Original Research

DIAGNOSTIC EFFICACY OF CELL BLOCK METHOD VERSUS CONVENTIONAL SMEAR CYTOLOGY IN MALIGNANT PLEURAL AND ASCITIC EFFUSIONS

Dr. Vinita Saharan[1], Dr. Ashumi Gupta[2], Dr. Mahima Patel[3]
[1,3]Post Graduate Resident, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India
[2]Professor, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India
Corresponding Author: Dr. Ashumi Gupta (MD Pathology),
Professor, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan – 313001, India
Email id: ashumi.gupta@gmail.com

ABSTRACT

Background: Cytological examination of serous effusions is the primary method for detecting malignant cells in pleural and ascitic fluids. Conventional smear cytology has limitations in sensitivity and architectural detail. The cell block technique, by concentrating cellular material into paraffin-embedded sections, offers superior morphological preservation.

Aims and Objectives: To compare the diagnostic efficacy of cell block preparation with conventional smear cytology in the detection of malignancy in pleural and ascitic effusions.

Materials and Methods: The study was conducted in Geetanjali Medical College and Hospital, Udaipur, over 18 months, in clinically suspected malignant cases. Eighty serous effusion specimens including 53 pleural and 27 ascitic fluid samples were processed by conventional smear cytology method as well as cell block. Specimens were classified as positive, suspicious, or negative for malignancy, after examination of morphological characteristics, and compared between conventional cytology smears and cell block sections.

Results: The mean patient age was 58.4 ± 14.0 years (range 13–85 years). Cell block detected malignancy in 75% of cases versus 61.3% by conventional smear ($p<0.05$). The false-negative rate decreased from 7.5% on conventional smear cytology to 1.2% on cell block. In scanty cellularity specimens, cell block sensitivity rose from 43.8% to 68.8% on cell block. The combined use of both techniques yielded an overall positivity rate of 80.0%.

Conclusion: The cell block technique is significantly superior to conventional smear cytology in detecting malignant effusions, particularly in low cellularity specimens. In allows better preservation of morphological details and and improves diagnostic yield. Combined use of both methods enhances the diagnostic efficacy of cytology and is strongly recommended during routine processing of suspected malignant effusion samples.

Keywords: Cell Block, Conventional Smear Cytology, Malignant Pleural Effusion, Malignant Ascites, Serous Effusion, Diagnostic Sensitivity.

INTRODUCTION

Serous effusions, defined as abnormal accumulation of fluid within body cavities, represent a frequent clinical presentation in both benign and malignant conditions.[1] Pleural and peritoneal fluids are the most commonly examined serous fluids in routine pathological practice. While benign causes such as congestive cardiac failure, cirrhosis, and tuberculosis are frequent, the identification of malignant cells in effusion specimens carries critical diagnostic and prognostic significance.[2]

Cytological examination of serous effusions is important in the diagnosis, staging, and prognostic assessment of malignant lesions.[2] Malignant effusions develop when tumor cells invade serosal surfaces or obstruct lymphatic drainage, resulting in exfoliation of neoplastic cells into the fluid. The most common primary sites implicated in malignant pleural effusion include carcinoma of lung, breast, and gastrointestinal tract, while ovarian, colorectal, and pancreatic carcinomas predominate in malignant ascites.[3,4]

Conventional smear cytology using Papanicolaou and Giemsa stains on centrifuged sediment smears remains an important tool in the diagnosis of effusion fluids.[4] However, there may be difficulty in distinguishing reactive mesothelial cells from malignant cells. Also, staining and fixation issues may affect sample preservation and morphology, leading to suboptimal sensitivity, particularly in low-cellularity specimens.[5-7]

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The cell block technique, processes the sedimented cellular material into a paraffin-embedded block similar to a tissue biopsy.[6] This preserves three-dimensional architectural patterns, enhances cellular morphology, and allows the application of immunohistochemical (IHC) panels — enabling sub-typing of carcinomas, differentiation of mesothelioma from adenocarcinoma, and identification of primary tumor sites.[7-10]

Despite the recognized superiority of cell block in numerous published studies, its routine adoption alongside conventional smear remains inconsistent across institutions. Therefore, the present study was undertaken to compare the utility of conventional smear and cell block methods for diagnosis of malignant effusion in pleural and peritoneal fluid specimens.

MATERIALS AND METHODS

The study was conducted in the Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, over a period of 18 months, following institutional ethical clearance. A total of 80 serous effusion specimens — 53 pleural fluid and 27 ascitic fluid samples — from clinically and/or radiologically suspected malignant cases were included. Poorly preserved or improperly labelled specimens were excluded.

All effusion specimens were examined for gross appearance and volume. The specimen was processed for conventional cytology by centrifugation at 2000 rpm for 10 minutes. Following centrifugation, the sediment was used for preparation of conventional cytology smears. Wet-fixed smears were stained with Papanicolaou stain, while air-dried smears were stained with Field stain. Remaining specimen was processed for cell block after centrifugation at 2000 rpm for 10 minutes. The supernatant was carefully discarded, and the residual sediment was resuspended by adding 2–3 drops of plasma, followed by 1–2 drops of thromboplastin reagent to facilitate clot formation. The formed clot was wrapped in filter paper, placed in a tissue cassette, and fixed in 10% neutral buffered formalin. The clot was then processed by the routine histopathology protocol, including dehydration, clearing, paraffin embedding, sectioning at 3–5 µm thickness, and staining with haematoxylin and eosin (H&E).

Cytological cellularity was divided as: abundant (many clusters and dispersed cells), moderate (clusters present with adequate cellular material), or scanty (rare clusters or scattered cells). Morphological features were studied in detail including cellular arrangement, nuclear and cytoplasmic details and background characteristics. Clinical details, laboratory investigations and radiological findings were taken into consideration. Diagnostic impressions were categorised as positive for malignancy, suspicious for malignancy, or negative for malignancy based on morphological findings.

Statistical analysis was performed using SPSS version 26.0. McNemar's test was applied for paired comparison of diagnostic positivity rates. Pearson's correlation coefficient assessed the relationship between cellularity grade and diagnostic yield. Cohen's kappa coefficient (κ) was used to quantify inter-method agreement. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included 80 patients with a mean age of 58.4 ± 14.0 years (range: 13–85 years). Female patients constituted 53.7% (n=43), with a female-to-male ratio of 1.16:1 (Table 1). The peak incidence was in the 60–69year age group (31.3%), followed by the ≥70 group (23.7%).

Table 1: Demographic Profile of Study Subjects (n=80)

Variables		**Frequency (n)**	**Percentage (%)**
Gender	Male	37	46.3
	Female	43	53.7
Age Group (years)	<40	12	15.0
	40–49	6	7.5
	50–59	18	22.5
	60–69	25	31.3
	≥70	19	23.7
Mean Age ± SD	58.4 ± 14.0 years	—	—
Total	—	80	100.0

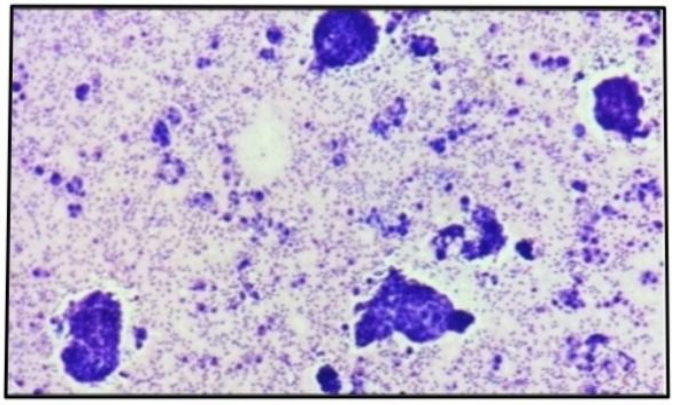
Pleural fluid constituted 66.3% of specimens while ascitic fluid comprised 33.7% (Table 2) of specimens. A significant gender-based disparity was observed (Chi-square, $p<0.05$): 83.8% of male

patients had pleural effusions versus only 51.2% in females.

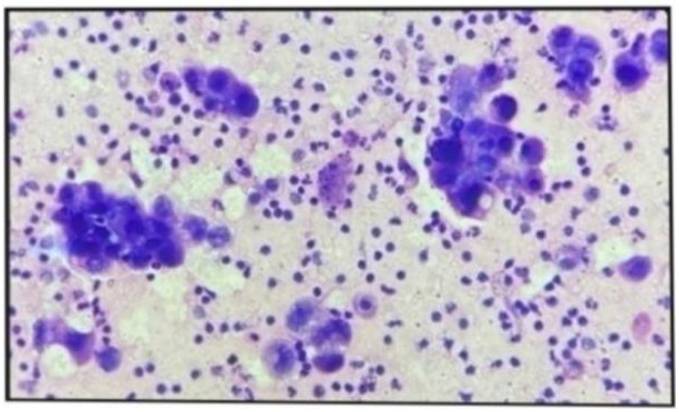
Table 2: Distribution of Body Fluid Type by Gender

Fluid Type	Male (n=37)	Female (n=43)	n (% of total)
Pleural Fluid	31 (83.8%)	22 (51.2%)	53(66.3%)
Ascitic Fluid	6 (16.2%)	21 (48.8%)	27(33.7%)
Total	37 (100%)	43 (100%)	80(100.0%)

Majority of fluid specimens showed moderate cellularity on conventional smear cytology (65.0%, n=52), followed by scanty cellularity (20.0%, n=16) and abundant cellularity (15%, n=12). Morphological features were studied in detail for cytology smears and cell block (Fig 1,2)



1(a)



1(b)

Figure 1(a) and 1(b): Malignant effusion with metastatic adenocarcinoma on conventional smear, Giemsa stain. (1(a): 10x, 1(b): 40x)

Conventional smear cytology diagnosed malignancy in 61.3% (n=49) of cases, with 31.3% (n=25) reported as suspicious and 7.5% (n=6) as negative (Table 3). The positivity rate was notably higher in ascitic fluid (85.2%) than in pleural fluid (49.1%).

Table 3: Conventional Smear Cytology — Diagnostic Impressions by Fluid Type

Conventional smear diagnosis	Pleural fluid	Ascitic fluid	Total (%)
Positive for Malignancy	26 (49.1%)	23 (85.2%)	49(61.3%)
Suspicious for Malignancy	21 (39.6%)	4 (14.8%)	25(31.3%)
Negative for Malignancy	6 (11.3%)	0 (0.0%)	6(7.5%)

Conventional smear diagnosis	Pleural fluid	Ascitic fluid	Total (%)
Total	53 (100%)	27 (100%)	80(100.0%)

The cell block technique demonstrated a higher diagnostic yield, detecting malignancy in 75.0% (n=60) of cases (Table 4). The architectural patterns and cellular morphology was well preserved (Fig 2).

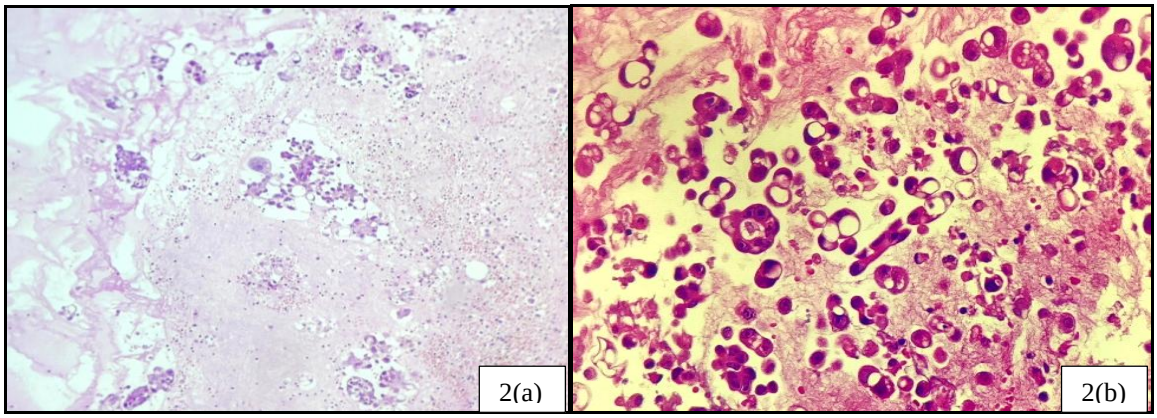


Figure 2(a) and 2(b) : Malignant effusion with metastatic adenocarcinoma, cell block section, H&E Stain.(2(a): 10x, 2(b) : 40x)

The proportion of negative cases decreased from 7.5% on conventional smear to 1.2% on cell block, and the suspicious rate declined from 31.3% to 23.8%. Ascitic fluid cell blocks achieved a positivity rate of 92.6%. The combined use of both methods yielded a maximal positivity rate of 80.0%.

Table 4: Cell Block Technique — Diagnostic Impressions by Fluid Type

Impression Category	Pleural (n=53)	Ascitic (n=27)	n(%)
Positive for Malignancy	35 (66.0%)	25 (92.6%)	60 (75.%)
Suspicious for Malignancy	18 (34.0%)	1 (3.7%)	19(23.8%)
Negative for Malignancy	0 (0.0%)	1 (3.7%)	1(1.2)
Total	53 (100%)	27 (100%)	80(100.0%)

The diagnostic yield, that is, percentage of specimens diagnosed as malignant, showed a significant positive correlation with cellularity grade on conventional smear (Pearson's r = +0.61, $p<0.05$). Diagnostic yield was highest in abundant (66.7%) and moderate (65.4%) cellularity groups and lowest in scanty specimens (43.8%), where the suspicious category was largest (50.0%). Cell block demonstrated superior diagnostic yield, which was particularly notable in scanty specimens, where yield increased from 43.8% on convention cytology to 68.8% on cell block. In moderate cellularity specimens, yield improved from 65.4% to 78.8%.

The cytological features, morphological details and architectural pattern were studied on conventional smear cytology and cell block. Cytological diagnoses in conventional smears were compared to cell block sections, and cell block was found to be diagnostically superior with significant increase in number of cases diagnosed as malignant (Table 5)

Table 5: Comparative Diagnostic Analysis — Conventional Smear vs. Cell Block

Diagnostic Parameter	Conventional Smear	Cell Block	p-value
Positive for Malignancy	49 (61.3%)	60 (75.0%)	<0.05
Suspicious for Malignancy	25 (31.3%)	19 (23.8%)	>0.05
Negative for Malignancy	6 (7.5%)	1 (1.2%)	<0.05
Diagnostic Sensitivity	61.3%	75.0%	<0.05
Abnormal Rate (Positive+Suspicious)	92.5%	98.8%	<0.05

McNemar's test; *Abnormal rate = Positive + Suspicious combined. CS = conventional smear; CB = cell block.

Overall concordance between conventional smear and cell block was 73.8% (59/80 cases), with a Cohen's κ coefficient of 0.58 (moderate agreement, $p<0.001$). Among 25 suspicious smear cases, 12 (48.0%) were upgraded to positive on cell block. All six cytologically negative cases were reclassified as either suspicious (n=5) or positive (n=1) on cell block — demonstrating that cell block can salvage fluid samples with false-negative smear cytology.

DISCUSSION

The present study comprised 80 patients with a mean age of 58.4 ± 14.0 years (range: 13–85 years), indicating a predominantly middle-aged to elderly population. This distribution is consistent with established epidemiological data showing that malignant effusions are encountered predominantly from the fifth decade onward, when the cumulative burden of solid tumors and haematological malignancies peaks. [9,11,12]

Female patients constituted a marginal majority (53.7%), with peak disease concentrated in the 60–69-year group (31.3%). Shivakumarswamy et al.[8] in their comparative cytological analysis of 44 ascitic effusion specimens documented a mean patient age in the sixth decade with a slight female preponderance attributable to ovarian carcinomas — the leading cause of malignant ascites in women. Female patients contributed a substantially greater proportion of ascitic fluid specimens in our study, consistent with the higher prevalence of gynaecological malignancies causing peritoneal seeding. [2]

Out of suspected malignant pleural fluid specimens, predominant patients were males (83.8%), reflecting the higher prevalence of lung, prostate, oesophageal, and lymphomatous malignancies in men that preferentially involve the pleural space. [2,4,10] Johnston[4] in a cytopathological review of 584 effusion specimens from 472 consecutive patients documented that lung and breast carcinomas were the dominant primary sites for pleural malignant effusions, while breast carcinoma and ovarian carcinoma were the most common primaries in female patients.

Cellularity exerted a demonstrable influence on conventional smear sensitivity. Scanty specimens showed a positivity rate of only 43.8% on conventional smear, with a suspicious rate as high as 50.0%. In contrast, cell block significantly improved yield in scanty specimens to 68.8%. Cell block provides increased cellularity, better morphological details and reduced degeneration, that leads to increase sensitivity, particularly in specimens with low cellularity.[2,8]

Motherby et al. [13] in a study of 300 pleural and 300 ascitic effusions reported a conventional cytology sensitivity of 50% for pleural fluid and 62.4% for ascitic fluid — closely approximating the 61.3% smear positivity observed in the present study. Conventional smear preparations alone carry an inherent sensitivity ceiling due to cellular overlap, poor preservation and loss of architectural detail — limitations that are addressed by the cell block method.[6-8,11]

Haemorrhagic pleural effusions carry a high risk of underlying malignancy, particularly in the absence of trauma or pulmonary infarction. [14] However, cell block technique is a valuable adjunct in haemorrhagic specimens, where conventional smear quality is suboptimal due to blood-obscured background. [15,16]

Conventional smear cytology yielded definitive malignancy diagnoses in 61.3% of cases in this study. The cell block technique demonstrated statistically and clinically significant superiority over conventional smear in this study, with a positivity of 75.0% versus 61.3% (McNemar's test, $p<0.05$). The false-negative rate was substantially reduced from 7.5% in conventional smear to 1.2% in cell block. Similar findings have been reported in previous studies.

Thapar et al.[6] in a study of 190 serous fluid samples found that combined use of conventional smear and cell block detected 13% more malignant cases than smear alone, and cell block helped identify the primary site of malignancy in 83.3% of cases. In the present study, the combined yield reached 80%, with cell block alone achieving 75.0%, a significant improvement over conventional smear (61.3%, $p<0.05$).

Chiatamone Ranieri et al.[17] in a retrospective multicentre study involving patients with malignant pleural effusion reported that combined smear and cell block techniques showed high diagnostic accuracy, with cell block detecting more malignant cases than conventional smear alone. Shivakumarswamy et al. in a prospective study of 60 pleural fluid specimens found that the cell block method yielded higher cellularity, better architectural features (glandular structures, cell sheets, three-dimensional clusters, and cell balls), and identified nine additional malignant cases not detected on conventional cytology, increasing the overall diagnostic yield by 15%.[18]

Pal and Murmu[19] in a study of suspected malignant ascitic effusions found that the cell block technique improved detection of malignant cells and yielded an additional 24% diagnostic rate for malignancy, with better cellularity and preservation of architectural patterns compared to conventional smear, consistent with the high ascitic cell block positivity of 92.6% observed in the present study. In another study, 44 peritoneal effusion cases were evaluated, and cell block identified an additional 6

malignant cases, a 14% increase in diagnostic yield, with difference observed in 8 cases where samples initially categorised as benign or suspicious on conventional smears were subsequently confirmed malignant.[8]

The main issues that lead to false-negative smear diagnoses in conventional smear cytology are abundance of inflammatory cells, reactive mesothelial overgrowth, and haemorrhagic background which can create difficulties during interpretation of cytology smears.[8,18] These limitations are addressed by the cell block concentration and architectural preservation mechanism. Cell block sections provide better morphological details with architectural patterns including glands, sheets or cell clusters that help in reaching accurate diagnosis.[18]

Chandan et al.[20] in a comparative study of 150 body fluid specimens found that the cell block method increased detection of malignant cases by 12% compared with conventional smear and allowed immunocytochemical studies. They recommended routine use of cell block in body cavity fluid evaluation.

Fetsch et al.[21] evaluated three cytological preparations including conventional smear, cytospin, and cell block for immunocytochemical analysis in effusion specimens using a panel of antibodies. Batool et al.[22] reported sensitivity of 92.31% with specificity of 98.95% on combining these techniques, highlighting the synergistic value of all three methods. Cell block, in combination with immunocytochemistry can increase the diagnostic yield and aids in detecting malignancy at an unknown primary site in effusion fluids.[22] Cell block not only provides superior preservation and cell morphology, but allows ancillary techniques including immunocytochemistry for tumor diagnosis and subtyping. Adding cell block to routine cytology smear examination, can enhance diagnostic efficacy, particularly when immunohistochemical techniques are applied.

Cytological smear examination is the primary diagnostic method for evaluation of effusion fluid specimens; however, conventional smear cytology has limited sensitivity and difficulty in distinguishing reactive mesothelial cells from malignant cells.[23] Conventional smear cytology smears may show suboptimal morphology in some cases due to obscuring haemorrrhage, or cellular degeneration. These limitations are significantly mitigated by the cell block method, as demonstrated in the present study. Cell block sections provide superior diagnostic material with better preservation of cellular architecture, lower background blood, and reduced cellular degeneration. [11,16] In the present study, the cell block technique was found to be significantly superior to conventional smear in overall positivity (75.0% vs. 61.3%, $p<0.05$), with significant reduction in false-negative rate from 7.5% to 1.2% ($p<0.05$), particularly in fluid specimens with scant cellularity on conventional cytology. Cell block demonstrated higher sensitivity and a significant upgrade rate for cases previously reported as suspicious or indeterminate on smear, particularly in the scanty-cellularity group. The cell block sections showed well preserved architectural and cytomorphological features. Combining of both techniques increased the positivity rate to 80.0%. Cell block additionally provides paraffin-embedded material for immunohistochemical sub-typing.

Cell block processing should be performed routinely in cases clinically and radiologically suspected to be malignant [11,12,16] – a recommendation supported by the present data, in which cell block sections provided superior diagnostic yield in specimens with scanty cellularity on conventional smears, and, combined cell block and conventional cytology was able to salvage cases with low cellularity.

CONCLUSION

Routine concurrent use of conventional smear cytology and cell block preparation is strongly recommended for the cytopathological evaluation of all serous effusions, particularly in clinically or radiologically suspected malignant cases. This dual-method approach significantly reduces false-negative diagnoses, upgrades equivocal smear reports, and provides the morphological and molecular data necessary for comprehensive oncological workup.

Conflict of Interest

The authors declare that they have no potential conflicts of interest to disclose.

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