paper.

Histopathology: The biopsy samples of patients suspected of ovarian cancer and ascites were sent to the pathology laboratory for histological findings. A tissue biopsy using the standard methods for histopathology was processed, and a five-micron section of CB was obtained and stained with an H&E stain. The SAAG system was followed for ascites classification [13].

All females of all age groups who were admitted to JNMC during the thesis period and were suspected cases of ovarian tumour and ascites based on clinical examination and ultrasonography were included in the study. All ovarian conditions with non-neoplastic ovarian pathology were excluded from the study.

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS programme for windows, version 28.0 (SPSS, Chicago, Illinois). Continuous

variables were presented as mean±SD, and categorical variables were presented as absolute numbers and percentages. Categorical variables were analysed using either the Chi-square test. The sensitivity, specificity, PPV, and NPV were calculated for conventional cytology smear comparing with the CB technique of ascitic fluid in the diagnosis of ovarian tumours. A p-value less than 0.05 was considered to indicate a significant difference.

RESULTS

Out of 45 patients, it was observed that 06 patients (13.30%) were in the age range between 20-40 years, while 24 patients (53.40%) were in the age range between 41-60 years, and 15 patients (33.30%) were >60 years with a mean age of 53.66 ± 14.15 [Table/Fig-1].

Age group (in years)	Frequency (n)	Percentage (%)	
20-40	06	13.3	
41-60	24	53.4	
>60	15	33.3	
Total	45	100	
Mean±SD	53.66±14.15		
Min-Max	20-83 years		
Median (IQR)	45-65 years		
[Table/Fig-1]: Distribution of patients according to age groups.			

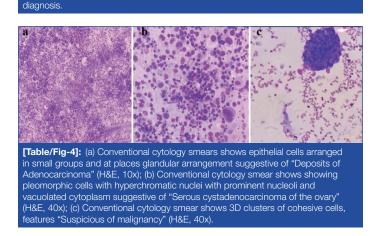
According to the clinical diagnosis, it was observed that 24 (53.40%) patients had ascites, 11 (24.40%) patients had abdominal pain with ascites, and 10 (22.20%) patients had ovarian mass with ascites [Table/Fig-2].

Clinical diagnosis	Frequency (n)	Percentage (%)	
Ascites	24	53.4	
Pain in the abdomen with ascites	11	24.4	
Ovarian mass with ascites 10 22.2			
Total	45	100	
[Table/Fig-2]: Distribution of patients according to the clinical diagnosis.			

According to the distribution of patients according to the conventional cytology smear diagnosis [Table/Fig-3] and representative images of conventional cytology smears [Table/Fig-4a-c], it was observed that 22 (48.9%) patients had infiltrates of serous cystadenocarcinoma, 5 (11.1%) patients had deposits (infiltrates) of epithelial malignancy, 4 (8.9%) had suspicion of malignancy, 3 (6.7%) patients each had serous cystadenoma, 4 (4.5%) patients each had a scant sample to comment upon and mucinous adenoma, 7 (2.2%) patients each had infiltrates of carcinoma cell with follicular features, infiltrates of mucinous cystadenocarcinoma with changes of pseudomyxoma peritonei, infiltrates of signet cell carcinoma, mucinous adenocarcinoma, infiltrates of adenocarcinoma, serous effusion material, and serous fluid with mesothelial cell reaction.

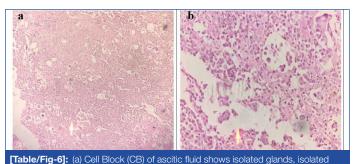
Conventional cytology smear diagnosis	Frequency (n)	Percentage (%)
Infiltrates of serous cystadenocarcinoma	22	48.9
Deposits (infiltrates) of epithelial malignancy	5	11.1
Suspicious of malignancy	4	8.9
Serous cystadenoma	3	6.7
Scant sample to comment upon	2	4.5
Mucinous adenoma	2	4.5
Infiltration of carcinoma cells with follicular features	1	2.2
Infiltrates of mucinous cystadenocarcinoma with changes of pseudomyxoma peritonei	1	2.2
Infiltrates of signet cell carcinoma	1	2.2
Mucinous adenocarcinoma	1	2.2
Infiltrates of adenocarcinoma	1	2.2

Serous effusion material	1	2.2	
Serous fluid with mesothelial cell reaction	1	2.2	
[Table/Fig-3]: Distribution of patients according to the conventional cytology smear			



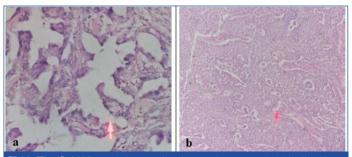
The distribution of patients according to the CB diagnosis [Table/ Fig-5] and representative images of the CB technique shows features of ovarian cancer [Table/Fig-6a,b]. Data analysis showed that 30 (66.7%) patients had serous adenocarcinoma, 9 (6.7%) patients each had mucinous adenocarcinoma, carcinoma of the ovary, and serous adenoma, 4 (4.4%) patients each had adenocarcinoma and mucinous adenoma, 2 (2.2%) patients each had a benign tumour of the ovary and mesothelial cell reaction. [Table/Fig-7] shows the distribution of patients according to the histopathological diagnosis. It was observed that 7 (15.6%) patients had serous papillary cystadenocarcinoma of the ovary [Table/Fig-8a], 5 (11.1%) patients had papillary adenocarcinoma of the ovary, 4 (4.5%) patients each had mucinous cystadenocarcinoma of the ovary and serous cystadenofibroma of the ovary, 6 (2.2%) patients each had carcinosarcoma of the left ovary, epithelial tumour of the ovary (borderline mucinous intestinal type), granulosa cell tumour of the right ovary [Table/Fig-8b], Malignant Brenner's tumour, papillary serous cystadenocarcinoma (left side of the ovary) with mixed epithelial cell tumour (right adnexal mass), and serous borderline tumour of the left ovary. Meanwhile, 23 (51.1%) histopathology samples were not available for examination.

Cell Block (CB) diagnosis	Frequency (n)	Percentage (%)
Serous adenocarcinoma	30	66.7
Mucinous adenocarcinoma	3	6.7
Carcinoma of ovary	3	6.7
Serous adenoma	3	6.7
Adenocarcinoma	2	4.4
Mucinous adenoma	2	4.4
Benign tumour of the ovary	1	2.2
Mesothelial cell reaction	1	2.2
[Table/Fig-5]: Distribution of patients according to the Cell Block (CB) diagnosis.		



cells, and rare small sheets of glandular epithelial cells suggestive of "Infiltrates of serous adenocarcinoma" (H&E, 10x); (b) CB of ascitic fluid shows isolated glands, isolated cells, and rare small sheets of glandular epithelial cells suggestive of "Infiltrates of serous adenocarcinoma" (H&E, 40x).

Histopathological diagnosis	Frequency (n)	Percentage (%)
Serous papillary cystadenocarcinoma of the ovary	7	15.6
Papillary adenocarcinoma of the ovary	5	11.1
Mucinous cystadenocarcinoma of the ovary	2	4.5
Serous cystadenofibroma of the ovary	2	4.5
Carcinosarcoma of the left ovary	1	2.2
Epithelial tumour of the ovary (borderline mucinous intestinal type)	1	2.2
Granulosa cell tumour of right the ovary	1	2.2
Malignant Brenner's tumour	1	2.2
Papillary serous cystadenocarcinoma (left-side of the ovary), mixed epithelial cell tumour (right adnexal mass)	1	2.2
Serous borderline tumour of left the ovary	1	2.2
Not available	23	51.1
[Table/Fig-7]: Distribution of patients according to the histopathological diagnosis.		



[Table/Fig-8]: (a) Histopathology section shows columnar to cuboidal cells with moderate cytoplasm and enlarged nucleus and prominent nucleoli suggestive of "Serous Papillary Cystadenocarcinoma of the ovary" (under 40x); (b) Histopathology section shows cells arranged in a diffused pattern suggestive of a "Granulosa Cell Tumour" (under 10x).

[Table/Fig-9] demonstrates the concordance between conventional cytology smear diagnosis and histopathological diagnosis of the patients. It was observed that there was a non-significant concordance between the findings of conventional cytology smear and histopathological diagnosis (p=0.63), and the cases were classified as follows: True positive (a)=18, False positive (b)=02, False negative (c)=02, True negative (d)=00. Due to the lack of available samples for histopathology, true negative cases could not be determined.

	Histopathological diagnosis			
	Malignant	Benign		
Conventional smear diagnosis	n (%)	n (%)	p-value	
Malignant	18 (90)	02 (100)		
Benign	02 (10)	0	0.22 p=0.63, NS	
Total	20 (100)	02 (100)		
Sensitivity; value (95% Cl): 90.00% (68.30% to 98.77%)				
Specificity; value (95% Cl): 0.00% (0.00% to 84.19%)				
Positive likelihood ratio; value (95% Cl): 0.90 (0.78 to 1.04)				
Negative likelihood ratio				
Disease prevalence (*); value (95% Cl): 00.91% (70.84% to 98.88%)				
Positive predictive value (*); value (*	Positive predictive value (*); value (95% Cl): 90.00% (68.30% to 98.77%)			
Negative predictive value (*); value (95% Cl): 0% (0% to 84.19%)				
Accuracy (*); value (95% Cl): 81.82% (59.72% to 94.81%)				
[Table/Fig-9]: Concordance between Conventional Smear (CS) diagnosis and histopathological diagnosis. NS: Non significant				

[Table/Fig-10] shows the association between CB and conventional cytology smear diagnosis of the patients. It was observed that there was a significant relation between the findings of CB and CS (p=0.0001), with sensitivity of 94.12%, specificity of 100%, PPV

100%, NPV 85.71%, and diagnostic accuracy of CB correlating with CS was 95.65%. [Table/Fig-11] shows the association between CB diagnosis and histopathological diagnosis of the patients. It was observed that there was a non-significant association between the findings of CB diagnosis and histopathological diagnosis, and the cases were classified as follows: true positive (a)=19, false positive (b)=02, false negative (c)=01, true negative (d)=0.

	Cell Block (CB)		
Conventional	Malignant	Benign	
smear	n (%)	n (%)	p-value
Malignant	16 (a) (94.12)	0 (b) (0)	
Benign	01 (c) (5.88)	06 (d) (100)	18.55 p=0.0001, S
Total	17 (100)	06 (100)	P
Sensitivity; value (95% Cl): 94.12% (71.31% to 99.85%)			
Specificity; value (95% Cl): 100.00% (54.07% to 100.00%)			
Positive likelihood ratio			
Negative likelihood ratio; value (95% Cl): 0.06 (0.01 to 0.39)			
Disease prevalence (*); value (95% Cl): 73.91% (51.59% to 89.77%)			
Positive predictive value (*); value (95% Cl): 100.00% (79.41% to 100.00%)			
Negative predictive value (*); value (95% Cl): 85.71% (42.13% to 99.64%)			
Accuracy (*); Value (95% Cl): 95.65% (78.05% to 99.89%)			
[Table/Fig-10]: Concordance between Cell Block (CB) and Conventional Smear (CS) diagnosis.			

True positive (a), False positive (b), False negative (c), True negative (d). S: Significant

	Histopathological diagnosis		
	Malignant	Benign	
Cell Block (CB) diagnosis	n (%)	n (%)	
Malignant	19 (94.4)	2 (100)	
Benign	01 (5.6)	0	
Total	20 (100)	2 (100)	
Sensitivity; value (95% Cl): 95.00% (75.13% to 99.87%)			
Specificity; value (95% Cl): 0% (0% to 84.19%)			
Positive likelihood ratio; value (95% Cl): 0.95 (0.86 to 1.05)			
Negative likelihood ratio			
Disease prevalence (*); value (95% Cl): 90.91% (70.84% to 98.88%)			
Positive predictive value (*); value (95% Cl): 90.48% (69.62% to 98.83%)			
Negative predictive value (*); value (95% Cl): 0% (0% to 97.50%)			
Accuracy (*); value (95% Cl): 86.36% (65.09% to 97.09%)			
[Table/Fig-11]: Concordance between Cell Block (CB) and histopathological diagnosis.			

Two cases diagnosed as benign tumours on CS, i.e., serous effusion material and scant sample to comment upon, were found to be malignant tumours on histopathology and diagnosed as mucinous cystadenocarcinoma of the ovary and papillary adenocarcinoma of the ovary, respectively. The reason for the false negative cases on CS was the scant amount of samples, which did not allow examination of representative areas. Two cases were diagnosed as malignant tumours on CS, as infiltrates of epithelial malignancy and infiltrates of serous cystadenocarcinoma, were found to be benign tumours on histopathology and diagnosed as serous cystadenofibroma. The reason for the false positive cases on CS was the misinterpretation of nuclear atypia of mesothelial cells as malignant and loosely adhesive cells as a three-dimensional cell cluster.

DISCUSSION

Ovarian carcinoma patients represents ascites as the typical presentation. Cytological examination of serous fluids can provide insight into early understanding of cancer aetiology. Two methods commonly used for cytological analysis are the CB method and the CS. Due to the lack of literature among the Indian population, we conducted a prospective study titled "Cyto-diagnosis of

ascitic fluid in ovarian tumours: A combined approach of routinely stained cytology smears and CB technique with histopathological correlation." The study was conducted at the Department of Pathology, JNMC, for two years, and a total of 45 patients were enrolled based on defined inclusion and exclusion criteria.

According to the conventional cytology smear diagnosis, patients were examined and distributed. It was observed that 48.9% of the patients had infiltrates of serous cystadenocarcinoma, 11.1% had deposits (infiltrates) of epithelial malignancy, 8.9% had a suspicion of malignancy, 6.7% of patients had serous cystadenoma, 4.5% of patients had a scant sample to comment upon along with mucinous adenoma, 2.2% of patients had infiltrates of carcinoma cells with follicular features, infiltrates of mucinous cystadenocarcinoma with changes of pseudomyxoma peritonitis, infiltrates of signet cell carcinoma, mucinous adenocarcinoma infiltrates, adenocarcinoma, serous effusion material, and serous fluid with mesothelial cell reaction. Further examination of patients was performed according to the conventional cytology smear. It was observed that a major proportion (80%) of the patients had malignant tumours, while only 20% of the patients had benign tumours. Patients were distributed based on age into three groups: 20-40 years, 41-60 years, and >60 years of age. Similar to observation of the present study, Udasimath S et al., found that the most commonly affected patients were from the 51-60 years age group and also reported a 13.63% higher detection of malignancy with the CB technique compared to the CS method [14]. In contrast, Dey S et al., observed a maximum proportion of patients in the age group of 61-70 years and reported a sensitivity and specificity of 88.88% and 86.98%, respectively, for CB compared to CS. They concluded that CB produced significantly better results (p=0.0271) in detecting malignant lesions [15].

On the diagnosis of CB, patients were further distributed. It was observed that 66.7% of the patients had serous adenocarcinoma, 6.7% of the patients each had mucinous adenocarcinoma, carcinoma of the ovary, and serous adenoma, 4.4% of the patients each had adenocarcinoma and mucinous adenoma, and 2.2% of the patients each had a benign tumour of the ovary and mesothelial cell reaction. In a recent study by Maseki Z et al., the histologic type determined by further biopsies, surgeries, and autopsies was correctly identified using the CB technique, which was consistent with the clinical and ultimate pathologic diagnosis. The sensitivity and specificity of the cellblock technique were 88.88% and 86.98%, respectively. They concluded that the CB approach greatly improved the identification of malignant lesions [16].

Patients distribution was performed based on the histopatholocial examination. It was observed that 15.6% of the patients had serous papillary cystadenocarcinoma of the ovary, 11.1% had papillary adenocarcinoma of the ovary, 4.5% each had mucinous cystadenocarcinoma of the ovary and serous cystadenofibroma of the ovary, 2.2% each had carcinosarcoma of the left ovary, epithelial tumour of the ovary (borderline mucinous intestinal type), granulosa cell tumour of the right ovary, Malignant Brenner's tumour, papillary serous cystadenocarcinoma (left side of the ovary) with mixed epithelial cell tumour (right adnexal mass), and serous borderline tumour of the left ovary. Meanwhile, 51.1% of the histopathology samples were not available for examination [6]. Based on the results obtained from the conventional cytology smear, patients were compared for age group distribution between the benign and malignant cytodiagnosis groups. It was observed that in the benign cytodiagnosis group, 22.2% of the patients were in the age group of 20-40 years, 33.4% in the age group of 41-60 years, and 44.4% of the patients were in the age group of >60 years [9].

The correlation between the conventional cytology smear diagnosis and histopathological diagnosis of the patients was performed. Subsequent analysis reported that there was a non-significant corelation between the finding of the conventional cytology smear and histopathological diagnosis (p=0.63) with 18 true positive cases, 2 false positive cases, 2 false negative cases, and none found in true negative cases due to the lack of availability of enough samples for histopathology [14].

Furthermore, the correlation between CB and conventional cytology smear diagnosis of the patients was performed. It was observed that there was a significant correlation between the findings of the cellblock and CS (p=0.0001) with a sensitivity of 94.12%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 85.71%, and a diagnostic accuracy of CB correlating with CS of 95.65%. Kumar SH et al., compared the CS technique to the CB method for malignant peritoneal and pleural effusions and observed a sensitivity of 90% and 75%, respectively, while the specificity was 68% and 79% [17]. They concluded that CB has a higher yield in diagnosing malignancy and aids in providing a clear diagnosis for cases suspected of malignancy on CS. Ascitic cytology was shown to have a sensitivity of 60% and a specificity of 100% [18].

Limitation(s)

Histopathological examination was not performed in nearly 50% of patients due to a lack of availability of samples, which could have affected our the results of the present study.

CONCLUSION(S)

The present study represents a combined approach of routinely stained cytology smears and the CB technique with histopathological correlation for cyto-diagnosis of ascitic fluid in ovarian tumours. The authors that this combined strategy could be a highly effective and efficient diagnostic approach for malignant ovarian tumours.

REFERENCES

 Janagam C, Atla B. Study of ascitic fluid cytology in ovarian tumours. Int J Res Med Sci. 2017;5(12):5227-31

- [2] Sangisetty SL, Miner TJ. Malignant ascites: A review of prognostic factors, pathophysiology and therapeutic measures. World J Gastrointest Surg. 2012;27;4(4):87-95.
- [3] Lin Z, Chen J, Liu Y. The efficacy of traditional Chinese medicine combined with hyperthermic intraperitoneal chemotherapy for malignant ascites: A systematic review and meta-analysis. Front Pharmacol. 2022;13:938472.
- [4] Monk BJ, Minion LE, Coleman RL. Anti-angiogenic agents in ovarian cancer: Past, present, and future. Ann Oncol. 2016;27(Suppl 1):i33-i39.
- [5] Záveský L, Jandáková E, Weinberger V, Hanzíková V, Slanař O, Kohoutová M. Ascites in ovarian cancer: MicroRNA deregulations and their potential roles in ovarian carcinogenesis. Cancer Biomark. 2022;33(1):01-16.
- [6] Ford CE, Werner B, Hacker NF, Warton K. The untapped potential of ascites in ovarian cancer research and treatment. Br J Cancer. 2020;123(1):09-16.
- [7] Ouyang HH, Pan ZY, Ma WD, Zhao LJ, Zhang T, Liu F, et al. Multidisciplinary treatment and survival analysis for 497 cases of pancreatic cancer with liver metastases. Zhonghua Yi Xue Za Zhi. 2016;96(6):425-30.
- [8] Grabowski JP, Martinez Vila C, Richter R, Taube E, Plett H, Braicu E, et al. Ki67 expression as a predictor of chemotherapy outcome in low-grade serous ovarian cancer. Int J Gynaecol Cancer. 2020;30(4):498-503.
- [9] Matreja SS, Malukani K, Nandedkar SS, Varma AV, Saxena A, Ajmera A. Comparison of efficacy of cell block versus conventional smear study in exudative fluids. Niger Postgrad Med J. 2017;24(4):245-49.
- [10] Padmavathi A, Prasad BV, Anuradha B. A comparative study of fluid cytology with smear and cell block preparation. J Evid based Med. 2016;3(65),3532-35.
- [11] Takanashi H, Suzuki K, Nakajima A, Saito R, Yamaguchi N, Kaya R, et al. Diagnostic value of cell block method in ascites fluid of ovarian cancer. J Clin of Diagn Res. 2020;14(3):QC01-QC04.
- [12] Takiar R. Status of ovarian cancer in India (2012–14). EC Gynaecol. 2019;8:358-64.
- [13] Younas M, Sattar A, Hashim R, Ijaz A, Dilawar M, Manzoor SM, et al. Role of serum-ascites albumin gradient in differential diagnosis of ascites. J Ayub Med Coll Abbottabad. 2012;24(3-4):97-99.
- [14] Udasimath S, Arakeril SU, Karigowdar MH, Yelikar BR. The role of the cell block method in the diagnosis of malignant ascitic fluid effusions. J Clin Diagn Res. 2012;6(7):1280-83.
- [15] Dey S, Nag D, Nandi A, Bandyopadhyay. Utility of cell block to detect malignancy in fluid cytology: Adjunct or necessity? J Cancer Res Ther. 2017;13(3):p425-29.
- [16] Maseki Z, Kajiyama H, Nishikawa E, Satake T, Misawa T, Kikkawa F. Is cell block technique useful to predict histological type in patients with ovarian mass and/or body cavity fluids? Nagoya J Med Sci. 2020;82(2):225-35.
- [17] Kumar SH, Sudhamani S, Shetty D, Rao R. Clinicopathological study of 117 body fluids: Comparison of conventional smear and cell block technique. Curr Health Sci J. 2020;46(4):336-43.
- [18] Pascual-Antón L, Cardeñes B, Sainz de la Cuesta R, González-Cortijo L, López-Cabrera M, Cabañas C, et al. Mesothelial-to-mesenchymal transition and exosomes in peritoneal metastasis of ovarian cancer. Int J Mol Sci. 2021;22(21):11496.

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