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A Study on Malignant Serous Fluid Effusions for a Period of One Year in a Tertiary Care Centre

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ABSTRACT
BACKGROUND: *The identification of cells as malignant or benign reactive mesothelial cells in serous effusions is a day to day diagnostic problem. Identification of these cells as benign or malignant is a diagnostic primary purpose of evaluation. Clinical history when taken into account while evaluating effusions can avoid inaccuratediagnosis.*
MATERIALS AND METHODS*: It was a prospective type of study. A total of 232 cases of serous effusions were cytologically evaluated following detailed history taking and clinical examination. Out of 232 cases all cases of benign and malignant effusions were segregated and categorized according to age, sex and site (peritoneal or pleural), based on The International System for Reporting Serous Effusions(TIS).*
RESULTS*: Total of 25 cases were positive for malignancy. Majority of primary tumors associated with malignant effusions were commonly from lung followed by GIT, ovary, breast and occult cases . Most common cause of malignant pleural effusion in males was lung cancer and in females was breast cancer respectively. Most common cause of malignant peritoneal effusion in males was carcinoma GIT and in females was carcinoma ovary respectively.*
CONCLUSION: *Malignant effusions were more common in males. Malignant effusions were mainly due to metastatic cancers, mostly adenocarcinomas. The most common cause of malignant pleural effusion in males was carcinoma lung and in females is carcinoma breast, while the most common cause of malignant peritoneal effusion in males was carcinoma GIT and in females was carcinoma ovary respectively. Thus, fluid cytology is an important diagnostic tool and complementary diagnosis for categorizing benign as well as malignant condition*

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I. INTRODUCTION:

Accumulation of fluid in various body cavities can occur in wide range of benign conditions and it is a frequent clinical presentation of Malignant and non-malignant disorders[1]. The studies of cells of effusion fluids were one of the first domains of cytology to draw the interest of clinicians. The first microscopic study of the cytology of effusions is now more than a century old. Cytological analysis of body cavity fluid is a quite cost effective procedure, rapid and easy to perform with another prime utility of serving both as a diagnostic as well as a therapeutic intervention[2].

Cytologic examination of a serous effusion is of paramount importance because the finding of cancer cells in such specimen denotes that patient has cancer that is not only advanced but also almost always incurable. Cytological assessment of serous fluids is an important investigation for diagnosis, staging, prognosis and management of malignancy as well as diagnosis of various non-neoplastic lesions[3,4]. Apart from the finding of cancer cells, cytologic examination of pleural, peritoneal, and pericardial effusions may also reveal information about inflammatory conditions of the serous membranes[5].

The identification of cells as malignant or benign reactive mesothelial cells in serous effusions is a day to day diagnostic problem. Because of its cytological nature and its exfoliation into a liquid, the cellular anarchy of mesothelial elements tend to overshadow the classic diagnostic criteria of cytological malignancy[5]

The definition of inadequate and benign samples is also mandatory. The International System for Reporting Serous Effusions (TIS) has been elaborated by an international work group formed by the collaboration of the International Academy of Cytology (IAC) and the American Society of Cytopathology (ASC) in order to clarify these issues and provide a universal reporting scheme following the prototype of

similar reporting schemes for cervical specimens and thyroid,salivary gland, breast, urinary and pancreatobiliary systems[6].

Thus, the purpose of this study was to establish the usefulness of clinicopathological evaluation of serous body effusions as a diagnostic method in malignant effusions.

II. MATERIAL AND METHODS

The study was carried out in the Department of Pathology, Siddhartha Medical College and Hospital after the approval of institutional ethical committee. This was a prospective type of study carried out from August 2021 to July 2022. The cases were collected from wards of medicine, surgery, TB & Chest. All the specimens of body fluids received in cytology unit of pathology department were included in the study.

Exclusion criteria:-

- Quantity less than 5ml.
- Synovial fluids.
- Frankly haemorrhagic fluids with no clinical suspicion of malignancy.

Detailed history was collected and clinical examination of the patient was done. General haematological investigations and specific investigations if needed were done. Physical and chemical examination of effusion fluids was properly performed. The standard handling for microscopic examination consists of conventional smearsand cell blocks were made using centrifugation. Two conventional smears were made, one ethanol fixed for H&E and other air dried for Leishman.In our study, the Neubauer chamber was used for manual cell counting.

The International System for Reporting Serous Effusions (TIS)[6]

After evaluation, each cytology report was classified into one of the following categories, according to the TIS:

- ND: Non-diagnostic specimen.
- NFM: Specimen negative for malignancy.
- AUS: Presence of atypical cells that, however, lack evidence of malignancy, with the atypical characteristics often attributed to inflammatory changes. Of note, specimens classified as AUS tend to lean closer to the benign end of the spectrum.
- SFM: Presence of cells with atypia not enough for a diagnosis of malignancy, but such diagnosis strongly indicates malignancy.
- MAL: Specimens containing clearly malignant cells.

Cytological diagnosis was made and malignant cases from the total cases were segregated and were then categorized according to sex, site(peritoneal or pleural), origin(primary or metastatic)

III. RESULTS

Out of the 232 cases of effusion studied 135 (58.1%) were male and 97 (41.9%) cases were females in the ratio of 1.38:1.In this study most of the pleural fluids has received between the age group of 41 to 50, in peritoneal fluids between the age group of 51 to 60 and only 2 pericardial fluids received in the age group of 31-40

202 (87 %) cases were benign and 25 (10.7%) cases were malignant. The cytology could not give a definitive diagnosis in 6 (2.3%) cases.

According to this study 111 (54.6%) cases of the benign lesions belong to the pleural fluid, 89 (44.4%) cases belong to peritoneal and 2(1%)cases are of pericardial fluid.

Among malignant effusions 14 (56%) cases of the malignant lesions belong to pleural and 11(45%) cases of malignant lesion belong to peritoneal fluid.

Table 1: Distribution on the basis of TIS reporting

CATEGORY	No. of Cases	Percentage
ND	5	2%
NFM	193	83.3%
AUS	4	1.7%
SFM	5	2%
MAL	25	11%
Total	232	100

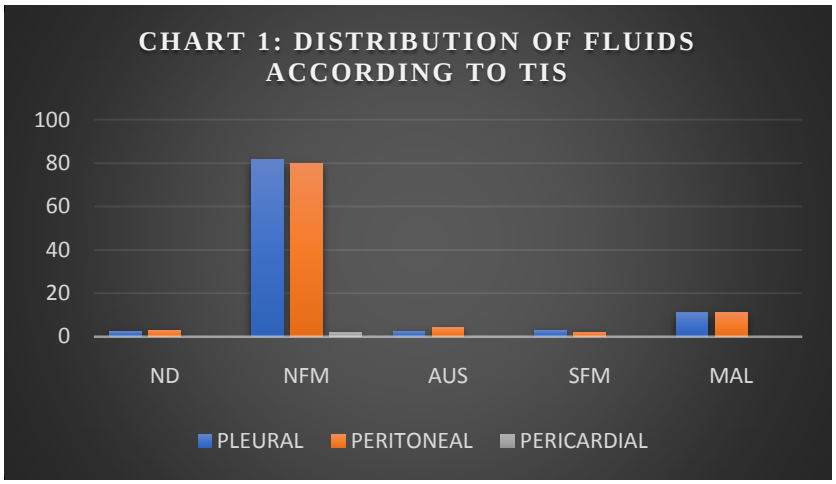
Pleural effusion:

Pleural effusion cases consisted of 130 patients, among them 3 were classified as ND (2.5%), 106 as NFM (81.5%), 3 as AUS (2%), 4 as SFM (3%), and 14 (11%) were positive for malignancy.The most common

site of malignancy origin was the lung (6), followed by the breast (3). Diagnostic performance in our laboratory was also evaluated for cases with data availability, considering ND, NFM and AUS as negative and SFM and MAL as positive results.

Peritoneal effusion:
As far as peritoneal effusion cases are concerned, 100 cases, 3 cases were categorized as ND (3%), 80 as NFM (80 %), 4 as AUS (4%), 2 as SFM (2%) and 11 as (11%) as MAL. The most common site of malignancy origin was the GIT (6), Lung (4) followed by ovaries (3)

Pericardial effusion:
There were only two cases of pericardial effusions, both are benign effusions only.

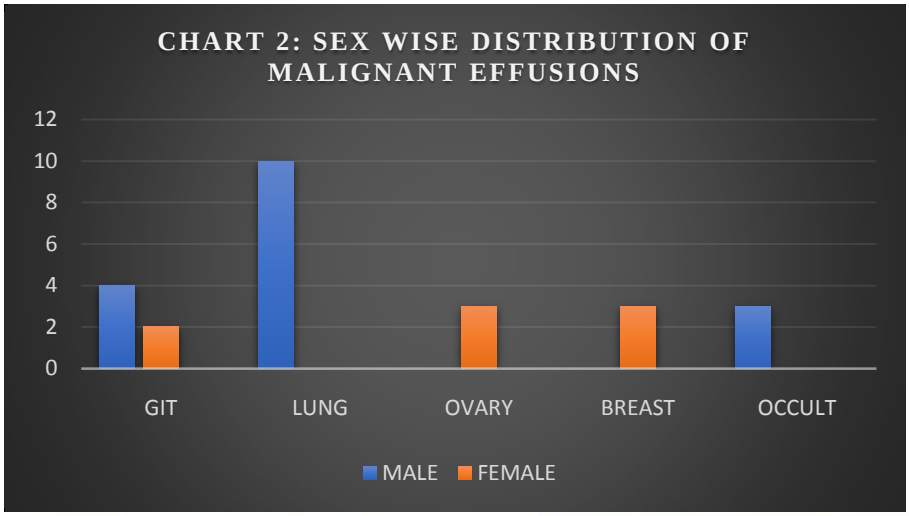


The common sites of primary malignancy giving rise to malignant effusions were from lung, GIT, ovary & breast.
Malignant effusions were more common in males than females. The most common primary tumour site associated with malignant effusions in males was carcinoma lung and in females is carcinoma ovary

Table 2: Distribution of malignant effusions according to the primary site

SITE	NO. OF CASES	PERCENTAGE %
Lung	10	40
GIT	6	24
Ovary	3	12
Breast	3	12
Occult	3	12
Total	25	100

Out of 11 cases of malignant peritoneal effusions 7 cases were males (64%) and 4 were females (36%). Out of 14 cases of malignant pleural effusions, 10 were males (71%) and 4 were females (29%). Most common cause of malignant pleural effusion in males was lung cancer (40%) and in females was breast cancer (12%). Most common cause of malignant peritoneal effusion in males was carcinoma GIT (24%) and in females was carcinoma ovary (12%). Carcinoma of unknown origin was noted in 3 cases (12%).



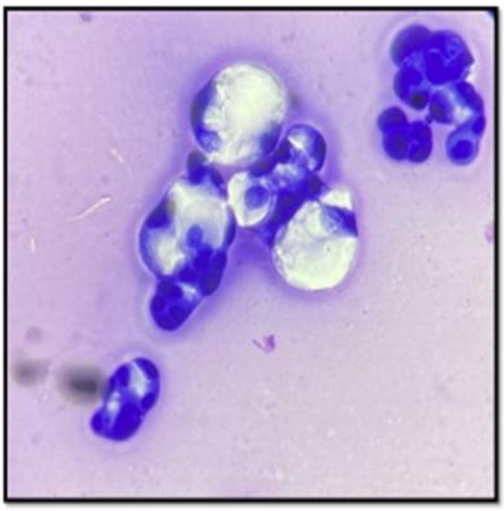


FIG : 1

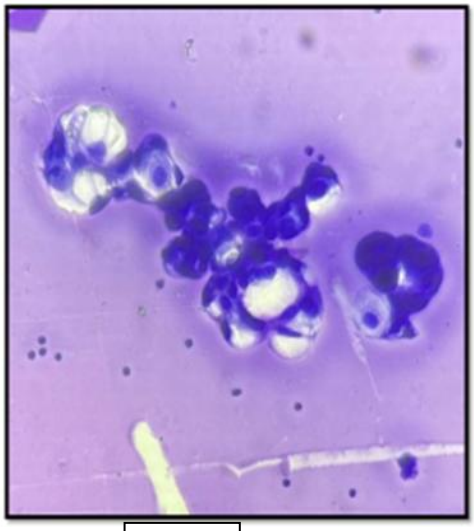


FIG: 2

Figures 1&2 : Atypical epithelial cells are arranged In sheets 3d balls with abundant mucin in cytoplasm , marked hyperchromatic nuclei and eccentrically pushed nucleus

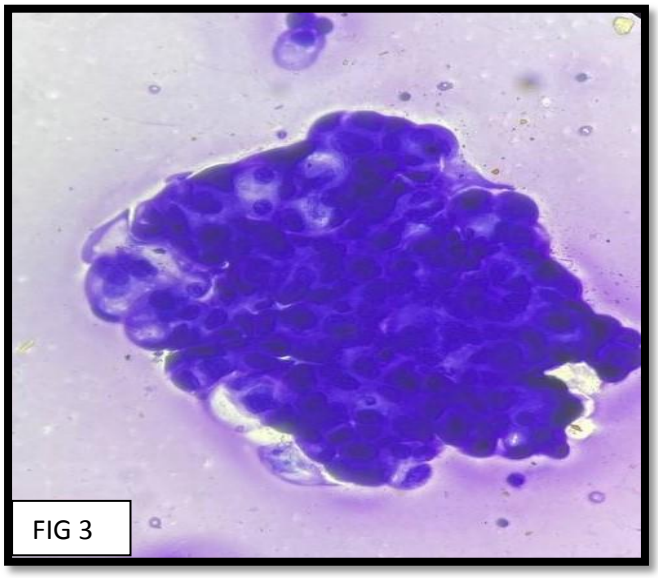


FIG 3

Figure 3: Atypical epithelial cells are arranged in sheets and cluster with increased nuclear to cytoplasmic ratio and eccentrically placed nuclei with abundant mucin in cytoplasm

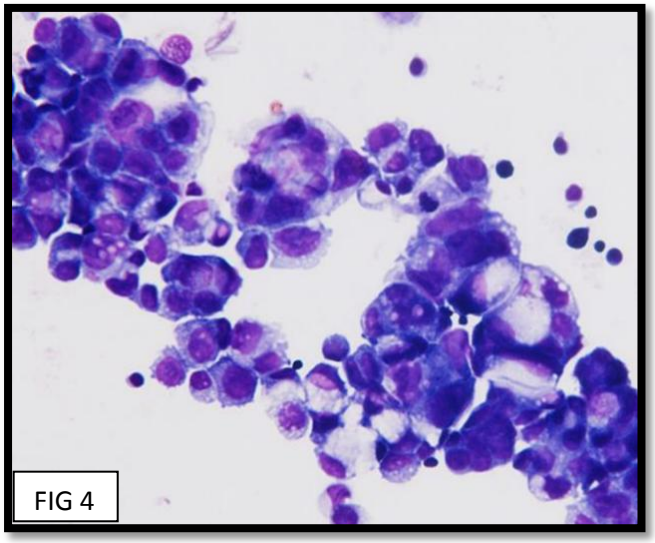


Figure 4: Atypical epithelial cells are arranged In sheets with abundant vacuolated cytoplasm with hyper chromatic nuclei

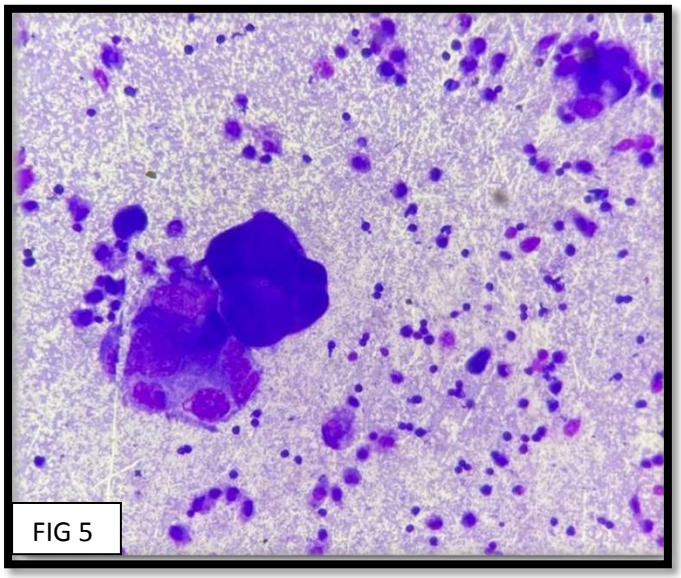


Figure 5: Atypical epithelial cells are arranged in 3d balls ,clusters and singly scattered cells

IV. DISCUSSION

Fluid cytology is mainly performed in order to see the type of inflammation and establish the presence or absence of malignancy[1]. The distinction between reactive mesothelial cells and malignant cells in cytological smears of serous effusion is a frequent cause of diagnostic difficulty.The present study was undertaken to study the significance of fluid cytology in the diagnosis of various neoplastic and non-neoplastic conditions .

In this study, the application of the International System for Reporting Serous Effusions (TIS) was evaluated[7,8]. During this period, 130 pleural, 100 peritoneal and 2 pericardial effusions were processed in the laboratory. Evaluation with distribution to the TIS categories showed that pleural effusions were 2.5% ND, 81.5% NFM, 2% AUS, 3% SFM and 11% MAL. Peritoneal effusions were 3% ND, 80% NFM, 4% AUS, 2% SFM and 11% MAL. Pericardial effusions only included two cases, both are NFM. Our results are compatible with those of other studies like Hou et al[7]and Kundu et al[8].

Out of the total 232 cases of effusions which were studied, 25 cases (10.7%) were malignant. This finding goes hand in hand with the findings of Bharat et al[2] and who reviewed 540 sample of effusions and found 50 samples (9.2%) to be positive for cancer cells.

In our study, pleural fluid was the commonest serous effusion (56%) followed by peritoneal fluid (43%) and pericardial fluid (1%). Similar studies conducted by Sharma, et al[19] and Ayagari sudha, et al[15]also found pleural effusion to be the most common effusion followed by peritoneal effusion.

In the present study most common age group of serous effusion was 60 to 69 years. Malignant effusion was also the highest in this age group. The increased number of cases in this age group could be due to increased incidence of malignancy in the elderly.

Out of the 25 positive cases of serous effusion on fluid cytology, fourteen were malignant pleural effusion (56%) and eleven were peritoneal effusion (44%). Malignant pleural effusion was more common in male (10 out of 14) than in females whereas malignant peritoneal effusion was more common in females (7 out of 11). This observation is supported by El sheik sa et al[19]and Sabha h et al[16].

Based on cytology alone we could not determine the primary site of malignancy. In our study, there was evidence of primary lung carcinoma in ten cases of malignant pleural effusion. Among the eleven cases of malignant peritoneal effusion, we could trace history of primary ovarian carcinoma in three cases, gastrointestinal carcinoma in another six cases and breast carcinoma in two cases. In the remaining three cases, there was no known primary site of tumour. Bharat et al[2] and Mahajan s et al[5] also found similar results of adenocarcinoma of lung being the most common malignant effusion followed by adenocarcinoma GIT.

The common primary tumors found to be associated with malignant effusions in the present study were Lung cancers(10;25%), GIT(6;24%), ovary(3;12%) and breast(6;24%). Naib[1] has reported that the tumors of the adult patients that frequently metastasize into the serous cavity are the adenocarcinomas of the ovary, GIT,Lung and breast.

The common primary tumors in males were lung (10/14;40%) and GIT (3/14;30%) and in females were gynaecologic site(3/11;40%) and breast (3/11; 33.3%). These findings were supported by Mahajan et al[5] who found adenocarcinoma lung as most common primary associated with malignant effusions in males and carcinoma of gynaecologic site in females.

Vargas et al[10] found carcinomas of lung, breast and lymphomas to be responsible for approximately 75% of all malignant pleural effusions. In this study they accounted for 71 % cases. Parsons et al[11]reviewed 164 patients with malignant ascites and found that ovarian ascites accounts for 28% of the total. In the present study it accounted for 27%.

In the present study the most common primary site associated with malignant pleural effusion in males was carcinoma lung and in females was carcinoma breast and the most common primary associated with malignant peritoneal effusion in males was carcinoma GIT and in females carcinoma ovaries. The observation is supported by Ringenberg et al[12] who reviewed cases of malignancy peritoneal effusion and found common primary site in females to be carcinoma ovary and in men to be colon, rectum and stomach(GIT)

Sears et al[4] and Ong et al[14] also reported that lung cancer is the most common cause of malignant pleural effusion in men, as is breast cancer in women and Sears et al also observed that pancreatic carcinomas were the most common cause of malignant peritoneal effusion in men, whereas in women the most common primary site was ovary. All these observations were matching with the observation in the present study except the one regarding pancreatic carcinoma.

In 3 out of 25 (2.3%) cases of malignant effusion the primary tumor was occult. The most common occult primary in both women and men who present with a malignant pleural effusion is lung cancer. It is extremely uncommon for breast cancer to manifest itself initially as a malignant effusion. The most common occult sources of a malignant peritoneal effusion were intestinal and pancreatic cancer in men and ovarian cancer in women[4,11]. In some patients the primary site was never discovered. Sears et al[4] reported an incidence of 15% of occult primary sites. Ong et al[14] reported an incidence of 9.7% of occult primaries.

Over all , the present study showed that , fluid cytology is very useful in classifying benign conditions, further it plays a major role in rapid diagnosis of malignant effusions

Fluid cytology although not a substitute for conventional histopathology but as complementary to it and is useful in categorizing benign conditions as well as in the diagnosis of malignant conditions.

V. CONCLUSION:

In the present study of serous effusions, 202 cases were benign, 25 were malignant.The primary tumor sites in malignant effusions were Lung (10), GIT(6) ovary (3), breast (3) and occult (3). The frequency of malignancy in our study was 10.77% with adenocarcinoma of lung being the common malignant lesion.

Most common age group is 6th decade with males to female ratio of 1.4:1 Maximum malignant lesions were noted in pleural fluid samples followed by peritoneal fluid samples while no malignancy was diagnosed in pericardial fluid samples

Malignant effusions were mostly due to metastatic cancers and most of them are adenocarcinomas. The most common cause of malignant pleural effusion in males was carcinoma lung and in females is carcinoma breast. The most common cause of malignant peritoneal effusion in males was carcinoma GIT and in females was carcinoma ovary

Thus, fluid cytology is an important diagnostic tool and can be applied as first line diagnostic procedure as it is simple, relatively painless, cost effective less time consuming and gives quick results.Fluid cytology is useful complementary diagnosis for categorizing benign as well as malignant conditions.

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