

## ORIGINAL ARTICLE

### CYTOLOGICAL STUDY OF PLEURAL FLUIDS AND ITS CLINICOBIOCHEMICAL CORRELATION

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**ABSTRACT:** A study of analysis of 50 pleural fluids was carried out at major teaching hospital, in Mumbai over a period of three years. Of these 50 fluids were 33 were transudates and 17 exudates. Male predominance (72%) was observed with the majority in 3<sup>rd</sup> decade. Tuberculosis (30 cases) was the commonest conditions associated with exudates followed by synpneumonic effusions. Majority of the tuberculous cases (80%) showed WBC count between 1000-5000 cells/cmm. Polymorphs were predominant in synpneumonic effusions. Of the 2 cases of malignant effusion, malignant cells (well differentiated adenocarcinoma) were detected in both the cases, with total WBC counts ranging between 1000-5000cell/cmm. The correct diagnosis of the fluid as transudate or exudate is important because if the fluid is exudative then further diagnostic procedures like cytopathology, pleural biopsy and other invasive procedure can be done for definite diagnosis. On the other hand, if the fluid is transudative then treatment for underlying conditions like CCF, nephrotic syndrome, cirrhosis is given. The presence of cancer cells in the fluid is a proof positive of malignancy related fluid but in 30 to 60 percent of cancer cases, cancer cells are not detected. Exfoliative cytology for malignant cells is highly specific though less sensitive (40-60%). Definitive diagnosis may depend upon clinical correlation and histological examination.

**KEYWORDS:** Pleural fluid, Tuberculosis, Malignancy, Etiological incidence.

**INTRODUCTION:** Pleural effusion means abnormal accumulation of fluid within pleural cavity. Normally it contains 0.1 to 0.2 ml/kg body weight of fluid.<sup>(1)</sup> Pleural effusion is a common clinical conditions and pose a diagnostic problem to the clinicians.

Some of the causes include congestive cardiac failure, cirrhosis, neoplasms and infections. Pleural effusions are classically divided into transudates and exudates. By traditional classification, if the fluid protein is more than 3gm% then it is exudate and fluid protein less than 3gm% is called transudate.<sup>(2)</sup>

Transudates are clear low protein content fluids and a glucose content similar to serum and are produced in disorders that cause increased hydrostatic pressure or decreased oncotic pressure. Exudates are slightly hazy fluids with a high protein content and low glucose level and are produced in conditions where the pleural pressure and lymphatic flow decreases and the pleural protein permeability increases.

The correct diagnosis of the fluid as transudate or exudate is important because if the fluid is exudative then further diagnostic procedures like cytopathology, pleural biopsy and other invasive procedure can be done for definite diagnosis so that specific therapy can be started. On the other hand, if the fluid is transudative then treatment for underlying conditions like CCF, nephritic syndrome, cirrhosis is given.

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Nearly all malignancies can occasionally present with or develop pleural effusion. The differentiation of the fluid into malignant or non-malignant fluid has a deep impact on the course of the treatment to be followed. The presence of cancer cells in the fluid is a proof positive of malignancy related fluid but in 30 to 60 percent of cancer cases, cancer cells are not detected. Exfoliative cytology for malignant cells is highly specific though less sensitive (40-60%). Definitive diagnosis may depend upon clinical correlation and histological examination. Benign conditions like ovarian cystadenoma may show psammoma bodies in one third cases.<sup>(3,4)</sup>

The present study is undertaken to detect malignancy, differentiate pleural fluids into transudates and exudates by using fluid protein parameter and also to correlate with clinical findings.

**MATERIALS AND METHODS:** A three years study which included one year retrospective study from May 2008 till April 2009 and two years of prospective study from May 2009 till April 2011 was carried out at the clinical laboratory of the teaching hospital in Navi Mumbai.

A total number of 50 cases of pleural fluids were studied.

## Every fluid was processed in the following way:

- ❖ Physical examination was done by noting the appearance and colour and also by observing the ability of pleural or peritoneal fluid to clot.
- ❖ Total WBC count and RBC count of fluid was carried out using Neubauer's chamber.
- ❖ Then fluid was centrifuged for 5 minutes at 1500/rpm. From the sediment, smears were prepared and stained by field's and leishman stain for differential count and papanicolaou stain for cytology.
- ❖ Supernatant was analysed for biochemical parameters (fluid protein).

**Criteria for Selection of Patients:** The patients presenting with pleural effusion were taken into account. All cases were clinically diagnosed.

## RESULTS:

| Diagnosis               | No. of Cases | %          |
|-------------------------|--------------|------------|
| Tuberculosis            | 30           | 60         |
| Synpneumonic effusion   | 9            | 18         |
| Liver cirrhosis         | 7            | 14         |
| Malignancy              | 2            | 4          |
| Anaemia-hypoproteinemia | 2            | 4          |
| <b>Total</b>            | <b>50</b>    | <b>100</b> |

Table 1: Etiological Classification of 50 Cases of Pleural Fluids

Tuberculosis (60%) was found to be the most common cause of pleural effusions.

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| Diagnosis               | Gender         |                | Age (years) |           |          |           |          | Total     |
|-------------------------|----------------|----------------|-------------|-----------|----------|-----------|----------|-----------|
|                         | Female         | Male           | 10-20       | 20-30     | 30-40    | 40-50     | >50      |           |
| Malignancy              | 1(50%)         | 1(50%)         | 0           | 0         | 0        | 0         | 2        | 2         |
| Tuberculosis            | 8(26.6%)       | 22(73.3%)      | 4           | 10        | 4        | 8         | 4        | 28        |
| Cirrhosis               | 1(14.3%)       | 6(85.7%)       | 0           | 2         | 3        | 2         | 0        | 7         |
| Synpneumonic Effusion   | 2(22.2%)       | 7(77.8%)       | 2           | 2         | 0        | 3         | 2        | 9         |
| Anaemia-hypoproteinemia | 2(100%)        | 0              | 0           | 1         | 0        | 0         | 1        | 2         |
| <b>Total</b>            | <b>14(28%)</b> | <b>36(72%)</b> | <b>6</b>    | <b>15</b> | <b>7</b> | <b>13</b> | <b>9</b> | <b>50</b> |

Table 2: Age and sex distribution of 50 pleural fluid cases

Male predominance was found in all the diseases (72%) causing pleural effusions. Majority of the cases were tuberculosis (20%) and found in the 3<sup>rd</sup> decade.

| Diagnosis               | Colour       |           |          |           | Total     |
|-------------------------|--------------|-----------|----------|-----------|-----------|
|                         | Haemorrhagic | Straw     | Turbid   | Yellow    |           |
| Malignancy              | 1            | 0         | 1        | 0         | 2         |
| Tuberculosis            | 0            | 20        | 0        | 10        | 30        |
| Liver cirrhosis         | 0            | 2         | 0        | 5         | 7         |
| Synpneumonic effusion   | 0            | 7         | 0        | 2         | 9         |
| Anaemia-hypoproteinemia | 0            | 1         | 0        | 1         | 2         |
| <b>Total</b>            | <b>1</b>     | <b>30</b> | <b>1</b> | <b>18</b> | <b>50</b> |

Table 3: Gross appearance of fluid in 50 pleural fluid

In tuberculosis majority of the cases (80%) showed W.B.C counts between 1000-5000cell/cmm. In synpneumonic effusion, polymorphs were predominant cells.

| Diagnosis                 | Total WBC counts |               |           | Total     |
|---------------------------|------------------|---------------|-----------|-----------|
|                           | <1000/cmm        | 1000-5000/cmm | >5000/cmm |           |
| Malignancy                | 0                | 2             | 0         | 2         |
| Tuberculosis              | 6                | 24            | 0         | 30        |
| Synpneumonic Effusion     | 2                | 7             | 0         | 9         |
| Liver cirrhosis           | 7                | 0             | 0         | 7         |
| Anaemia – Hypoproteinemia | 2                | 0             | 0         | 2         |
| <b>Total</b>              | <b>17</b>        | <b>33</b>     | <b>0</b>  | <b>50</b> |

Table 4: Distribution of Leucocyte Count in 50 Cases of Pleural Fluid of Various Etiologies

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| No. of Pleural fluid cases            | Histopathological diagnosis        | Malignant cells detected |
|---------------------------------------|------------------------------------|--------------------------|
| 1                                     | well differentiated adenocarcinoma | Detected                 |
| 2                                     | well differentiated adenocarcinoma | Detected                 |
| Table 5: Cytology of Malignant Fluids |                                    |                          |

**DISCUSSION:** Pleural effusion represents a very common diagnostic problem. It occurs in a variety of diseases.

**ETIOLOGICAL INCIDENCE:** Light et al has reported 68.7% of the cases belonging to exudative group and remaining 31.3% to transudates.<sup>[5]</sup> In my study only 66% were exudative and 34% transudative. Tuberculosis was the most common cause of pleural effusion, (60%) which is comparable to findings of Leuallen E.C and Carr D.T et al.<sup>[6]</sup>

The incidence of malignancy in the study was 4% which is comparatively lower than the findings of Hirsch A.et al (39%) and Light et al (43%).<sup>[7,5]</sup>

The incidence of synpneumonic effusion and liver cirrhosis in the study was 18% and 14% respectively comparable to findings of Romeo et al (16% and 14%).<sup>[8]</sup>

Valdes et al <sup>[9]</sup> has reported 1% of anaemia–hypoproteinemia cases whereas in my study, it was 4% incidence.

**AGE AND SEX INCIDENCE:** Males were affected more (72%) than the females (28%).

In malignancy, Hirsch A.et al has reported 64.1% involvement of males and 35.9% females with the average age of 53 years.<sup>[7]</sup> In the present study incidence of malignancy was 4% with males and females were equally affected and were beyond 5<sup>th</sup> decade. The incidence of tuberculosis was found to be 60% with male predominance (73.3%) and also the leading cause in all the age groups.

Male predominance was seen in synpneumonic effusion (77.8%) and liver cirrhosis which is in accordance with Romero et al<sup>(8)</sup> and Hirsch et al<sup>(7)</sup> whereas female predominance was observed in severe anaemia-hypoproteinemia (100%).

**PLEURAL FLUID GROSS EXAMINATION:** In tuberculosis, the pleural fluid were clear yellow to straw coloured in all which is similar to the reports of Baganha M. F et al.<sup>(10)</sup>

In malignant effusion, all the cases showed turbid to hemorrhagic fluid whereas synpneumonic effusion, liver cirrhosis and anaemia-hypoproteinemia, it was yellow to straw coloured.

**PLEURAL FLUID CYTOLOGY:** Total WBC count >1000 cells/cumm was observed in 80% of the tuberculosis cases and <1000 cells/cumm were seen in 20% of the cases. Polymorph predominance may also occur in pulmonary embolism, asbestos exposure related effusions.<sup>(11)</sup>

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In malignancy total WBC >1000cells/cumm were observed whereas in liver cirrhosis and anaemia-hypoproteinemia, <1000 cells/cumm were observed

In synpneumonic effusion, 77.7% cases showed 1000-5000 cells/cumm and remaining cases showed <1000 cells/cumm.

All these findings are in accordance with findings of Light et al. Lymphocytic predominance was found in the cases of TB and malignancy. In synpneumonic effusions, 88.9% of the cases showed polymorph predominance.

In case of malignancy, malignant cells were found in both of the cases. Hirsch et al and few other studies have stated that cytological examination reveals positivity in 50-60% cases of the cases of malignancy.<sup>(7,10,12)</sup> Repeat sample examination markedly increases the diagnostic yield has been stated by some authors.<sup>(13)</sup> Bielsa et al<sup>(14)</sup> found that tumor markers in pleural fluid could be useful independent survival predictor.

**CONCLUSION:** Tuberculosis was the commonest conditions causing pleural effusion and male predominance (72%) was observed with the majority in 3rd decade. It was followed by synpneumonic effusions. Majority of the tuberculous cases (80%) showed WBC count between 1000-5000 cells/cmm. Of the 2 cases of malignant effusion, malignant cells (well differentiated adenocarcinoma) were detected in both the cases, with total WBC counts ranging between 1000-5000cell/cmm. The correct diagnosis of the fluid as transudate or exudate is important as further line of management will differ. Exfoliative cytology for malignant cells is highly specific though less sensitive (40-60%). Definitive diagnosis may depend upon clinical correlation and histological examination.

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