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Co-Relation OfCytomorphology With Absolute Ldh Gradient And Fluid Ada Levels In Determining The Type Of Pleural Effusion.

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Abstract:
Present Study is done with an aim to co-relate the cytomorphology with Absolute LDH gradient and Fluid ADAlevels in determining the type of pleural effusion.
On calculating the mean Absolute LDH gradient (serum-fluid LDH after dropping the negative sign)along with standard deviation after performing the biochemical analysis of pleural fluid, the exudative effusion fluid had an absolute LDH gradient value of 3356.20+4985.20 U/L (highest), tubercular effusion fluid had an absolute LDH gradient value of 1361.36+ 1609.50 U/L, malignant/ suspicious of malignancy effusion fluid had an absolute LDH gradient value of 1376+1181.79 U/L while transudative fluid had an absoluteLDH gradient value of 107.91+61.60U/L (lowest).
On calculating the mean ADA levels along with standard deviation after performing the biochemical analysis, the exudative effusion fluid (including tubercular) had an ADA value of 54.37+56.71U/L (highest), malignant/ suspicious of malignancy effusion fluid had an ADA value of 31.09+02.81U/L while transudative effusion fluid had an ADA value of 23.46+15.22U/L (lowest).
The mean and standard deviation values of ADA according to cytology reports showed that it was highest in chronic inflammatory smear (exudates- tubercular) and least in case of inflammatory smears (transudate).
The mean and standard deviation values of Absolute LDH gradient according to cytology reports showed that it was highest in acute inflammatory smears (exudates) and found to be least in case of inflammatory smears (transudate).
Using the Biserial correlation method, when the cytologic types of pleural fluid were correlated with absolute LDH gradient values the p- value (0.011) was found to be statistically significant in acute inflammatory smears (exudates). Alternatively, when the cytologic types of pleural fluid were correlated with pleural fluid ADA values the p- value (0.001) was found to be statistically significant in chronic inflammatory smears (tubercular-exudates).
Cytomorphological analysis of body fluids is an important investigation which is very convenient, cost effective, accurate and also safe . It gives a clue to diagnose any underlying neoplastic or non- neoplastic diseases that may change prognosis, further management or outcome of patient. In cases of malignant effusion it is crucial in staging and deciding further protocol of treatment.

Keywords: Pleural effusion, Correlation, Cytomorphology,Absolute LDHGradient, Fluid ADA.
Study Design: Observational Study.

1. INTRODUCTION:-

Pleural fluid occupies the space enclosed by the visceral (inner) and parietal (outer) membranes surrounding the lungs[1]. Formation of the fluid occurs by filtration of plasma across the capillary walls and the pleural mesothelial cells in the parietal membranes, following a hydrostatic pressure gradient[1]. Lymphatics opening through the parietal membranes actively drain the pleural spaces, generating the negative hydrostatic pressure in the pleural space[1]. In healthy individuals, there is less than 10ml pleural fluid in each pleural space[1].

NORMAL COMPOSITION OF PLEURAL FLUID[2]:-
Volume:- 0.1-0.2ml/kg
Cells/mm^3 :- 1000-5000
% Mesothelialcells :- 3-70%
% Monocytes :- 30-75%
% Lymphocytes :- 2-30%
% Granulocytes :- 10%
Protein:- 1-2 g/dl
% Albumin :- 50-70%
Glucose :- Same as plasma level.
LDH :- <50% of plasma level.
pH :- >plasma pH.

HISTORY:-

Pleural effusion was first described by Hippocrates as early as in 5th century B.C. in a patient with pneumonia[3]. Later in 1820, Laennec described pneumothorax and haemorrhagic pleurisy and association of pthysis and pleurisy with effusion[4]. Armand Troussseau in 18th century aspirated fluid from pleural cavity for the first time[4]. Georges Dieulafoy used trocar in the aspiration of the pleural fluid[4]. Defrancis and associates used a Vim Silvermann needle for the first time for obtaining biopsies from parietal pleura[4]. Abraheus performed a pleural biopsy using Harrifield biopsy needle[4]. Emerson described pleural effusion due to lymphatic obstruction (Yellow Nail Syndrome)[4]. Gaensler and Kaplan described benign pleural effusion due to exposure to asbestos[4]. Light and Ball described measurement of pleural fluid lactate dehydrogenase to differentiate transudates and exudates[4].

Transudates have been differentiated from exudates by using established Light's criteria since long[5]. Light's criteria defines exudative pleural effusions as having either – (a)a ratio of >0.5 between total pleural and plasma protein, (b) a ratio >0.6 between pleural and plasma lactate dehydrogenase (LDH) and (c) pleural LDH higher than two thirds (>200U/L) of the normal serum level[6]. The sensitivity of Light's criteria in identifying exudative pleural effusions is high (98%); however its ability to exclude transudates remains low[6]. This classification as transudates or exudates ; reflects the likely location of the pathological process causing the effusion[6]. Thus the presence of an exudates usually implies pleural disease, likely to need further investigation, whereas a transudate reflects disease outside the pleural space, which is often clinically apparent[6]. Heffner et al carried out a patient level meta – analysis of studies and showed (a) pleural fluid protein >2.9g/dl, (b) pleural fluid cholesterol >45mg/dl and (c) pleural fluid LDH >45% of upper limits of normal plasma levels[7].

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CAUSES OF PLEURAL EFFUSION[8]:-

A. Transudative pleural effusion.

a. Increased hydrostatic pressure.
1. Congestive cardiac failure.
2. Constrictive pericarditis.
3. Pericardial effusion.
4. Constrictive cardiomyopathy.
5. Massive pulmonary embolism.

b. Decreased capillary osmotic pressure.
1. Cirrhosis of liver.
2. Nephrotic syndrome.
3. Malnutrition.
4. Protein losing enteropathy.
5. Small bowel disease.

c. Transmission from peritoneum.
1. Any cause of ascitis.
2. Peritoneal dialysis.

d. Increased capillary permeability.
1. Small pulmonary emboli.
2. Myxedema.

e. Miscellaneous.
1. Acute atelectasis.
2. Wet Beriberi.
3. Idiopathic.

B. Exudative pleural effusion.

a. Infections.
1. Bacterial infections.
2. Lung Abscess.
3. Pulmonary Tuberculosis.
4. Fungal &Actinomycotic disease.
5. Viral infections.
6. Hepatic Amoebiasis.
7. Parasitic infection.

b. Neoplasms.
1. Bronchogenic carcinoma.
2. Metastatic disease.
3. Pulmonary secondaries.
4. Mesothelioma of pleura.
5. Lymphoma.
6. Leukemia.
7. Pleural sarcoma.
8. Chest wall tumors.

c. Collagen Vascular Disease.
1. Post Myocardial Infarct.
2. Rheumatoid disease.
3. Systemic Lupus Erythematosus.

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4. Rheumatic Fever.
5. Drug Induced Lupus.
6. Sjogren Syndrome.
7. Churg- Strauss Syndrome.
8. Sarcoidosis.

d. Gastrointestinal Disease.

1. Acute Pancreatitis.
2. Esophageal perforation.
3. Diaphragmatic Hernia.
4. After abdominal surgery or liver transplant.
5. Malignant mesothelioma of peritoneum.
6. Hepatic Abscess.

e. Pulmonary embolism and infarction.

f. Miscellaneous.

1. Meigs Syndrome.
2. Drug reactions.
3. Radiation therapy.
4. Asbestos exposure.
5. Yellow Nail Syndrome.
6. Hemothorax.
7. Iatrogenic injury.
8. Chylothorax.

Both malignant and non- malignant cases of pleural effusion can be identified by pleural fluid cytology[9].

Lactate Dehydrogenase (LDH) is widely distributed in many body tissues. It is a hydrogen transfer enzyme that catalyzes the oxidation of L- lactate to pyruvate with the mediation of NAD+ as a hydrogen acceptor[10]. It is a tetramer composed of four polypeptide chains[10]. There are five component isoenzymes as a result of the five different combinations produced by two polypeptide chains encoded by separate genes (M and H)[10]. In the heart H gene is more active than the M gene, latter being strongly expressed in the skeletal muscle[10]. As the number of M over H chains increases, the LDH isoenzyme becomes more efficient in catalyzing the conversion of pyruvate to lactate (LDH-5), while an increase in H over M chains (LDH-1) favours the conversion of pyruvate to acetyl- coenzyme A that enters into the citric acid cycle[10].

The various types of LDH and their locations in human body are[10] :-

1. LDH -1(4H) : In the heart, RBC's and brain.
2. LDH -2 (3H1M) : In the reticuloendothelial system.
3. LDH -3 (2H2M) : In the lungs.
4. LDH -4 (1H3M) : In the kidneys, placenta and pancreas.
5. LDH -5 (4M) : In the liver, striated muscles and brain.

When the LDH levels are elevated , it means that tissues may have been damaged or are diseased[11].

The normal range of total serum LDH is[11]:-

- Newborns: 160-450U/L.
- Children : 60-170U/L.
- Adults : 140-280U/L.

A cholesterol concentration above 55 mg/dl combined with an LDH concentration above 200U/L is highly specific for the presence of an exudate[12].

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Since, LDH is a marker of inflammation or cellular injury and is a sensitive but non- specific pathological marker[13], so LDH levels of greater than 3 times the upper limit of normal (often >1000U/L) are often indicative of pleural infection, in the appropriate clinical scenario and can also be associated with rheumatoid pleurisy, tuberculous pleurisy or malignancy[14,15].

The **Absolute LDH gradient** means difference between serum and pleural fluid LDH levels and it neglects the negative sign of difference between serum and fluid LDH.

Adenosine deaminase (ADA) is an enzyme catalyzing the conversion of the adenosine and deoxyadenosine to the inosine and deoxyinosine in the purine degradation pathway and plays an important role in the differentiation of lymphoid cells. Its quantity increases in the immature and non- differentiated T- lymphocytes following mitogenic and antigenic stimulation[16].

ADA is a T-cell (CD4+) metalloenzyme whose presence in high levels within pleural fluid strongly indicates tuberculosis particularly in high prevalence areas[17]. High pleural ADA is also detected in non- TB settings including malignancy, rheumatoid arthritis, systemic lupus erythematosis and parapneumonic effusions[17]. In view of this, it is important to acknowledge that two ADA isoenzymes exist; ADA-1 and ADA-2 (found only in monocytes and macrophages) with the latter related in increased levels in the tuberculous setting. In meta-analysis of 63 studies, ADA is reported to have a sensitivity of 92% and a specificity of 90%, whilst within the setting of a lymphocytic predominant effusion, ADA>40U/L is almost exclusively secondary to tuberculosis[17]. Paradoxically retrospective study of 221 patients has illustrated that ADA levels >250U/L do not generally occur in tuberculosis related effusion[18]. Such levels are in fact found in patients with empyema or lymphoid –related malignancies[19]. Therefore, pleural fluid ADA should be interpreted in parallel with clinical findings and other traditional methods such as tuberculin skin test to reach a diagnosis[19]. Such a combination of clinical features with pleural ADA measurement has excellent diagnostic value with a sensitivity and specificity rates of 95% and 97% respectively[18]. Hence, experts have recommended, if measured ADA levels in low- prevalence areas have a concentration <40U/L, it almost exclusively rules out tuberculosis- driven effusions[19].

ADA activity may be dependent more on the pathologic stimulus e.g. TB and rapidity of T-lymphocyte proliferation, and not on amount of lymphocytes present[20].

The biochemical analysis of pleural fluid should be done within 4 hours after the sample is obtained[21]. If a delay is anticipated , a specimen collected in tubes containing an anticoagulant (heparin or EDTA) can be refrigerated at $4^{o}C$ for upto 1 day with no significant effects on white blood cell count and differential[21]. ADA measurement and cytologic interpretation remains reliable after a longer refrigeration time (upto 28 days and 14 days respectively)[21].

2. MATERIAL &METHOD :-

MATERIAL:-

Patients presenting into the hospital (OPD &IPD) in the department of Pulmonary Medicine having fluid collection in pleural space.

METHOD:-

50 cases of pleural effusion were studied over a period of 3 months.

a. BIOCHEMICAL TESTS:-

Determination and calculation of serum to fluid LDH gradient and ADA levels was done.

b. FIXATION AND STAINING:-

Conventional Smear Technique (DIRECT SMEAR):

Pleural fluid was first centrifuged at 2000rpm for 5 minutes.

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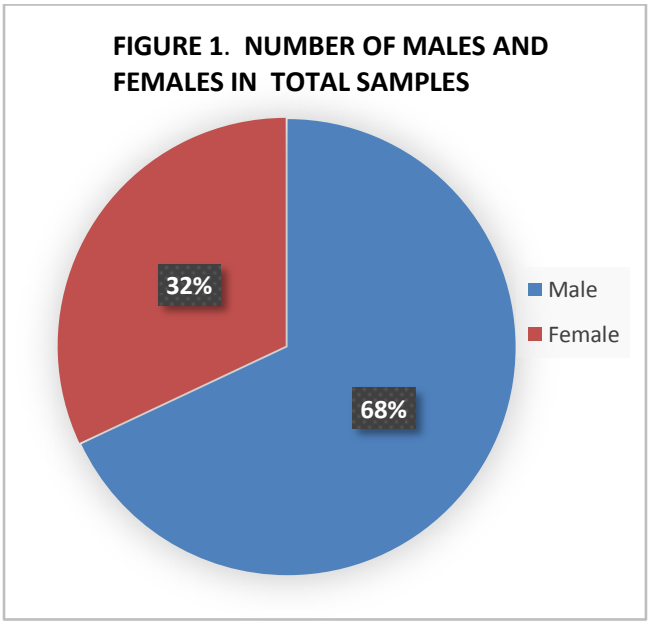
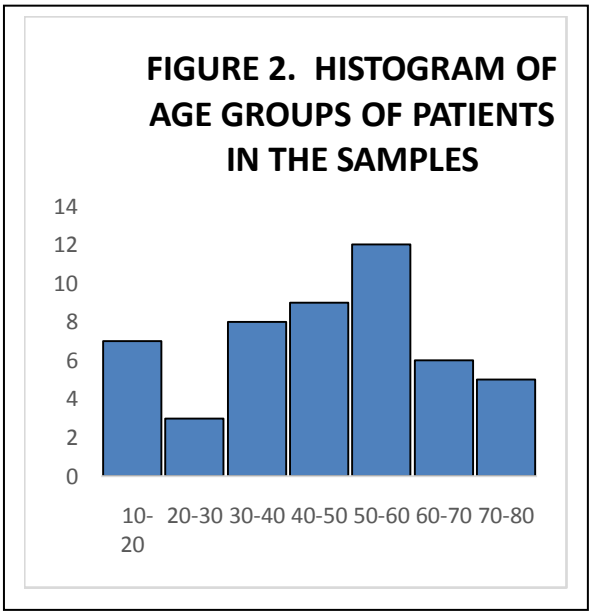
Supernatant was transferred to another tube.
Sediment was used for direct smear preparation and smears were being labelled.
At least 2 smears were immediately kept in fixative (methanol) for 10 minutes and then stained using Modified Leishman-Giemsa and Papanicolaou stains.
The smears were then examined under low power for overall cell population and predominant pattern.
Cell morphology was studied under high power.

INCLUSION CRITERIA:-
Patients attending OPD or admitted under Pulmonary medicine department and referred for both cytomorphological study and biochemical tests.
EXCLUSION CRITERIA:-
Body fluids other than pleural fluid were excluded.

3. RESULT AND DISCUSSION:-

A total of 50 patients were included in this study. **(Figure1)**Out of these 34 were males and 16 were females.**(Figure 2)** Amongst various age groups, the maximum number of patients were between 50-60 years of age (12subjects) followed by 40-50yrs(9subjects) and 30-40yrs(8subjects).





(Figure 3) The clinical diagnosis amongst patients varied from frank pleural effusion alone to pleural effusion associated with pulmonary tuberculosis(Pul.TB), diabetes mellitus(DM), rheumatoid arthritis(RA), empyema, pneumonia, chronic obstructive pulmonary disease(COPD), chronic kidney disease(CKD), hypertension(HTN), coronary artery disease(CAD), carcinoma ovary(Ca.ovary) and carcinoma breast(Ca. breast).

(Figure 4) The various clinical abnormalities or clinical features in patients with pleural effusion included cough, fever, breathlessness or dyspnoea (most common clinical complaint), chest pain, loss of weight, loss of apetite, swelling in lower limbs, associated abdominal distension and yellowish discolouration of sclera.

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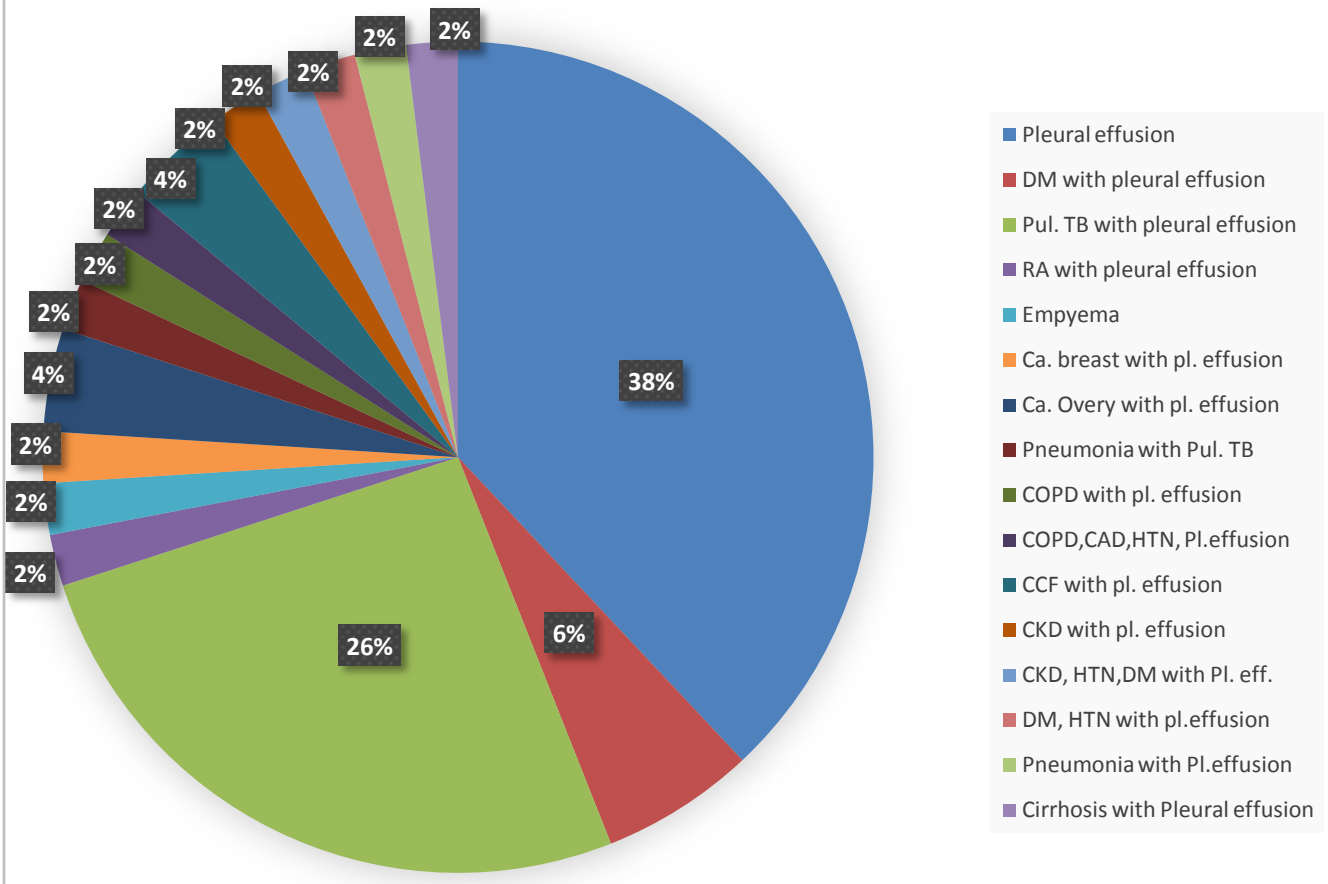
FIGURE 3. CLINICAL DIAGNOSIS IN VARIOUS SUBJECTS



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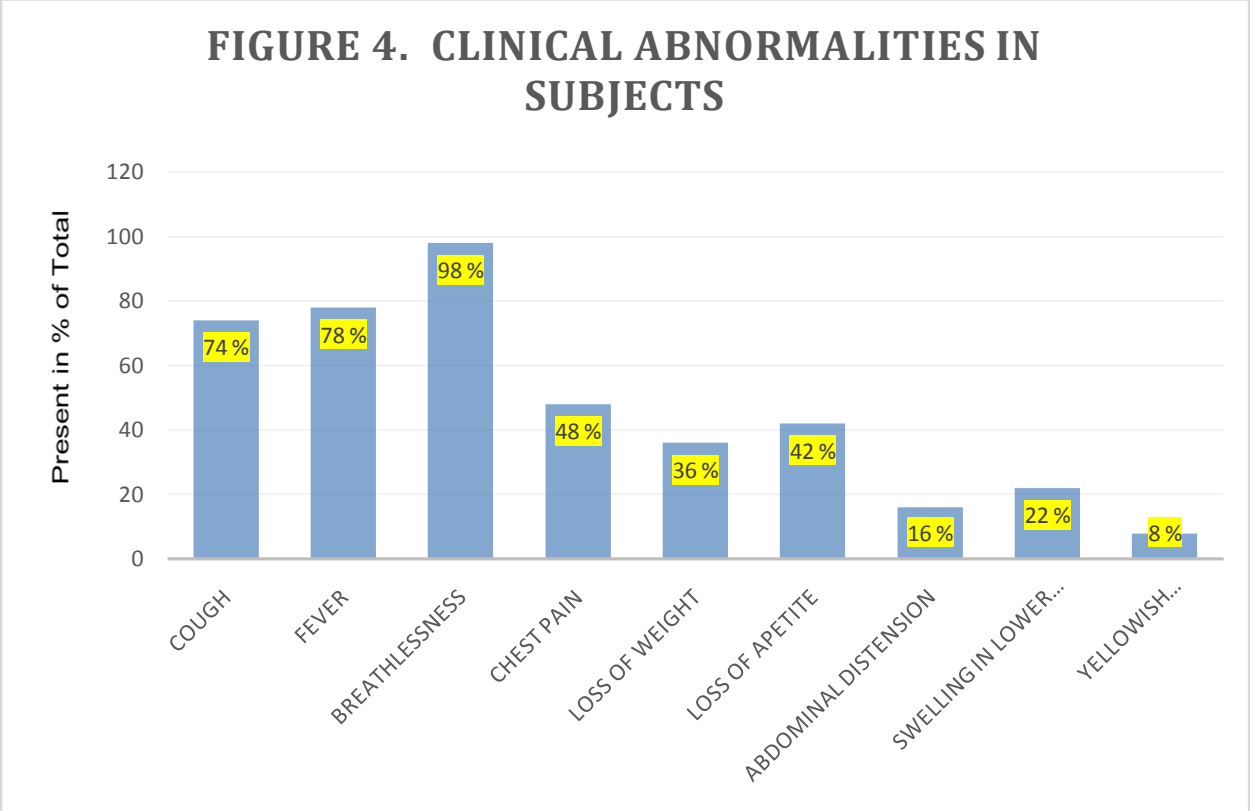


- **(Figure 5)** The colour of pleural fluid ranged (maximum to least) from yellow, reddish yellow, reddish, pale yellow and chocolate brown.
- **(Figure 6)** The appearance of pleural fluid ranged from turbid (maximum), slightly turbid to clear or straw coloured (least).

FIGURE 5. COLOUR OF PLEURAL FLUID IN SAMPLES

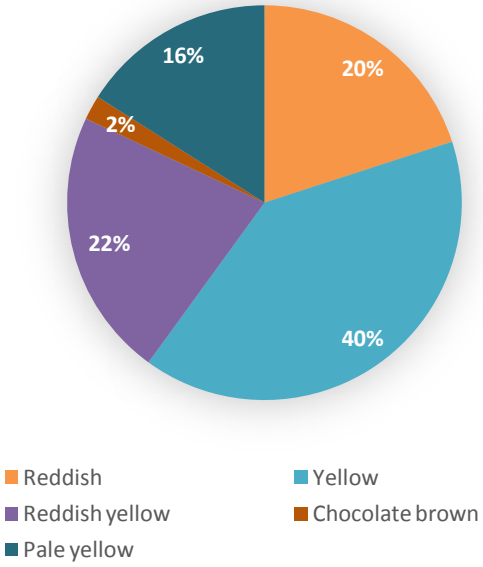
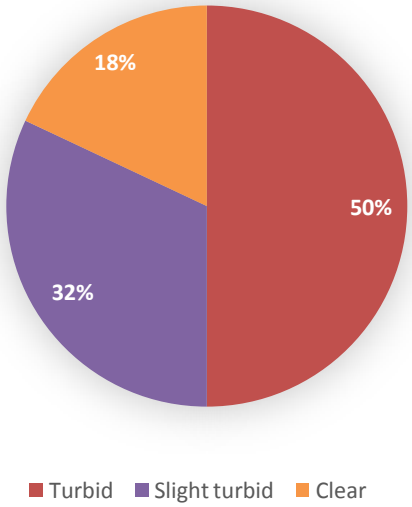
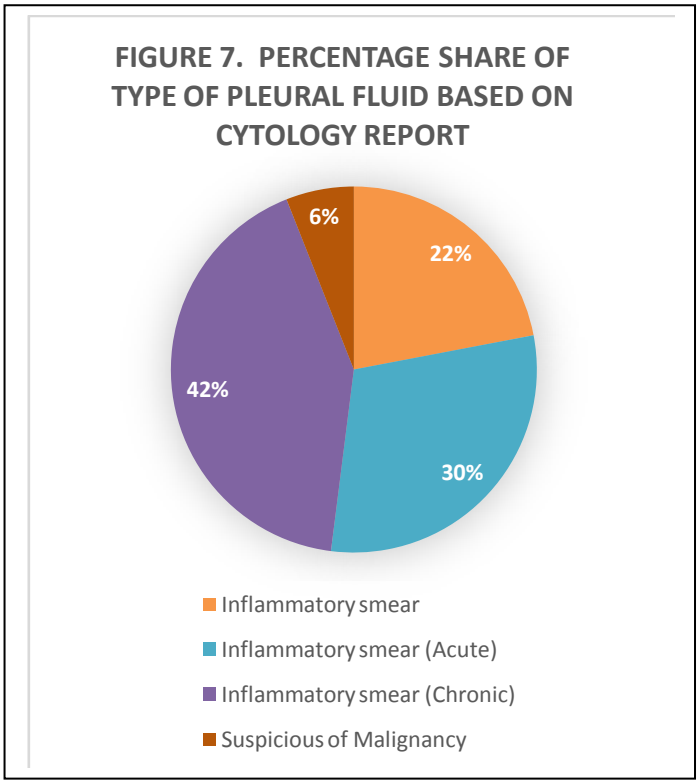
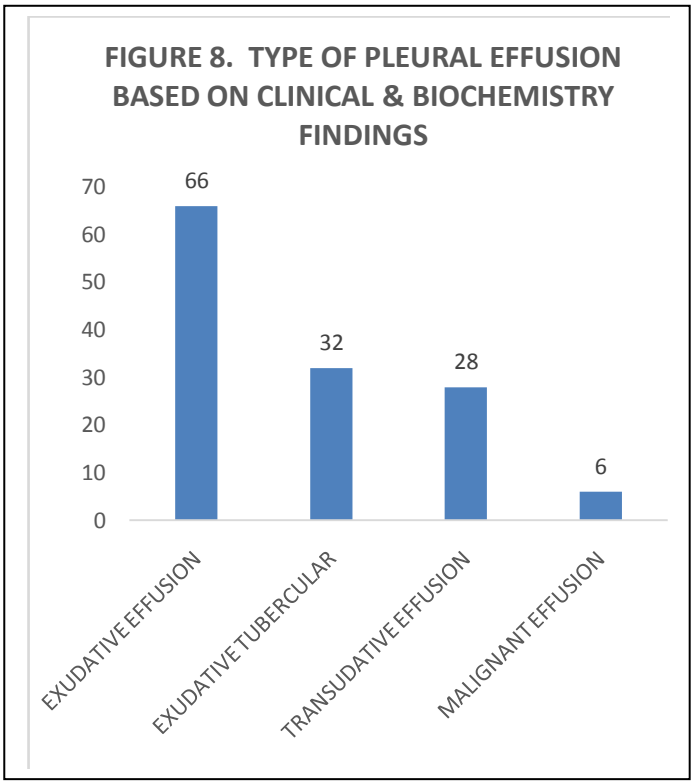


FIGURE 6. APPEARANCE OF PLEURAL FLUID IN SAMPLES



- **(Figure 7)**Most of the pleural effusions were exudative in nature. Tuberculosis was the most common cause of exudative effusion. The other causes were malignancy, pneumonia, empyema, trauma, abscess or organ disease (mostly liver) etc.
- **(Figure 7)**The Fluid Cytology Report showed either inflammatory smear (transudate-with less cellularity), acute inflammatory smear (neutrophilic predominant), chronic inflammatory smear (lymphocytic predominant) or suspicious of malignancy/ malignant effusion(atypical mesothelial cells in 3-D clusters).
- In more than half of the malignant effusions predominant cells were lymphocytes while the polymorphonuclear cells were predominant in pneumonic effusions. The malignant pleural effusion fluid showed clusters and papillary groups of large abnormal epithelial cells with large dense nuclei, conspicuous nucleoli and coarse nuclear chromatin.
- **(Figure 8)** Amongst the samples of pleural fluid after clinical and biochemical assessment the percentage share of various pleural fluid types were exudative (66%-maximum) out of which 32% were tubercular, transudative (28%) and susupicious of malignancy/ malignant effusion (06%).





- The biochemical analysis of pleural fluid was performed for fluid ADA, fluid LDH and serum LDH levels. Following this mean with standard deviation values of fluid ADA, fluid LDH, serum LDH and Absolute difference of serum and fluid LDH gradient were calculated.
- **(Table no. 1)** The mean and standard deviation for ADA levels of exudative fluid (including tubercular) was 54.37 ± 56.71 U/L (highest), of malignant/suspicious of malignancy fluid was 31.09± 02.81 U/L and of transudative fluid was 23.46±15.22 U/L.
- **(Table no. 2)** The mean and standard deviation for LDH levels of exudative fluid was 3201 ± 3889 U/L, of malignant/ suspicious of malignancy fluid was 1692±1179 U/L and of transudative fluid was 130.2±52.30 U/L.
- This shows that the fluid LDH levels are higher in exudative effusion followed by malignant effusion and least in transudative effusion. The ADA levels are found to be

TABLE 1. ADA VALUES OF VARIOUS TYPES OF PLEURAL EFFUSION:-

CYTOLOGY REPORT	**N**	**Mean ± SD**
EXUDATE	33	54.37 ± 56.71
TRANSUDATE	14	23.46± 15.22
MALIGNANT	3	31.09 ± 02.81
TOTAL	**50**	**45.76 ± 48.72**

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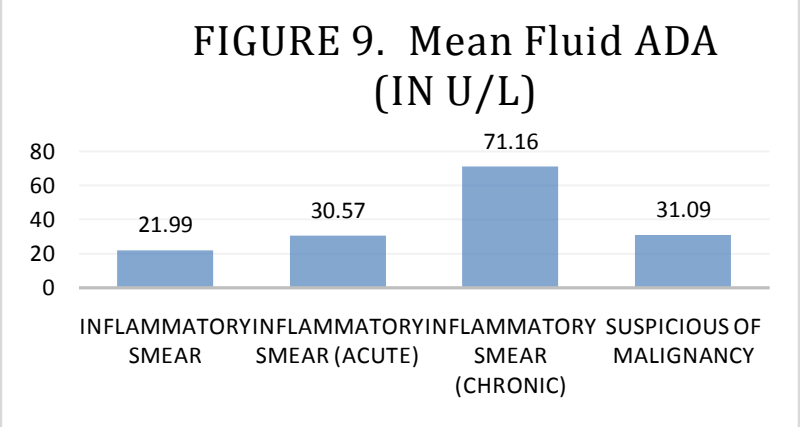
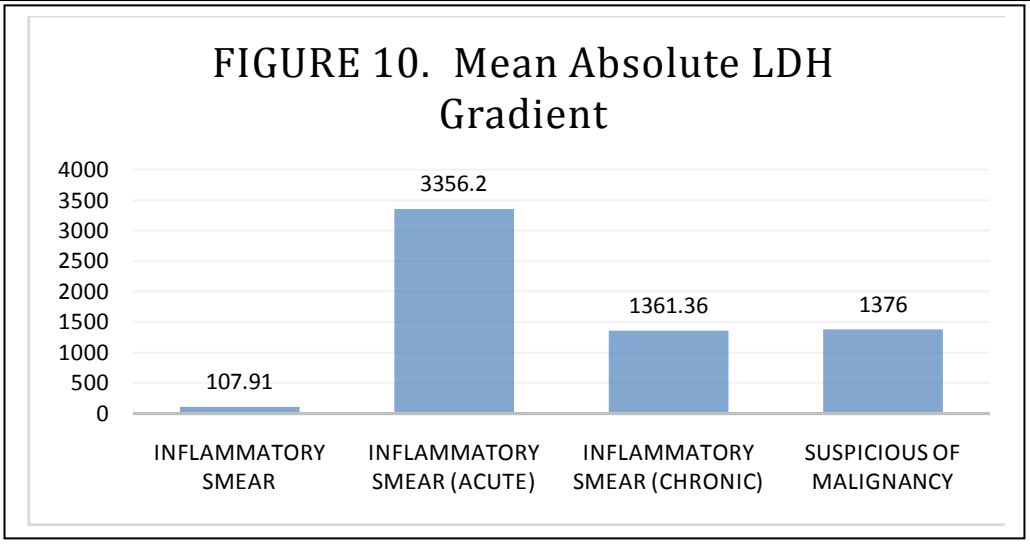


- **(Table no. 2)** The pleural fluid LDH values reflected that it was highest in exudative effusion (including tubercular) followed by suspicious of malignancy/ malignant effusion and least in transudative fluid.

TABLE 2.FLUID LDH VALUES OF VARIOUS TYPES OF PLEURAL EFFUSION:-

TYPE OF PLEURAL EFFUSION	N	Mean ± SD
EXUDATE	33	3201 ±3889
TRANSUDATE	14	130.2 ± 52.30
MALIGNANT	3	1692 ± 1179
TOTAL	**50**	**2560 ± 3442**

- **(Table no. 3)** On calculating the mean**"Absolute LDH gradient"**(Neglects the negative sign of difference between serum and fluid LDH) by performing the biochemical analysis of pleural fluid, the exudative effusion fluid had an absolute gradient value of 3356.20±4985.20 U/L, tubercular effusion fluid had an absolute gradient value of 1361.36± 1609.50 U/L, malignant/ suspicious of malignancy effusion fluid had an absolute gradient value of 1376±1181.79 U/L while transudative fluid had an absolute gradient value of 107.91±61.60 U/L .On calculating



- **(Table no. 3)** The mean and standard deviation values of ADA according to cytology reports showed that it was highest in chronic inflammatory smear followed by those suspicious of malignancy/ malignant smears and acute inflammatory smear. The ADA values were least in case of inflammatory smears (transudate).
- **(Table no. 3)** The mean and standard deviation values of Absolute LDH gradient according to cytology reports showed that it was highest in acute inflammatory smears followed by those suspicious of malignancy/ malignant smears and chronic inflammatory smears. The absolute LDH gradient values were found to be least in case of inflammatory smears (transudate).

TABLE 3.ADA AND ABSOLUTE LDH GRADIENT VALUES ACCORDING TO CYTOLOGY REPORTS:-

CYTOLOGY REPORT	N	MEAN ± SD (ADA)	MEAN ± SD (ABSOLUTE LDH GRADIENT)
INFLAMMATORY SMEAR (TRANSUDATE)	9	21.99 ± 16.30	107.91 ± 61.60
INFLAMMATORY SMEAR (ACUTE- EXUDATE)	14	30.57 ± 20.47	3356.20 ± 4985.20
INFLAMMATORY SMEAR (CHRONIC- EXUDATE)	16	75.21 ± 73.23	1361.36 ± 1609.50
SUSPICIOUS OF MALIGNANCY	1	31.09 ± 2.81	1376.00 ± 1181.79
TOTAL	**50**	**45.76 ± 48.72**	**1684.93 ± 3111.24**

- In this study, to find out whether there is a correlation between various cytologic pleural fluid smear types and their absolute LDH gradients "**Biserial Correlation Method"** for calculating the correlation coefficient was used. Thereafter the p- value was also calculated. Since, the comparative groups had two variables- one was a Dichotomous type variable and another was a Continuous type variable therefore the method of finding out the Correlation Coefficient was the "**Biserial Correlation Method".**
- Calculating the **"Pearson's Correlation Coefficient"** requires the assumption that the relationship between the two variables is linear.
- In this study, a p- value of < 0.05 was considered to be significant to consider a correlation between two variables. A p- value of < 0.05 level of significance means that there is only 5% chance that results from your sample occurred due to chance.
- Here for dichotomous variable we Assume 0 as Not Exudates and 1 as Exudates so the correlation coefficient signifies that if we move from 0 to 1 we shall expect a statistically significant change in Absolute LDH gradient values which means, if the values observed the positive significant correlation then we can say the absolute LDH Gradient values exceeds from lower to higher.
- And similarly we can proceed for the other dichotomous variables like Inflammatory smear (acute)/Not Inflammatory smear (acute), Inflammatory smear (chronic)/Not Inflammatory smear (chronic), suspicious of malignancy/Not Suspicious of malignancy, Inflammatory smear (transudate) / Not Inflammatory smear etc.

- **(Table no. 4)** The study results showed that the p- value of acute inflammatory smear was 0.011 indicating a significant correlation between absolute LDH gradient and the cytologic type of pleural fluid. This means that if the absolute LDH gradient value of a sample of pleural fluid is high then that type of pleural fluid is more likely to be an acute inflammatory smear (exudative) or vice versa.

Table 4. Correlation Between Cytology Report (Inflammatory Smear/Inflammatory Smear (Acute)/Inflammatory Smear (Chronic)/Suspicious Of Malignancy) And Absolute LdhGradient :-

CYTOLOGICAL REPORT	**PEARSON'S CORRELATION COEF.**	**P VALUE**	**SIGN/NS**
Inflammatory smear (tansudate)	-0.272	0.056	N.Sig.
Inflammatory smear (acute- exudate)	0.355	0.011*	Sig.
Inflammatory smear (chronic- exudate)	-0.089	0.537	N.Sig.
Suspicious of Malignancy	-0.025	0.861	N.Sig.

NOTE:- As p-value is $<\alpha = 0.05$ (which means a 5 % Level of significance)hence, we can reject Null Hypothesis and assume to be a significant correlation between the variables.

- **(Table no. 5)** On correlating the cytologic type of pleural fluid with the fluid ADA values, the p-value of chronic inflammatory smear was found to be statistically significant at 0.001 indicating inflammatory smear (tubercular) or vice versa.

Table 5. Correlation Between Cytology Report (Inflammatory Smear/Inflammatory Smear (Acute)/Inflammatory Smear (Chronic)/Suspicious Of Malignancy) And Fluid Ada :-

CYTOLOGICAL REPORT	**PEARSON'S CORRELATION COEF.**	**P VALUE**	**SIGN/NS**
Inflammatory smear (transudate)	-0.262	0.066	N.Sig.
Inflammatory smear (acute- exudate)	-0.207	0.150	N.Sig.
Inflammatory smear (chronic- exudate)	0.449	0.001*	Sig.
Suspicious of Malignancy	-0.078	0.589	N.Sig.

NOTE:-As p-value is $<\alpha=0.05$ (which means at 5 % Level of significance)hence, we can reject the Null Hypothesis and assume to be a significant correlation between the variables.
In this way Hypothesis testing is carried out with,
Null Hypothesis: There is no significant correlation between two variables.

- Hence, on carefully analyzing the data obtained from cytology reports and biochemical analysis of pleural fluid for ADA and absolute LDH gradient levels it was found that the ADA levels were highest in chronic inflammatory smears (exudative- tubercular) followed by acute inflammatory smears (exudative), suspicious for malignancy/malignant smears and least in inflammatory smears (transudative).
- The fluid LDH levels in patients with exudative pleural effusion (non- tubercular and tubercular) were found to be more profoundly elevated than their corresponding serum LDH levels thereby giving negative gradient values. Hence, in this study Absolute LDH gradient (serum-fluid LDH) was taken into account by dropping the negative sign.
- In patients with suspicious malignancy /malignant effusion both fluid and serum LDH levels were found to be elevated but to a lesser extent when compared to the exudative effusion.

4. CONCLUSION:-

- Cytomorphological analysis of body fluids is an important investigation which is very convenient, cost effective, accurate and also safe . It gives a clue to diagnose any underlying neoplastic or non- neoplastic diseases that may change prognosis, further management or outcome of patient. In cases of malignant effusion it is crucial in staging and deciding further protocol of treatment.
- Pleural fluid accumulation occurs when any pathologic process causes imbalance of hydrostatic pressure gradient, capillary membrane permeability and lymphatic drainage resulting in either a protein poor transudate or inflammatory exudates.
- The present study shows that the most useful tests in establishing the diagnosis of the type of pleural effusion are pleural fluid cytology, ADA levels and LDH levels along with absolute LDH gradient. Pleural fluid pH is the most useful marker of infection although LDH is also used. Study of cytomorphological features of various metastatic malignant cells in pleural fluid gives definite clues regarding the primary site.
- Although, if the absolute pleural fluid LDH values alone are taken instead of serum values alone for comparison, they may give erroneous results because the pleural fluid levels are influenced by changes in the serum.
- In this study, the pleural effusion showed a male preponderance with maximum number of subjects within the age group of 50-60years.
- The clinical diagnosis amongst patients in this study varied from frank pleural effusion alone to pleural effusion associated with pulmonary tuberculosis(Pul.TB), diabetes mellitus(DM), rheumatoid arthritis(RA), empyema, pneumonia, chronic obstructive pulmonary disease(COPD), chronic kidney disease(CKD), hypertension(HTN), coronary artery disease(CAD), carcinoma ovary(Ca.ovary) and carcinoma breast(Ca. breast).
- Amongst the various clinical abnormalities or clinical features in patients with pleural effusion breathlessness or dyspnoea was the most common clinical complaint.
- Most of the pleural effusions were exudative in nature and amongst those " tuberculosis" was the most common cause of exudative effusion.

- The transudative effusions are usually characterized by majority of lymphocytes or other mononuclear cells. When exudative effusions are considered all tuberculous effusions had more than 50% small lymphocytes.
- The mean and standard deviation values of ADA according to cytology reports showed that it was highest in chronic inflammatory smear followed by those suspicious of malignancy/ malignant smears and acute inflammatory smear. The ADA values were least in case of inflammatory smears (transudate).
- The mean and standard deviation values of Absolute LDH gradient according to cytology reports showed that it was highest in acute inflammatory smears followed by those suspicious of malignancy/ malignant smears and chronic inflammatory smears. The absolute LDH gradient values were found to be least in case of inflammatory smears (transudate).
- Using the Biserial correlation method, when the cytologic types of pleural fluid were correlated with absolute LDH gradient values the p- value was found to be statistically significant in acute inflammatory smears (exudates).
- Alternatively, when the cytologic types of pleural fluid were correlated with pleural fluid ADA values the p- value was found to be statistically significant in chronic inflammatory smears (tubercular-exudates).

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