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Original Research Article

Evaluation of pleural fluid cytology for the diagnosis of pleural effusion: A retrospective study

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ABSTRACT

Background: Cytological examination of pleural fluid has good specificity for the diagnosis of malignant pleural effusion (MPE).
Aims & Objective: (1). To study the incidence of non-neoplastic and neoplastic effusions; (2). To study most common cause of neoplastic effusions.
Materials and Methods: This study is an Observational retrospective study that was conducted from April 2021 to October 2022 (1.5 years). This study was conducted in the Cytology section, Pathology Department, of a tertiary care centre, Gujarat, India.
Results: A total of 248 pleural fluid samples were studied among them 186 were benign effusions, 48 were malignant effusions, 10 cases were unsatisfactory for evaluation and 4 cases were suspicious for malignancy.
Conclusion: A descriptive study was performed to know the incidence of benign and malignant effusion in the pleural fluid sample. Pneumonia was the most common clinical diagnosis followed by tuberculosis and malignancy. Lung was the most common primary site for pleural effusion. In females, ovarian carcinoma was the primary aetiology followed by breast carcinoma. Cytodiagnosis of pleural fluid represents the cell population from a much larger representative area than obtained from the needle biopsy.

1. Introduction

Pleural fluid cytology is a minimally invasive technique used in the diagnostic evaluation of pleural effusions to establish a differential diagnosis. It can lead to a final diagnosis and provide valuable information for treatment. The diagnostic yield of cytological analysis is high due to the representative cell population present in the sediment. It is a crucial initial step in managing pleural effusion cases and can help identify non-malignant and transudative effusions. Collaboration with clinical, radiological, and laboratory results can increase sensitivity.

This study aimed to assess the diagnostic utility of pleural fluid cytology in identifying the underlying causes of pleural effusion. Pleural effusion is a common clinical condition that can be detected through clinical and radiological examinations.[1,2] Radiological investigations such as ultrasound and chest CT scans are essential for diagnosis. Effusions can be of pulmonary origin or related to other conditions like cardiac, liver, renal, endocrine diseases, malignancies, and connective tissue disorders.[1,3,4]

Clinical presentation of pleural effusion can vary from asymptomatic to severe dyspnea and chest pain. Cytological evaluation of pleural fluid is crucial for confirming the

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etiology of the condition. The most common causes of pleural effusion are infectious and tuberculosis-related. The initial analysis involves differentiating between transudate and exudate to determine the underlying pathological process. The primary goal of cytological analysis is to detect malignant cells and confirm or rule out infectious causes.

2. Materials and Methods

We conducted a retrospective cohort study of 248 patients. This study is an Observational retrospective study that was conducted from April 2021 to October 2022 (1.5 years). This study was conducted in the Cytology section, Pathology Department, of a tertiary care center, Gujarat, India. The collection of samples of Pleural fluid was obtained by thoracocentes is by inserting a needle in the sixth or seventh intercostal space by the physician in the clinical wards and submitted to our laboratory were studied. In all patients, history, physical examination of pleural fluid, color of fluid, amount, and nature of fluid was collected from patient record. Physical examination of the fluids regarding the colour, volume and odour were noted. Smears obtained from the fluids without centrifugation to produce uniform suspension of cells. The sample was centrifuged for five minutes at 2000rpm. Smears were made from the drop of the sediment after discarding the supernatant fluid. Smears were fixed in 95% alcohol and stained with Hematoxylin and Eosin (H&E) and Papanicolaou stain (Pap), with the remaining sediment, cell blocks were made and sections reviewed after H&E staining by pathologist.

3. Result

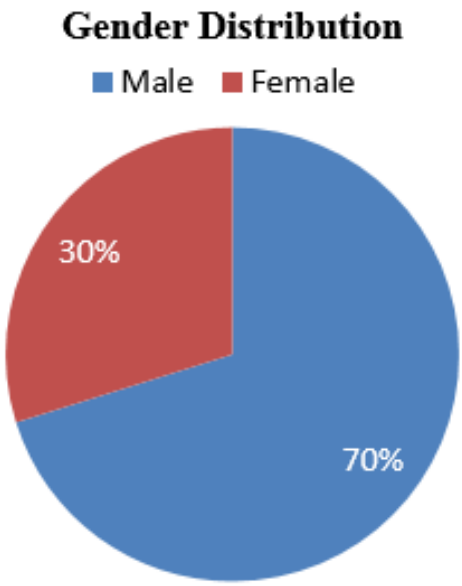
In the span of April 2021 to October 2022, a total of 248 pleural fluids were studied. The demographic data of these cases is shown in Graph 1. The pleural fluids were obtained from 174 (70%) males and 74 (30%) with M: F ratio of 2.3:1.

Table 1 shows age distribution of the patients from whom pleural fluid were obtained. The age of the patient ranged from 9months to 97 years with the maximum number of cases 86 (35 %) patients in 61-80 years followed by 82 (33%) in 41-60 years and 48 (19%) in 21-40 years. The mean age of presentation was 54.4 years.

Table 1: Shows age-wisedistribution of pleural fluid study (N=248)

Ageinyears	No. of cases and percentage (%)
0-20	10(4%)
21-40	48(19%)
41-60	82(33%)
61-80	86(35%)
>80	22 (9%)

Table 2 shows the clinical diagnosis of the cases whose pleural fluid was received for the study. The most



Graph 1: Shows gender distribution (N=248)

common clinical diagnoses were pneumonia in 90(36%) patients, followed by malignant effusion in 50 (20 %) and tuberculous effusion in 36 (15 %) patients. The diagnosis of tuberculosis cases was based on clinical examination, chest x-ray findings, ESR, sputum examination for Acid fast bacilli.

Table 2: Shows clinical diagnosis of pleural effusion (N=248)

Clinical diagnosis	No. of cases and percentage (%)
Pneumonia	90(36 %)
Congestive cardiac failure	36(15 %)
Hypo proteinemia	18 (7 %)
Tuberculosis	36(15 %)
Cirrhosis of liver	12 (4 %)
Collagen disorder	4(2 %)
Pancreatic disorder	2 (1 %)
Malignant effusion	50(20 %)

Table 3 and Graph 2 shows the physical and chemical characteristics of pleural fluid. 80 (32%) pleural fluids were classified as transudate and 168 (68%) as exudate. Straw colour fluid was found in 48 samples (40 transudates and 8 exudates). Turbid, yellow fluid was noted in 118 (48%) samples (92 exudates and 26 transudates). Turbid and reddish fluid was found in 64(26%) samples (52 exudates and 12 transudates).Turbid and brownish fluid was found in 18 (7%) samples (transudates 2 and 16 exudates).

Table 4 shows cytological findings in pleural fluid. The maximum number of cases 88 (35%) showed lymphocyte-rich smears, they were diagnosed as chronic inflammation (Figure 1) followed by positive for malignant cells in

Table 3: Showsphysical and chemical characteristics of Pleural fluid (N=248)

Gross appearance	No. of Cases (N=248) and %	Transudate (N=80)	Exudate (N=168)
Clear and Straw colour	48(19%)	40	8
Turbid, Yellow	118(48%)	26	92
Turbid, Reddish	64(26%)	12	52
Turbid, Brown	18(7%)	2	16

Table 4: Shows cytological pattern and diagnosis of pleural effusion (N=248)

Predominant cytological pattern	Cytological impression	No. of cases%
Predominantly Lymphocytes	Chronic inflammation	88 (35%)
Predominantly Polymorphs	Acute inflammation	24 (10%)
Lymphocytes, Polymorphs, and Mesothelial cells	Inflammation	30 (12%)
Chiefly mesothelial cells	Reactive effusion	44 (18%)
Malignant cells	Positive for malignancy	48 (19%)
Atypical cells	Suspicious for malignancy	4 (2%)
Degenerative and few cells	Unsatisfactory for evaluation	10 (4%)

Table 5: Shows comparison of gender composition in pleural effusion of various studies

Authors, Ref. No.,Year of publication	Number of fluids studied	Male	Female
Sandeep Vetal.[5](2020)	65	67%	33%
Lekha M B et al.[6](2020)	120	60%	40%
Snehalbhade et al[7](2018)	146	63%	37%
Shobha SN et al[8](2017)	100	62%	38%
Mahima Sharma et al[9](2017)	228	71%	29%
Sadullahoğlu et al.[10](2017)	264	61%	39%
Present study	124	70%	30%

Table 6: Showscomparison of gender composition in pleural effusion of various studies

Authors, Ref. No.	0-20	21-40	41-60	61-80	>80
Sandeep V et al.[5]	9%	26%	34%	40%	6%
Lekha MB et al.[6]	9%	28%	41%	16%	3%
SunitaG et al.[11]	6%	32%	47%	14%	1%
Shaukin et al.[12]	4%	19%	32%	41%	4%
Shobha SN et al.[8]	13%	26%	41%	19%	1%
SudhaAetal.[13]	9%	29%	29%	32%	
Satvik B et al.[14]	7%	37%	42%	15%	0%
Chakrabarti et al.[15]	4%	49%	24%	21%	
Present study	4%	19%	33%	35%	9%

Table 7: Shows clinical diagnosis in patient with pleural effusion invarious studies

Clinical Diagnosis	Gayathri MN et al.[16]	Shobha SN et al.[8]	Sadullahoğlu et al.[10]	Loveland P et al.[17]	ParikhP et al.[18]	Present study
Pneumonia	11 %	22 %	25 %	7.8 %	10 %	36 %
CCF	2 %	5 %	4 %	10 %	5 %	15 %
Hypo proteinemia	2 %	6 %	3 %	2.0 %	1 %	7 %
Tuberculosis	35 %	52%	4 %	2 %	62 %	15 %
Cirrhosis of liver	7 %	-	1 %	3 %		4 %
Collagen disorder	3 %	-	1 %	-	-	2 %
Pancreatic disorder	1 %	-	-	-		1 %
Malignant effusion	20 %	13 %	49 %	40 %	18 %	20 %

Table 8: Shows comparison of physical findings of pleural effusion

Gross appearance	Chakrabarti et al.[19]	Wasim et al.[20]	Mulkalwar M et al.[21]	Akhila P et al.[22]	Cuneyt T et al.[23]	Present study
Clear and Straw color	5%	30%	26%			19%
Turbid, Yellow	43%	45%		74%	79%	48%
Turbid, Brown	-	-	74%			7%
Turbid, Reddish	19%	26%		26%	21%	26%

Table 9: Shows classification of pleural fluid (transudate and exudate)

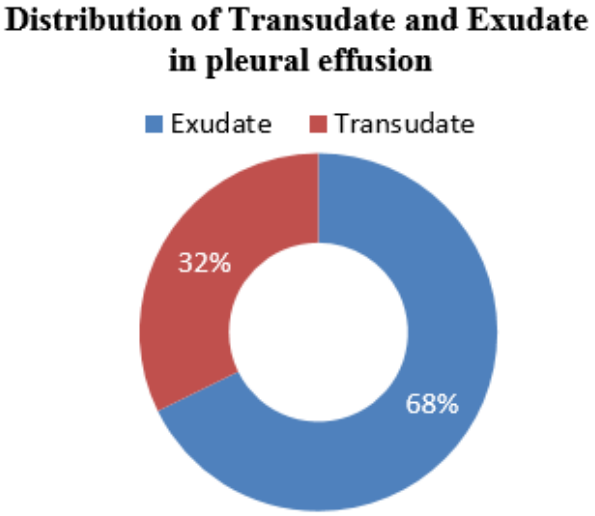
Authors, Ref. No.	Transudate	Exudate
Valdes et al.[24]	26%	74%
RamKN et al.[25]	32%	67%
Pujan Parikh et al.[18]	9%	91%
Jaisonk et al.[26]	39%	61%
Ambresh et al.[27]	23%	77%
Dharwadkar et al.[28]	16%	84%
Mahima Sharma et al.[9]	37%	63%
Present study	32%	68%

Table 10: Shows cytological pattern and diagnosis of pleural fluid

Predominant cytological pattern	Cytological impression	Ayyagari Sudha et al.[13]	Sandeep V et al.[5]	Lekha MB et al.[6]	Present study
Predominantly Lymphocytes	Chronic inflammation	57%	46%	52%	35%
Predominantly Polymorphs	Acute inflammation	5%	32%	17%	10%
Lymphocytes, Polymorphs, Mesothelial cells	Inflammation	13%	-	-	12 %
Chiefly mesothelial cells	Reactive effusion	9%	4%	19%	18%
Malignant cells	Positive for malignancy	14%	14%	7%	19%
Atypical cells	Suspicious for malignancy	2%	-		%
Degenerative and few cells	Unsatisfactory for evaluation	-	2%	5 %	4 %

Table 11: Shows primary site of malignancy showing malignant cells in pleural effusion in various studies.

Authors, Ref. No.	Lung	Breast	Ovarian
Pairman L et al.[29]	40%	15%	10%
Sunita G et al.[11]	29%	18%	0%
Khan et al.[30]	69%	12%	0%
Sudha A et al.[13]	46%	12%	17%
Loveland P et al.[17]	44%	7%	11%
Chakrabarti et al.[19]	45%	27%	18%
ArnoldDT et al.[31]	39%	17%	15%
PorntipJ et al.[32]	61%	33%	0%
Presentstudy	71%	13%	16%



Graph 2: Shows distribution of Transudate and Exudate in pleural effusion

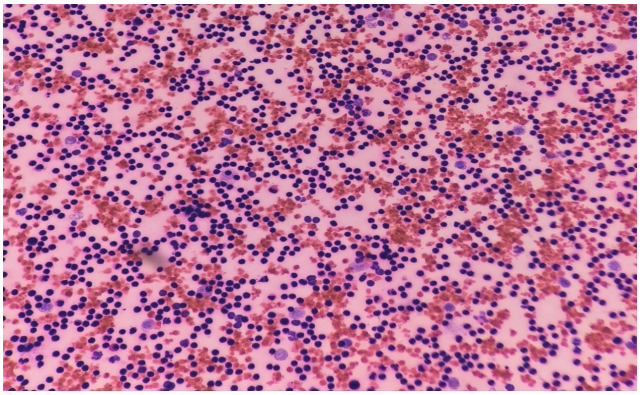


Figure 1: Shows plenty of lymphocytes (Chronic inflammation) [H&EX400]

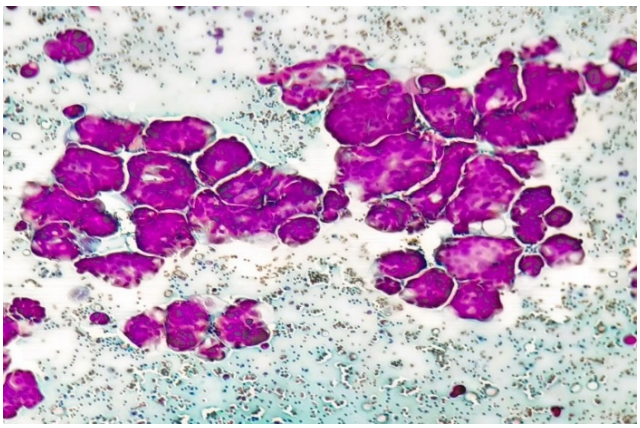


Figure 2: Shows tight cluster of malignant cells with a smooth contour in case of lung carcinoma [PAP X 100]

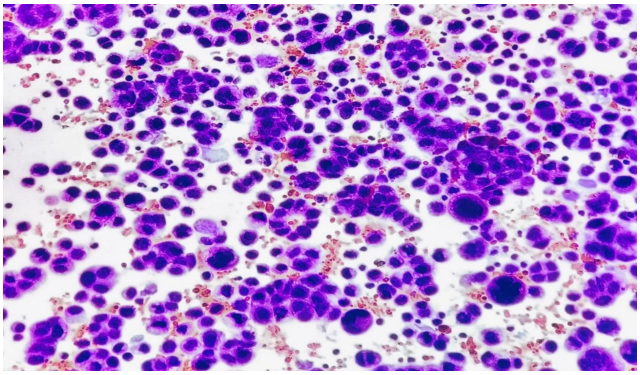


Figure 3: Shows malignant cells arranged in acini, sheets, cluster, and singly scattered in a case of lung carcinoma [H&E X 400].

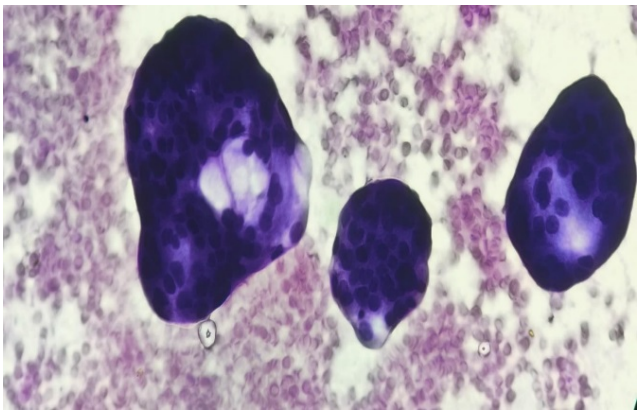


Figure 4: Shows a 3-D ball cluster of malignant cells in a case of breast carcinoma [H&E X 400]

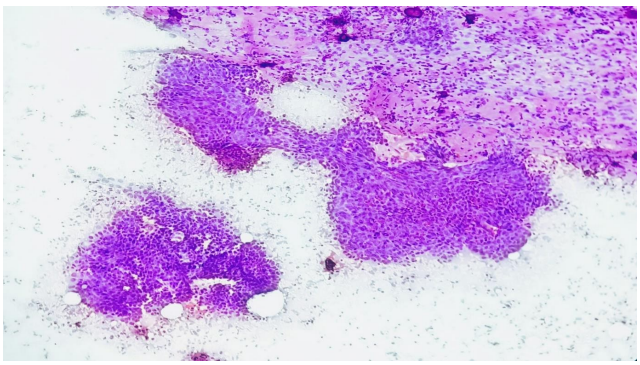


Figure 5: Shows metastatic carcinoma with papillary configuration in case of primary ovarian malignancy [H&E X 400]

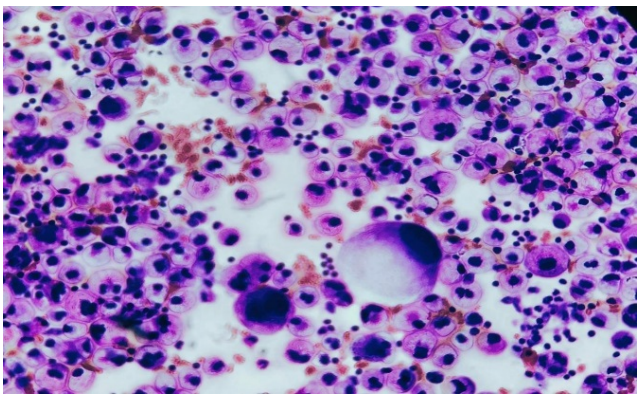


Figure 6: Shows sheets of reactive mesothelial cells having vacuolated eosinophilic cytoplasm background shows lymphocytes. [H&E X 400]

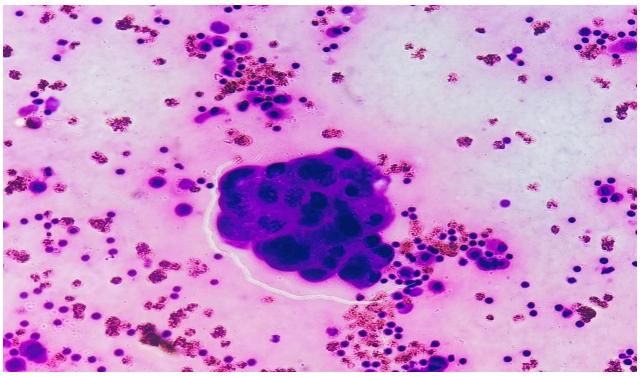


Figure 7: Shows a cluster of reactive mesothelial cells with knobby contour, background shows scattered mesothelial cells and lymphocytes [H&E X 400]

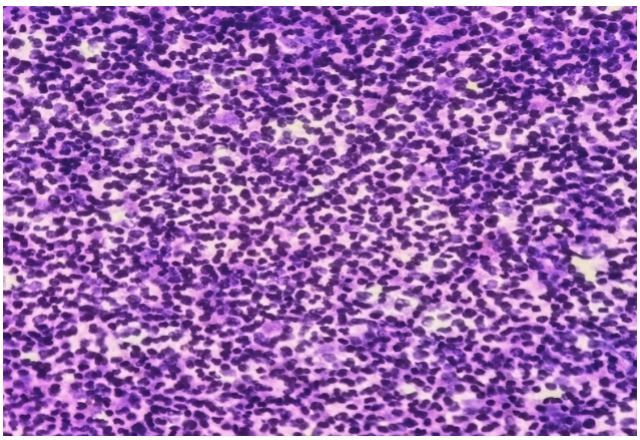


Figure 8: Shows plenty of Polymorphs (Acute inflammation). [H&EX400]

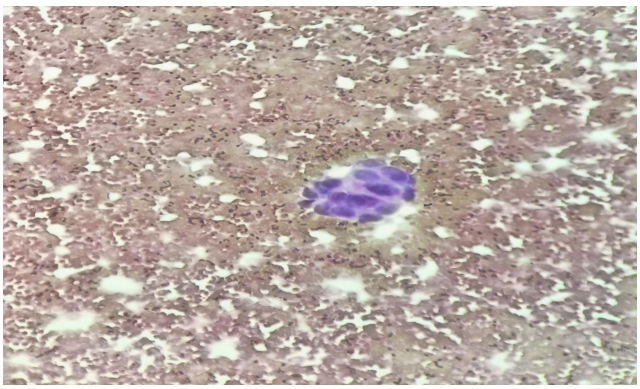


Figure 9: Show sanoccasional cluster of malignant cells in the hemorrhagic background- Suspicious for malignancy [H&E X 400]

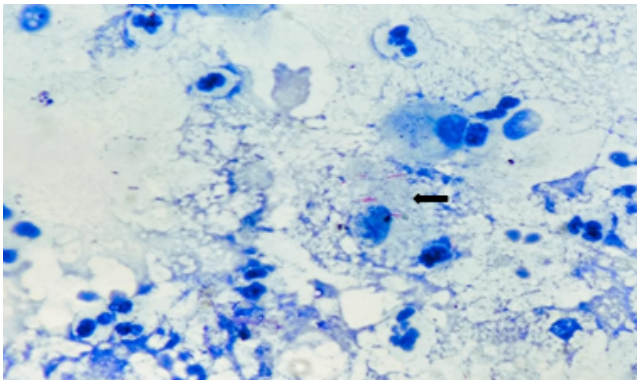


Figure 10: shows Acid-fast bacilli (arrow) in case of tuberculosis [Ziehl Neelsen stain X 1000]

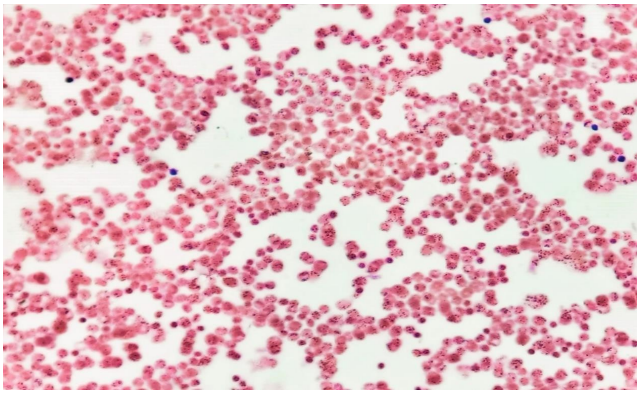


Figure 11: Shows plenty of red blood cells, Unsatisfactory for evaluation [H&E X 400]

48 (19%) cases. These smears showed high nucleus: cytoplasmic ratio, hyperchromatic nuclei, coarse chromatin arranged in a cluster, 3 db all cluster of tumour cells and tumour cells forming papillary configuration (Figures 2, 3, 4 and 5). Retrospective evaluation of malignant effusion for the primary site, lung cancer 34/48 (71%) was the commonest cause followed by ovarian carcinoma 8(16%), and breast carcinoma 6 (13%). All malignant effusion cases were adenocarcinoma type. In 44 (18%) cases reactive effusion comprising reactive mesothelial cells were noted. The reactive mesothelial cell were arranged incluster with knobby cont our, clefts or "windows" in between mesothelial cells, the mesothelial cells had round and single central or eccentric nucleus (Figures 6 and 7). Smears predominantly showing polymorphs 24 (10%) cases were diagnosed as acute inflammatory cells (Figure 8). 4 cases were suspicious for malignancy which showed either singly scattered bizarre cells or cluster of atypical cells with a high N: C ratio (Figure 9). Only two cases out of 36 cases with clinical diagnosis of tuberculous effusion showed acid-fast bacilli in the smear (Figure 10). 10 cases were unsatisfactory for evaluation which showed only RBCs and degenerative cells (Figure 11).

In the present study total of 36 clinically diagnosed cases of tuberculous effusion, 32 cases were>40U/L value of ADA and 4 cases were <40U/L. The mean value of fluid protein was 3.9gm/dl and ADA was 12.65U/L in the malignant effusion. In pneumonia cases mean value of protein was 5.3 gm/dl.

4. Discussion

Investigations of the pleural effusions by cytologic examination are of much importance in the diagnosis of diseases as well as for the exclusion of neoplasia. A cytologic examination of the pleural fluid performed on the smears of centrifuged specimens helps in differentiating benign from malignant effusions. Cyto-diagnosis of pleural fluid represents the cell population from a much larger representative area than obtained from the needle biopsy. It also aids in establishing the nature of malignancy in many cases and helps in the planning of treatment. It eliminates the need for invasive procedures and unnecessary surgical intervention, thus making the pathologist contribute positively to the clinical diagnosis and management of patients. There are many techniques used in the processing of fluid specimens. They include conventional centrifugation, cyto-spin preparations, membrane filtration, cellblocks, and LBC. Most of the laboratories still use conventional techniques because it is more convenient, cost-effective, and easy to perform. In our laboratory, we routinely use conventional centrifugation techniques for preparing smears from fluid samples.

The demographic data in various studies carried out on pleural fluid is shown in Table 5. Different studies showed male predominance in the range of 60 to 70% and female in the range of 30 to 40%. In the present study the gender composition comprised of 70% males and 30% females. Our findings are comparable with other reports.[5–10]

Table 6 shows comparative study of age distribution of the cases. The youngest patient in our study was 9-month-old boy and the oldest patient 97 years old male. 35% of our patient were in the age range of 61 to 80 years followed by (33%) in the age range of 41 to 60 years. Only 4% patients were in 0–20-year age group, and 19 % were in 20 – 40 years age group. 3-7% patient was in 0-20 age group seen in studied done by Chakrabarti et al.,[15] Satvik B et al.,[14] Sunita G et al.[11] And Shaukin et al.[12] Compared with our study and 9-13% cases seen in others studies was not compare with our study.[5,6,13] In age group 21-40 year, our study was in concordance with studies done by Sandeep V et al.,[5] Shaukin et al.,[12] Lekha M B et al.,[6] Shobha SN et al.[8] and 29-50 % case was seen in other studies was differed from our study.[13,26] 24-34% patient were in 41-60 age group seen in studied done by Sandeep V et al.,[5] Shaukin et al.,[12] Sudha A et al.,[13] and Chakrabarti et al.[15] Comparable with present study and 40-42% cases seen in other studies was not comparable with our study.[6,11] In present study 35% patient were seen in 61- 80 age group was compared with study done by Sandeep V et al.,[5] Shaukin et al.[12] 15-19% cases were seen in 61-80 age group in other studies.[6,8,11] In more than 80 age group 9% case were seen in our studies and1–6% cases were seen in other studies.[5,6,11–13]

Table 7 shows clinical diagnosis of pleural effusion in various studies. Non-malignant causes such as pneumonia, tuberculosis, heart failure, and liver diseases are found in 79% of cases while malignancy-related reasons make up the remaining 21%. In our study pneumonia was, the most common cause followed by malignant and tuberculous effusion. In our study pneumonia 36% cases was higher than other studies cases 7 to 25%.[8,10,16–18] Patient of tuberculosis 35-62% was found in other studies was not comparable with our study (15% cases). 2 to 5% cases of tuberculosis found in studies of Loveland P et al.[17] and Sadullahoğlu et al.[10] Our study was in concordance with studies done by Gayathri M N et al.,[16] Parikh P et al.,[18] and Shobha SN et al.[8] where malignant effusion cases was 13-20%. Malignant effusion 39-49% cases found in Sadullahoğlu et al.,[10] and Loveland P et al. studies.[17] The disparity observed between other studies may be attributed to the common clinical diagnosis of pneumonia in the present study and varied sample size as well as a selection criterion in the different studies.

Table 8 shows physical finding of pleural fluid in various studies. In the present study, we found 48 % samples of pleural fluid having turbid and yellow in appearance were in the concordance with the study of Wasim et al.,[20] and Chakrabarti et al.[19] Turbid, reddish fluid contains 26% cases in the present study, which was similar with the study of Akhila P et al.,[22] Cuneyt T et al.,[23] Wasim et al.[20] and

Chakrabarti et al.[19] Present study has 19% clear and straw-coloured pleural fluid appearance which was in concordance with the study of Mulkalwar M et al.[21] and Wasim et al.[20] while it was less in the study of Chakrabarti et al.[19]

Table 9 shows transudate and exudate fluid in various study. According to the study, exudate was predominant to transudate with the former having a percentage of 68% and the latter with 32%. This is comparable with the previous studies done by Ram KN et al.,[9] Mahima Sharma et al.,[24] Valdes et al.[25] and Jaisonk et al.[26] Exudate effusion 84-91% cases found in other studies was not compare with our study.[18,28]

Table 10 in the present study, the predominant cytological pattern diagnosis. In the present study predominant cytological pattern found was lymphocyte rich 35 % cases which is discordance with the study of Ayyagari Sudha et al.,[13] Sandeep V et al.[5] and Lekha M B et al.[6] Predominantly lymphocytic cytological pattern is followed by malignant cells found in 19% cases which is similar to the study of Ayyagari Sudha et al.[13] and Sandeep V et al.[5] Smear with chiefly mesothelial cells (18%) cases were concordance with Lekha M B et al.[6] Ayyagari Sudha et al.,[13] & Sandeep V et al.,[5] found only 4-9% cases. Lekha MB et al.,[6] found only 6% cases of effusion having malignant cell differed from our study. We found 12% cases of mix inflammatory cells effusion which is in compare with Ayyagari Sudha et al.[13] In the present study, we found 2% cases suspicious for malignancy which is in correlation with the study of Ayyagari Sudha et al.[13] while Sandeep V et al.,[5] and Lekha M B et al.,[6] did not find any atypical cell pattern. In our study 4% cases of unsatisfactory for evaluation found which is in compare with Lekha MB et al.[6]

Table 11 shows malignant pleural fluid for the primary site in various studies. In the present study, 24 cases were malignant effusion and lung carcinoma cases 71 % was the most common primary site which agrees with the study of Khan et al.,[30] and Porntip J et al.[32] and 29-46 % cases seen in various other studies.[11,13,17,19,29–32] In our study, 13 % cases found of breast carcinomas primary site which is concordance with the study of Pairman L et al.,[29] Khan et al.,[30] Sunita G et al.,[11] Sudha A et al.[13] and Arnold DT et al.[31] 27-33% breast malignancy cases found as primary in Chakrabarti et al.,[19] and Porntip J et al.,[32] studies which are not compared with our study. In the present study, 16% cases found of carcinomas as a primary site which is compared with Sudha A et al.,[13] Chakrabarti et al.,[19] and Arnold DT et al.[31] Fewer cases 9 to11% found in studies done by Pairman L et al.,[29] and Loveland P et al.[17]

5. Conclusion

Cytological analysis of pleural fluid is crucial for diagnosing various lesions. Differentiating between transudate and exudate helps determine the underlying cause. Detecting malignant cells is a key goal, while also identifying inflammatory and infective conditions. Non-neoplastic effusions are common, with adenocarcinoma being the most prevalent malignancy. In resource-limited settings, pleural fluid analysis remains a cost-effective and safe initial investigation for suspected malignant effusions. It can aid in diagnosing primary and metastatic pleural malignancies when combined with clinical history and other tests.

6. Data and Material Availability

Department of Pathology, of a tertiary care centre, Gujarat, India.

7. Authors' Contributions

All the authors including corresponding author have contributed equally towards data collection, data analysis, and preparation of the draft and approval of the final manuscript of this article.

8. Source of Funding

None to disclose.

9. Conflict of Interest

None declared.

10. Acknowledgement

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