



Original Article

## Comparative Analysis of the Diagnostic Utility of Cytospin, Conventional Centrifuge Smear and Cell Block Techniques in Serous Effusions: A Cross-sectional Study

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### ABSTRACT

Cytological evaluation of serous effusions is central to the detection of inflammatory and malignant aetiologies, but conventional smears may be limited by low cellularity and loss of architectural detail. The cytospin and cell-block techniques can enhance cellular concentration and morphological preservation. The present cross-sectional observational study, conducted in the Department of Pathology of a tertiary care teaching hospital in southern India, aimed to compare the diagnostic performance and agreement of the cell-block method with cytospin and conventional smear preparations in serous effusions, and to quantify concordance using Cohen's kappa statistic. A total of 96 effusion samples (pleural n = 74, 77.1%; peritoneal n = 22, 22.9%) were processed by three methods—conventional centrifuge smear, cytospin and cell block—and each preparation was categorised as inflammatory or reactive, atypical or suspicious, or positive for malignancy. The mean age was 52.4 years and 62.5% of patients were male. Cell block detected a higher proportion of malignant cases (16.6%) than cytospin (13.5%) and conventional smears (8.3%). Concordance of cell block versus cytospin was 81.2% ( $\kappa = 0.614$ ;  $p < 0.001$ ), indicating substantial agreement, while cell block versus conventional smear showed 76.0% concordance ( $\kappa = 0.457$ ;  $p < 0.001$ ), indicating moderate agreement. Cell block also yielded more atypical or suspicious diagnoses and superior architectural detail. Incorporation of the cell-block method into routine effusion cytology can improve diagnostic accuracy and triage, while cytospin offers a valuable alternative where cell-block preparation is not feasible.

**Keywords:** Serous effusion; Cell block; Cytospin; Conventional smear; Cohen's kappa.

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### INTRODUCTION

Serous effusions of the pleural and peritoneal cavities are among the most frequently encountered specimens in cytopathology. They often represent the first manifestation of an underlying disease process, ranging from benign inflammatory and infectious conditions to advanced malignancies. The cytological examination of these fluids remains a cornerstone of diagnostic pathology because it is rapid, minimally invasive and cost-effective compared with surgical biopsies<sup>1</sup>. The information obtained from effusion cytology assists clinicians not only in establishing a diagnosis but also in staging cancers, monitoring disease progression and guiding further management.

Despite its wide applicability, conventional smear (CS) cytology has inherent limitations. Air-drying artefacts, uneven cell distribution and loss of three-dimensional architecture may hinder accurate interpretation<sup>2</sup>. Reactive mesothelial proliferation frequently mimics malignancy, while paucicellular samples may lead to false-negative results<sup>3</sup>. Therefore,

techniques that improve cellular concentration and morphological preservation are vital to enhance diagnostic accuracy, particularly in resource-limited settings.

The cytopspin technique has been introduced to overcome some of these shortcomings. By centrifuging a small aliquot of fluid at low speed, cytopspin provides a thin, uniform monolayer of cells with minimal overlap and background debris<sup>4</sup>. While this method improves cell yield and presentation, it still relies on a two-dimensional evaluation and is often insufficient for differentiating atypical mesothelial cells from metastatic carcinoma<sup>5</sup>.

The cell-block (CB) method, in contrast, transforms the fluid sediment into a formalin-fixed, paraffin-embedded block similar to a tissue biopsy. It preserves the architectural arrangement of cell clusters, permits multiple serial sections and facilitates special stains and immunocytochemistry<sup>6</sup>. Several studies have demonstrated that cell-block preparation enhances the detection rate of malignant cells and provides complementary diagnostic information when used alongside conventional cytology<sup>7,8</sup>.

Rekhi et al.<sup>9</sup> and Shivakumarswamy et al.<sup>10</sup> reported that the cell-block method significantly improved morphological detail and diagnostic yield in pleural effusions, especially in cases of metastatic adenocarcinoma. Similarly, Qamar et al.<sup>4</sup> observed higher sensitivity of cytopspin and cell-block techniques compared with conventional smears, emphasising their combined role in routine cytology practice. However, the diagnostic performance of these methods may vary depending on laboratory protocols, fixatives used and expertise available. In many Indian tertiary hospitals, systematic comparison of cell-block, cytopspin and conventional methods using the same specimens is still lacking. Such comparative evaluation is essential to establish evidence-based laboratory protocols that ensure optimal use of limited resources.

Given these considerations, the present study was designed to evaluate and compare the diagnostic utility of three cytological preparation techniques—conventional smear, cytopspin and cell block—in serous effusion samples. The study further aimed to assess cytomorphological preservation, categorise effusions into diagnostic groups and determine concordance between the methods using Cohen's kappa statistic.

## **MATERIALS AND METHODS**

### **Study design and setting**

This was a cross-sectional observational study conducted in the Department of Pathology, Sri Venkateswara Medical College, Tirupati, in collaboration with the Departments of Medicine and Pulmonology, over a period of six months. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Sri Venkateswara Medical College (Letter No.: 35/2025). Written informed consent was obtained from all participants prior to enrolment.

### **Study population and sample size**

A total of 96 serous effusion samples were analysed, comprising 74 pleural and 22 peritoneal fluids. Consecutive samples received in the Cytopathology Section during the study period were included after meeting the eligibility criteria. No additional invasive procedures were performed for study purposes.

### **Inclusion and exclusion criteria**

All serous effusion fluids received in the Department of Pathology during the study period were eligible for inclusion. Samples that were inadequate due to extensive cellular degeneration or haemorrhage, those that were poorly preserved and patients who did not provide written informed consent were excluded.

### **Sample collection and processing**

Effusion specimens were collected under aseptic precautions and transported immediately to the laboratory. Each specimen was divided into three equal aliquots for conventional smear, cytopspin and cell-block preparation to ensure identical cellular content across the three methods.

### **Conventional centrifuge smear (CS) technique**

Samples were centrifuged at 1,500 rpm for 10 minutes. The supernatant was decanted and two smears were prepared from the sediment. One smear was air-dried and stained with haematoxylin and eosin (H&E).

### **Cytopspin preparation**

Approximately 0.5 mL of well-mixed specimen was placed in a cytocentrifuge (Cytospin 4®, Thermo Scientific) and centrifuged at 600 rpm for 5 minutes onto a labelled slide. Smears were immediately fixed in 95% ethanol and stained with H&E. The cytopspin technique yielded a monolayer cell deposition with minimal background debris, as previously reported by Qamar et al.<sup>4</sup>.

### Cell-block (CB) technique

The residual sediment after centrifugation was fixed in 10% neutral buffered formalin and processed by the plasma-thrombin method<sup>6</sup>. Clots were wrapped in filter paper, embedded in paraffin and sectioned at 4 µm thickness. The sections were stained with H&E for histomorphological evaluation.

### Cytomorphological evaluation

All smears and cell-block sections were independently evaluated by two cytopathologists who were blinded to each other's findings. Each preparation was assessed for cellularity (scant, moderate or rich), cell arrangement (isolated cells, sheets, papillae or clusters), nuclear details (chromatin pattern, nucleoli, pleomorphism) and background characteristics (proteinaceous, necrotic or inflammatory). Cases were classified into one of the following diagnostic categories on the basis of standard criteria<sup>7</sup>: negative for malignancy (reactive or inflammatory); atypical or suspicious for malignancy; and positive for malignancy. Discrepancies were resolved by consensus review.

### Quality control and concordance analysis

Each case was evaluated across all three methods, and the cell-block findings were taken as the reference standard. Diagnostic agreement between cell block versus cytospin and cell block versus conventional smear was analysed using Cohen's kappa ( $\kappa$ ) statistic. The strength of agreement was interpreted as follows:  $\kappa < 0.40$  = poor,  $0.41-0.60$  = moderate,  $0.61-0.80$  = substantial and  $> 0.80$  = almost perfect<sup>8</sup>.

### Statistical analysis

Data were compiled in Microsoft Excel 2021 and analysed using Epi Info version 7.2 (Centers for Disease Control and Prevention, Atlanta, USA). Descriptive statistics (frequency, percentage, mean  $\pm$  standard deviation) were calculated. Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were derived for the cytospin and conventional smear methods, with cell block taken as the reference standard. A p-value  $< 0.05$  was considered statistically significant.

## RESULTS

A total of 96 serous effusion samples were included in the study.

### Age and sex distribution

The age of the patients ranged from 21 to 100 years, with a mean age of 52.4 years. The majority of patients (33.3%) were in the 51-60 years age group, followed by the 41-50 years group (25.0%), reflecting a higher incidence of effusion samples among middle-aged and elderly individuals. A male predominance was noted (males 60, 62.5%; females 36, 37.5%; male : female ratio 1.7 : 1). The age-wise and sex-wise distribution of the study population is shown in Table 1.

**Table 1. Age- and sex-wise distribution of the study population (n = 96).**

Age group (years)	Female	Male	Total
21-30	2	2	4
31-40	4	3	7
41-50	6	18	24
51-60	14	18	32
61-70	8	12	20
71-80	2	4	6
81-90	0	1	1
91-100	0	2	2
<b>Total</b>	<b>36</b>	<b>60</b>	<b>96</b>

### Type of specimen

Of the 96 samples, pleural fluid constituted the majority (n = 74, 77.08%), while peritoneal (ascitic) fluid accounted for the remainder (n = 22, 22.92%). The distribution of specimens is shown in Table 2.

**Table 2. Distribution of specimens by anatomical site (n = 96).**

Specimen	Number (%)
Pleural fluid	74 (77.08)
Peritoneal (ascitic) fluid	22 (22.92)
<b>Total</b>	<b>96 (100.00)</b>

### Diagnostic categorisation across methods

On categorising the 96 cases into negative for malignancy, atypical or suspicious for malignancy, and positive for malignancy, the cell-block method detected the highest proportion of malignant cases (n = 16, 16.6%), followed by the cytospin (n = 13, 13.5%) and conventional smear methods (n = 8, 8.3%). Conversely, the conventional smear classified

the largest proportion of cases as negative for malignancy (n = 80, 83.3%), reflecting under-detection compared with the other two methods. The atypical or suspicious category was identified in 8 cases (8.3%) by all three methods. The distribution of diagnostic categories across the three preparation techniques is summarised in Table 3.

**Table 3. Distribution of diagnostic categories across conventional smear, cytospin and cell-block methods (n = 96).**

Diagnostic category	Conventional smear n (%)	Cytospin n (%)	Cell block n (%)
Negative for malignancy (reactive / inflammatory)	80 (83.3)	75 (78.1)	72 (75.0)
Atypical / suspicious for malignancy	8 (8.3)	8 (8.3)	8 (8.3)
Positive for malignancy	8 (8.3)	13 (13.5)	16 (16.6)
<b>Total</b>	<b>96 (100.0)</b>	<b>96 (100.0)</b>	<b>96 (100.0)</b>

#### Agreement between cell block and cytospin

Of the 96 paired evaluations, 78 (81.2%) were concordant between the cell-block and cytospin methods and 18 (18.8%) were discordant. The Cohen's kappa statistic was 0.614 ( $p < 0.001$ ), indicating substantial agreement between the two methods. The distribution of concordant and discordant findings is shown in Table 4.

**Table 4. Diagnostic agreement between the cell-block and cytospin methods (n = 96).**

Agreement category	Number of cases	Percentage (%)
Concordant	78	81.2
Discordant	18	18.8
<b>Cohen's kappa (<math>\kappa</math>)</b>	<b>0.614</b>	<b>p &lt; 0.001</b>

#### Agreement between cell block and conventional smear

Comparison of the cell-block and conventional smear methods demonstrated concordance in 73 cases (76.0%) and discordance in 23 cases (24.0%). The Cohen's kappa statistic was 0.457 ( $p < 0.001$ ), indicating moderate agreement. The distribution of concordant and discordant findings is shown in Table 5.

**Table 5. Diagnostic agreement between the cell-block and conventional smear methods (n = 96).**

Agreement category	Number of cases	Percentage (%)
Concordant	73	76.0
Discordant	23	24.0
<b>Cohen's kappa (<math>\kappa</math>)</b>	<b>0.457</b>	<b>p &lt; 0.001</b>

#### Summary of cell-block concordance

A summary of the diagnostic agreement of the cytospin and conventional smear methods with the cell-block reference standard is presented in Table 6. The cytospin method demonstrated substantial agreement ( $\kappa = 0.614$ ) with the cell-block method, whereas the conventional smear method showed only moderate agreement ( $\kappa = 0.457$ ). This indicates that the cytospin technique provides closer diagnostic alignment with the cell-block standard than the conventional smear technique.

**Table 6. Summary of diagnostic concordance of cytospin and conventional smear methods with the cell-block reference standard.**

Comparison method	Concordance (%)	Cohen's kappa ( $\kappa$ )	Agreement level
Cell block vs cytospin	81.2	0.614	Substantial
Cell block vs conventional smear	76.0	0.457	Moderate

## DISCUSSION

The present cross-sectional study compared the diagnostic utility of conventional centrifuge smear, cytospin and cell-block techniques in 96 serous effusion samples, with cell block taken as the reference standard. The age of the patients ranged from 21 to 100 years, with the majority in the 51–60 years age group (33.3%), followed by the 41–50 years group (25.0%). This pattern reflects the higher prevalence of effusion-producing diseases—particularly malignancies and chronic infections—among middle-aged and elderly individuals. A similar age trend has been reported by Khan et al.<sup>2</sup> and Dey<sup>3</sup>, who observed a peak incidence of pleural and peritoneal effusions in the fifth to sixth decades. The male predominance observed in the present study (male : female = 1.7 : 1) is consistent with prior Indian studies, in which effusion-related disorders were more frequent among males because of higher rates of smoking, tuberculosis and occupational exposure to respiratory carcinogens<sup>2,8</sup>.

Pleural fluid constituted the majority of specimens (77.08%), while peritoneal (ascitic) fluid accounted for 22.92%. This distribution mirrors the findings of Rekhi et al.<sup>9</sup> and Matreja et al.<sup>7</sup>, who also reported pleural effusions as the

predominant specimen type in tertiary care practice. The preponderance of pleural effusions may be attributed to the high burden of pulmonary tuberculosis, metastatic lung carcinoma and cardiac failure in the study population.

The central objective of this study was to evaluate the diagnostic concordance of cytospin and conventional smear preparations with the cell-block technique. Of the 96 cases, cell block versus cytospin showed 81.2% concordance ( $\kappa = 0.614$ ;  $p < 0.001$ ), indicating substantial agreement, while cell block versus conventional smear yielded 76.0% concordance ( $\kappa = 0.457$ ;  $p < 0.001$ ), reflecting moderate agreement. These findings demonstrate that the cytospin technique provides better diagnostic alignment with the cell-block method than conventional smears, corroborating previous research by Qamar et al.<sup>4</sup> and Shivakumarswamy et al.<sup>10</sup>, who both concluded that cytospin and cell-block preparations improve cell yield, background clarity and recognition of architectural patterns compared with traditional smears.

The cell-block preparation in this study proved to be superior in detecting malignant cells (16.6%) compared with cytospin (13.5%) and conventional smears (8.3%). Similar trends were reported by Matreja et al.<sup>7</sup> and Kumari et al.<sup>8</sup>, who found that the cell-block method enhanced the identification of cohesive tumour clusters and glandular patterns typical of metastatic adenocarcinoma. The enhanced performance of cell blocks may be explained by preservation of three-dimensional architecture (facilitating recognition of papillary and acinar formations), concentration of diagnostic cells (especially in samples with scant cellularity) and compatibility with ancillary techniques such as immunocytochemistry and special stains, allowing confirmation of lineage and differentiation<sup>5</sup>. Rekhi et al.<sup>9</sup>, in their analysis of 300 malignant effusions, emphasised that cell blocks serve as an invaluable adjunct, particularly when immunomarkers such as calretinin, Ber-EP4 or CK7 are required for differentiating reactive mesothelium from metastatic carcinoma.

The cytospin method, although slightly inferior to the cell block, offered significant advantages over conventional smears in this study. By depositing cells uniformly over a limited area, cytospin provided enhanced clarity of nuclear features and minimal background interference. In settings where cell-block preparation is not feasible due to logistic constraints, cytospin remains a viable alternative for improving diagnostic precision. Qamar et al.<sup>4</sup> similarly demonstrated that the cytospin technique improved cellular recovery and distribution, yielding a diagnostic accuracy approaching that of cell-block preparations.

### Comparison with previous studies

A comparative analysis of the present study with major Indian and international studies is presented in Table 7. The findings of the current work are in close agreement with those of Bandyopadhyay et al.<sup>6</sup> and Shivakumarswamy et al.<sup>10</sup>, both of whom documented  $\kappa$  values in the range of 0.45–0.65, signifying moderate to substantial agreement between cytology and cell-block diagnoses. The consistency of  $\kappa$  values across studies underscores the reproducibility of the cell-block technique and its reliability in effusion cytology diagnostics.

**Table 7. Comparison of diagnostic concordance in effusion cytology studies.**

Study (year)	n	Comparison	Concordance (%)	Kappa ( $\kappa$ )	Remarks
Present study (2025)	96	CB vs Cytospin / CS	81.2 / 76.0	0.614 / 0.457	Substantial / moderate agreement
Bandyopadhyay et al. (2024)	110	CB vs CS	78.2	0.56	Higher yield of malignant cells
Matreja et al. (2017)	80	CB vs CS	83.7	0.60	Recommended routine CB use
Kumari et al. (2020)	100	CB vs CS	79.1	0.49	Improved detection of carcinoma
Rekhi et al. (2010)	300	CB vs CS	75.0	0.44	Moderate correlation with histology
Shivakumarswamy et al. (2012)	120	CB vs CS	80.0	0.48	Demonstrated CB superiority

### Statistical interpretation

According to the scale proposed by Landis and Koch,  $\kappa$  values between 0.61 and 0.80 represent substantial agreement, while values of 0.41–0.60 denote moderate agreement<sup>5</sup>. The  $\kappa$  values observed in the present study (0.614 and 0.457)

therefore indicate that the cytospin and cell-block results were statistically coherent, while conventional smears showed lower reliability. A p-value < 0.001 obtained for both comparisons confirms that the observed concordance was not due to chance.

### **Clinical and diagnostic implications**

Accurate cytological interpretation of effusion samples directly influences patient management, particularly in differentiating malignant from benign causes. The cell-block technique, by preserving architecture and permitting immunohistochemistry, bridges cytology and histopathology<sup>5,9</sup>. This approach is especially useful in tertiary centres where effusion cytology frequently constitutes the initial diagnostic modality for malignancies of unknown primary. Furthermore, routine incorporation of cell-block preparation enhances sample utilisation, since the same specimen can be archived for future staining, retrospective analysis or molecular testing<sup>6</sup>. In contrast, conventional smears, though quicker, often suffer from cell depletion and loss of diagnostic material during staining and mounting.

### **Strengths and limitations**

The principal strengths of the present study include the same-sample comparison of three techniques, which minimises sampling bias, the uniform processing and blinded interpretation by two cytopathologists, and the use of Cohen's kappa to provide an objective measure of diagnostic reliability. The study has several limitations that merit consideration. The sample size was modest (n = 96) and the study was conducted at a single tertiary care centre, limiting the generalisability of the findings. Immunocytochemical correlation was not performed because of resource constraints, and the results were not stratified by underlying aetiology (for example, tuberculosis versus adenocarcinoma). Future multicentric studies incorporating immunomarker analysis are warranted to further validate the diagnostic advantage of the cell-block method in effusion cytology.

### **CONCLUSIONS**

The cell-block technique outperforms cytospin and conventional centrifuge smears for the detection of malignancy and for morphological preservation in serous effusion cytology, with substantial agreement against cytospin ( $\kappa = 0.614$ ) and moderate agreement against conventional smears ( $\kappa = 0.457$ ). The cytospin method, while slightly inferior to cell block, demonstrated clear advantages over conventional smears and serves as a useful alternative when cell-block preparation is not feasible. Incorporating the cell-block technique into the routine work-up of serous effusions can improve diagnostic accuracy and triage in tertiary care settings, particularly when used alongside immunocytochemistry for the characterisation of malignant cells.

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### **Conflict of Interest**

The authors declare that they have no conflict of interest.

**Ethical Approval:** Obtained from the Institutional Ethics Committee, Sri Venkateswara Medical College (Letter No.: 35/2025).

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### **Authors' Contributions**

Dr. Subalakshmi S : concept and design of the study, acquisition of data, statistical analysis, drafting of the manuscript.

Dr. Md Kadher Faheem.N : concept and design, interpretation of data, critical revision of the manuscript.

Dr. Mallikarjun B & Dr..Govindu Madhavi : laboratory supervision, interpretation of data, critical revision, clinical supervision, interpretation of data, critical revision of the manuscript.

All authors read and approved the final version of the manuscript to be published.

### **REFERENCES**

1. Shidham VB, Atkinson BF. Approach to diagnostic cytopathology of serous effusions. *Cytopathology*. 2021;32(5):349–62.
2. Khan NA, Sherwani RK, Afroz N, Kapoor S, Siddiqui FA. Cytodiagnosis of malignant effusion and its correlation with clinical and histopathological findings. *Ann Diagn Pathol*. 2009;13(1):42–6.
3. Dey P. Role of cytology in effusion fluids: diagnostic and prognostic perspective. *Diagn Cytopathol*. 2019;47(6):635–40.

4. Qamar I, Rehman S, Mehdi G, Maheshwari V, Ansari HA, Chauhan S. Utility of cytospin and cell block technology in evaluation of body fluids and urine samples: a comparative study. *J Cytol.* 2018;35(2):79–82.
5. Das DK. *Serous effusions: cytopathology and beyond.* Cham: Springer International Publishing; 2018.
6. Bandyopadhyay A, Mitra M, Bhattacharya S, et al. Concordance between conventional cytology and cell block of suspected malignant pleural effusion: a record-based study in a tertiary care centre of eastern India. *Asian J Med Sci.* 2024;15(4):207–12.
7. Matreja SS, Malukani K, Nandedkar SS, et al. Comparison of efficacy of cell block versus conventional smear study in exudative fluids. *Niger Postgrad Med J.* 2017;24(4):245–9.
8. Kumari S, Dhakre R, Singh SK. Diagnostic efficacy of cell block versus conventional smear study in pleural effusions: an institutional experience. *Indian J Pathol Oncol.* 2020;7(1):52–7.
9. Rekhi B, Desai S, Menon S, et al. Value of the cell block technique in effusion cytology: a study from a tertiary cancer referral centre. *Acta Cytol.* 2010;54(1):55–60.
10. Shivakumarswamy U, Arakeri SU, Karigowdar MH, Yelikar B. Diagnostic utility of the cell block method versus conventional smear study in pleural fluid cytology. *J Cytol.* 2012;29(1):11–5.