Cytomorphological and Biochemical Profile of Serous Effusions: A Cross-Sectional Study at a Tertiary Care Center in Chitwan, Nepal

ISSN: 3059-9733
DOI: 10.3126/jobh.v2i1.94399

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ABSTRACT

Background

Serous effusions are frequently encountered clinical conditions with diverse non-neoplastic and neoplastic causes, often indicating advanced disease in malignancy. Their evaluation is important for both diagnostic and prognostic purposes. This study aimed to assess protein concentration, classify effusions as transudates or exudates, and correlate these findings with cytomorphological features.

Methods

A hospital-based cross-sectional study was conducted at the Department of Central Clinical Laboratory, College of Medical Sciences-Teaching Hospital, Bharatpur, Nepal, including 96 serous effusion samples collected from June to August 2023. Total protein and cell counts were measured, and cytological evaluation was performed using standard staining techniques. Data were analyzed using SPSS version 16 with descriptive statistics, Pearson's correlation, and Mann-Whitney U test, considering $p < 0.05$ as statistically significant.

Results

Of the 96 samples, 52 (54.2%) were peritoneal, 43 (44.8%) pleural, and 1 (1.0%) pericardial fluid. Total protein ranged from 0.06 to 5.96 g/dl (mean ± SD: 2.65 ± 1.03 g/dl), with 42 (43.8%) exudates and 54 (56.2%) transudates. Total cell count ranged from 10 to 22,720 cells/cu mm and showed a significant positive correlation with total protein ($r = 0.525$, $p < 0.001$). Exudates had significantly higher total protein, total cell count, and neutrophil percentage. Most cases (96.9%) were negative for malignancy, with three exudative cases showing atypia, suspicion, or malignancy.

Conclusions

Biochemical and cytomorphological evaluation plays a crucial role in diagnosing serous effusions, with malignant effusions typically presenting as exudates. However, cytological assessment should be guided by both fluid characteristics and clinical context for accurate diagnosis.

Keywords: Cytomorphology; Effusion; Exudate; Serous; Transudate.

Correspondence: Dr. Binita Goyal, Department of Pathology, College of Medical Sciences-Teaching Hospital, Bharatpur, Chitwan, Nepal. Email: binitagoyal@yahoo.com, Phone: +977-98610167741 **Article received**: 2026-03-21. **Article accepted**: 2026-05-12. **Article published**: 2026-06-30.

INTRODUCTION

The pleural, pericardial and peritoneal cavities are serous cavities lined by a single layer of mesothelial cells, which normally contain a very small amount of fluid enough to lubricate the surfaces. [1] When the fluid collected is larger than normal, it is termed effusion, which may be a presentation in systemic and local pathological processes which need to be investigated both for diagnosis and management. [1, 2] Clinically, these effusions may be classified as transudates and exudates, which can be differentiated biochemically based on protein estimation of these effusions. Transudates result due to imbalance in hydrostatic and oncotic pressures in conditions like congestive heart failure, cirrhosis and nephrotic syndrome and have low protein concentration, low specific gravity and little or no cellular debris. Exudates result due to injury to mesothelium in conditions like malignancy, infections, autoimmune diseases, pulmonary infarction and trauma and have higher protein and more cellular debris.[1, 3] The biochemical analysis of these effusions along with clinical information helps in arriving at a differential diagnosis.[2] Cytological examination is also commonly performed as it helps in differentiating benign from malignant disease and has an advantage of being minimally invasive, easy availability and cost effectiveness.[4] Biochemical analysis is equally important as further cytological examination may not be missing in transudative effusion as malignancy results in exudate.[5] Hence, this study is aimed to see protein concentration of these effusions, classify them as transudate and exudate and compare with cytomorphological findings.

METHODS

Study Design

A hospital-based cross-sectional study was conducted to evaluate the biochemical and cytological characteristics of serous effusion fluids and their correlation with total protein concentration.

Study Area

The study was carried out in the Department of Central Clinical Laboratory, College of Medical Sciences, Bharatpur, Chitwan, Nepal. The study was conducted over a period of two and a half months, from 1 June to 15 August 2023.

Study Population

The study population comprised all serous effusion fluid samples received in the Central Clinical Laboratory during the study period. Peritoneal, pleural, and pericardial fluid samples were included. Recurrent cases were excluded from the study.

Sample Size

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

Sampling Technique

A consecutive sampling technique was employed, whereby all eligible serous effusion samples received during the study period that fulfilled the inclusion criteria were included until the required sample size was achieved.

Data Collection Tools and Technique

Relevant demographic and clinical information, including age, sex, clinical diagnosis, type of fluid, and the site and laterality (for pleural effusions), was obtained from laboratory requisition forms and recorded using a predesigned data collection proforma. Total protein estimation was performed using a fully automated biochemistry analyzer (Biosystems BA 400, Barcelona, Spain) based on the spectrophotometric principle. Effusion fluids were classified as transudates when the total protein concentration was <3 g/dL and as exudates when the concentration was ≥3 g/dL. Total cell count (TC) was determined using an improved Neubauer counting chamber by counting cells in the four corner squares. Five milliliters of each fluid sample was centrifuged at 2500 rpm for 5 minutes. The supernatant was used for biochemical analysis, while the sediment was evenly spread onto two clean glass slides. One slide was air-dried, fixed in 90% ethanol, and stained with May-Grünwald-Giemsa stain. The second slide was wet-fixed in 90% ethanol and stained using the Papanicolaou staining method. Differential cell count (DC) and cytomorphological examination were performed by a pathologist under 40× magnification. Cytological diagnoses were categorized according to the International System for Reporting Serous Fluid Cytopathology.

Variables/Measurements

The primary variables measured included total protein concentration, total cell count, differential cell count, cytological diagnosis, and classification of serous effusions as transudates or exudates. Additional variables included age, sex, clinical diagnosis, type of serous fluid, and the site and laterality of pleural effusions.

Statistical Analysis Used

Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 16. Continuous variables were summarized as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages.

Pearson's correlation coefficient was used to assess the relationship between total protein concentration and total cell count. Comparisons of total protein concentration, total cell count, and differential cell count between transudative and exudative effusions were performed using the Mann-Whitney U test. A p-value of <0.05 was considered statistically significant at the 95% confidence level.

Ethical Consideration

Ethical approval for the study was obtained from the Institutional Review Committee (IRC) of the College of Medical Sciences, Bharatpur, Chitwan, Nepal (Reference No. COMSTH-IRC/2023-19). Patient confidentiality was maintained throughout the study by using anonymized laboratory data and restricting data access to the research team.

RESULTS

Out of the 96 consecutive samples of serous effusions received, majority were peritoneal fluid comprising 52 (54.2%) cases (Figure 1).

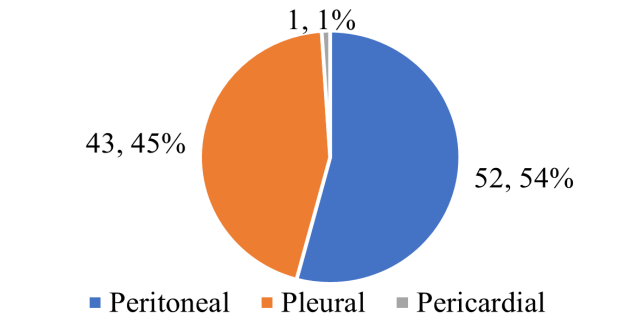

Figure 1. Types of effusion (n=96).

The mean ± SD age of the patients was 55.4 ± 17.4 years, ranging from 16 to 87 years. The highest number of cases, 23 (24.0%), was observed in the 51-60 years age group (Figure. 2).

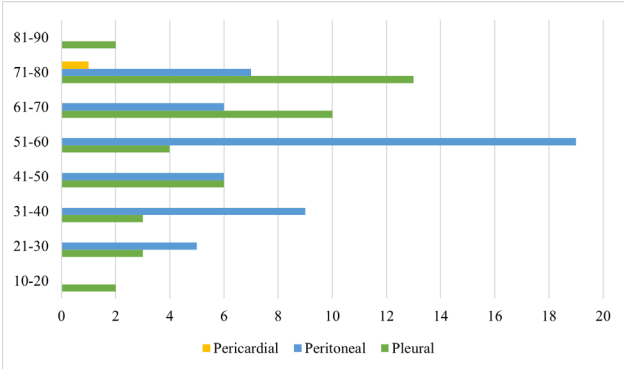

Figure 2. Age distribution in various types of fluids (n=96).

There were 56 (58.3%) males and 40 (41.7%) females, with a male-to-female ratio of 1.4:1 (Figure. 3).

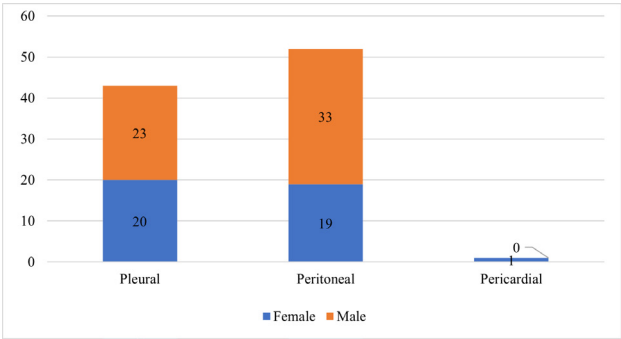

Figure 3. Gender distribution in various types of fluid (n=96).

Total protein ranged from 0.06 to 5.96 g/dl with mean ± SD of 2.65 ± 1.03 g/dl. There were 42 (43.8%) exudates and 54 (56.2%) transudates (Table 1).

Table 1. Distribution of exudate and transudate in different types of fluid (n=96).

Type of fluid	Exudate n (%)	Transudate n (%)
Pleural	27 (28.1)	16 (16.6)
Peritoneal	14 (14.6)	38 (39.6)
Pericardial	1 (1.0)	0 (0)

TC ranged from 10 to 22,720 cells/cu mm, with a mean ± SD of 1407.15 ± 3639.21 cells/cu mm. There was a significant correlation between total protein and total cell count, with a Pearson correlation coefficient of 0.525 and a p-value < 0.001 at a 99% confidence interval. Among the 42 cases of exudates, differential count (DC) showed the presence of

mesothelial cells in 36 (85.7%) cases, lymphocytes in 40 (95.2%) cases, neutrophils in 27 (64.3%) cases, histiocytes in 30 (71.4%) cases, and eosinophils in 3 (7.1%) cases. Among the 54 cases of transudates, DC showed the presence of mesothelial cells in 53 (98.1%) cases, lymphocytes in 54 (100%) cases, neutrophils in 17 (31.5%) cases, and histiocytes in 47 (87.0%) cases. On Mann-Whitney U test, there was a statistically significant difference between exudates and transudates in total protein, TC, and the percentages of mesothelial cells, neutrophils, and histiocytes, with higher total protein, TC, and neutrophil percentage observed in exudates (Table 2).

Table 2. Comparison of Total protein, TC and DC in exudates and transudates (n = 96).

Parameters	Exudate	Transudate	Mann-Whitney U value	p-value*
Total Protein (g/dl)				
Range	3.0-5.96	0.06-2.90	< 0.001	< 0.001
Mean rank	75.5	27.5		
Total count (cells/cu mm)				
Range	128-22720	10-410	52	< 0.001
Mean rank	74.26	28.46		
Mesothelial cells (%)				
Range	0-72	0-70	815	0.018
Mean rank	40.9	54.41		
Lymphocytes (%)				
Range	0-100	Sep-96	938.5	0.149
Mean rank	43.85	52.12		
Neutrophils (%)				
Range	0-84	0-4	626	< 0.001
Mean rank	60.6	39.09		
Histiocytes (%)				
Range	0-73	0-35	853	0.037
Mean rank	41.81	53.70		

A total of 93 (96.9%) cases were negative for malignancy. One case (1.0%) each was reported as atypia of undetermined significance, suspicious for malignancy, and positive for malignancy (Fig. 5); all of these were exudative in nature (Fig. 4).

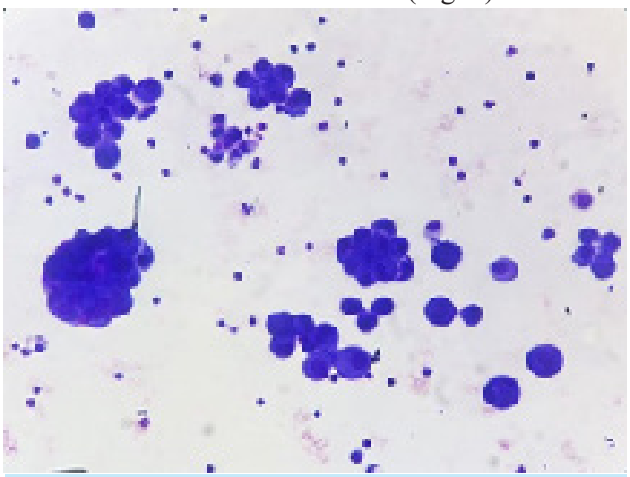

Figure 4. Suspicious for malignancy (Giemsa x 100X)

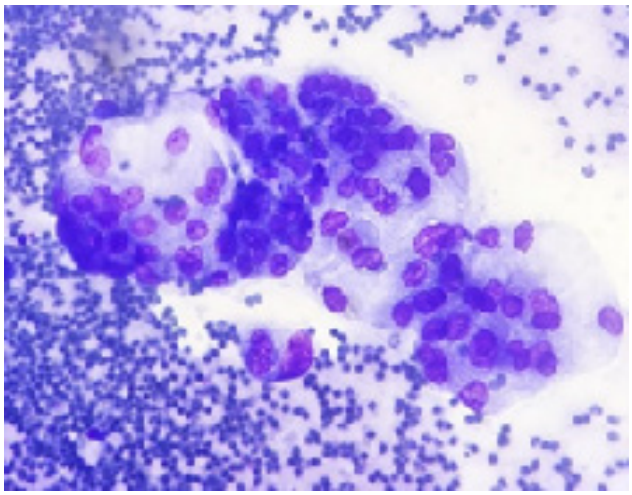

Figure 5. Positive for malignancy (Giemsa x 100X)

DISCUSSION

The serous body cavities (pleural, peritoneal and pericardial) are lined by visceral and parietal layers

which are collapsed in normal state and contain a very small amount of fluid inside enough for frictionless free movement of enclosed organs within during activities like respiration, peristalsis and heart beats.[1] Increased amount of fluid known as effusion sufficient for tapping indicates a pathological process. Effusion may result from various mechanisms like increased hydrostatic pressure, decreased colloid oncotic pressure, increased vascular permeability, lymphatic obstruction and secretion by tumor cells. [9] The effusion may be a transudate with low protein content (< 3g/dl) and little cellular debris resulting from imbalance between hydrostatic pressure and colloid oncotic pressure or it may be an exudate with high protein content (> 3g/dl) and higher cellular content resulting from damage to the capillaries.[1, 9, 10] If on biochemical analysis, the effusion turns out to be transudate, then further line of management is to treat the underlying cause and if exudate, then finding out the aetiology whether inflammatory or malignant is necessary for which cytological examination becomes necessary. [9] This study was conducted on 96 serous effusions in which 54.2% were peritoneal fluids followed by 44.8% pleural and 1.0% pericardial fluids. Age of the patient ranged from 16 to 87 years with mean 55.4 years. Transudates were more common comprising 56.2% cases and exudates 43.8% cases. Similarly, in a study conducted by Anita B and Ahuja JM on serous effusions,peritoneal effusion comprised 48.5% of the cases with pleural and pericardial effusions made up 44.3% and 7.1% of cases respectively. Age ranged from 8 to 90 years with a mean of 50.36 years. However, 52.9% cases were exudative and 47.1% were transudative. [11] In study conducted by Chandan et al., pleural fliud were more common makin up 64.7% of cases followed by 32% of cases of peritoneal fluid. Mean age was 53.3 years. They also had higher 60.7% cases as transudate and 39.3% cases exudate. [10] The first manifestation of ovarian or lung malignancy and mesothelioma may be an effusion whereas, in others effusion may occur in the course of disease, hence guide in prognosis. The cells which may be seen in an effusion may be lymphocytes, neutrophils, eosinophils, macrophages, mesothelial cells and malignant cells. [9] In present study, TC ranged from 10-22720 cells/cu mm with mean ± SD of 1407.15 ± 3639.21 cells/cu mm. 93 (96.9%) cases were negative for malignancy. 1 (1.0%) case each was atypia of undetermined significance, suspicious for malignancy and positive for malignancy, all were exudates in nature. In study conducted by Anita B and Auja JM, TC ranged from 57-1,50,000/cu mm with a higher mean ± SD of 3151.5 ± 17974.06 and 7.14% cases were malignant which was higher as compared to present study. All the malignant cases were exudative in nature in their study as well.[11] Also, in a study conducted by Sulbha VS and Dayanand BS, all 10 cases of malignant effusion were exudative in nature. [12] In study conducted by Chandan et al., malignancy was seen at a much higher rate of 18.7% cases. Moreover, 6 out of 28 (21.4%) malignant cases were transudative in their study. [10] In a study conducted by Ryu et al., 3.1% cases of malignant effusions were transudative. However, they found no clinical implication of cytology in transudative effusions in their study. [13] Though malignant pleural effusions are mostly exudative in nature, this is not always the case. Transudative effusions may also result because of pleural seeding, lymphatic obstruction by malignancy or by exacerbation of coexisting medical disease due to malignancy. [14] Cytological examination of effusion is an important diagnostic tool in malignant effusion and may even be superior to pleural biopsy. [15]

Conclusions

Biochemical and cytomorphological examination of serous effusions are important diagnostic tool in their evaluation. Malignant effusions are generally exudative. Decision to requirement of cytological analysis should not be based alone on exudative or transudative nature and should take clinical information also in account.

Acknowledgement: We are grateful to all participants for their cooperation.

Conflicts of Interest: Abstract of the manuscript was presented as poster in the 62nd IAP-Thailand Annual Meeting 2023 and the abstract was published

in official journal of IAP Thailand, Asian Archives of Pathology in Volume 6, Number 1, January - March 2024 (Supplement Issue). https://www.asianarchpath.com/storage/issue/AAP_Volume_6_Number_1_January-March2024Supplement.pdf

However, the full manuscript with detailed methodology, results and discussion has not been published elsewhere.

Source of funding: This study did not receive any external funding.

Ethical and Publication Integrity: Ethical approval was obtained from Institutional Review Committee (Ref. No.: COMSTH-IRC/2023-19). Anonymity of patient identification was maintained. Informed consent was not required as the study was based on laboratory findings (secondary data). The study was based on routinely performed tests on effusion fluids and did not incur any added cost to the patient.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. Due to institutional policies and participant confidentiality considerations, raw data are not publicly available.

Authors' Contributions

Conceptualization: Dr. Binita Goyal.
Methodology: Dr. Binita Goyal.
Data curation: Dr. Binita Goyal.
Investigation: Dr. Binita Goyal.
Formal analysis: Dr. Binita Goyal.
Supervision: Dr. Binita Goyal.
Writing-original draft: Dr. Binita Goyal.
Writing-review and editing: Dr. Binita Goyal, Dr. Akshunna Rup Shrestha.

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Citation: Goyal B, Shrestha AR. Cytomorphological and Biochemical Profile of Serous Effusions: A Cross-Sectional Study at a Tertiary Care Center in Chitwan, Nepal. JoBH, Nepal. 2026; 2(1): 28-34