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Original Research Paper

Comparing between serum-pleural effusion albumin gradient and Light's criteria in differentiating exudative from transudative pleural effusion

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ABSTRACT:

Background: Approximately about 10% of patients with internal diseases suffer from pleural effusion, For diagnosing and treatment plan the first step is to determine whether the effusion is exudate or transudate. If this classification is not correct, it may result in severe complications. **Aim:** This study is conducted to evaluation the diagnostic value of Serum Effusion Albumin Gradient (SEAG) criteria in comparison to Light's criteria to differentiate exudative from transudative pleural effusion. **Methods:** In this prospective study, population was grouped as exudative and transudative effusions depending on their confirmed aetiology, and was compared with the classification of Light's criteria and SEAG. Sensitivity and specificity of each indicator of Light's criteria were also compared with those of SEAG. **Results:** 41 of 45 exudates and 36 of 38 transudates were classified correctly using SEAG, the sensitivity and specificity were 91.1% and 94.7% respectively, meanwhile 43 exudates and 28 transudates were classified correctly using Light's criteria with sensitivity 95.6% and specificity 73.7%, pleural fluid protein/serum protein ratio had sensitivity of 86.05%, specificity of 80%, Pleural fluid to serum LDH ratio had sensitivity of 88.57%, specificity of 70.83%, Pleural fluid LDH index was found to have sensitivity of 84.44%, specificity of 84.21%. **Conclusion:** SEAG is better in identifying the transudative effusions than Light's criteria, but the latter still have a slight advantage in identifying exudative effusions.

Key words: Serum effusion albumin gradient, Light's criteria, exudates, transudates.

INTRODUCTION:

Pleural effusion is one of the commonest findings in the internal medicine, and is found in about 10% of patients with internal diseases [1], About 1.5 million cases are diagnosed annually in the United States[2]. Patients with pleural effusion are a very heterogeneous group in terms of clinical symptoms, diagnosis, and management [3]. Pleural effusions are divided into two basic types: exudative and transudative depending on the pathogenesis[4]. Congestive heart failure is the most common cause of transudative effusions, followed by hepatic hydrothorax and nephrotic syndrome, while parapneumonic effusions (PPE) is the commonest among exudative effusions, followed by malignant pleural effusions (MPE), tuberculous pleural effusions (TPE) and many other causes[1]. The classification of the effusion into exudative and transudative is the first and essential step to determine the cause of the effusion due to the fundamental differences in follow-up and management between these two types [5], and for this classification, Light's criteria rule was used fifty years ago and is still considered as a gold standard [6]

According to this rule, the effusion is considered as exudative when one of the following is met: pleural fluid protein/serum protein >0.5 , pleural fluid LDH/serum LDH >0.6, pleural fluid LDH > two-thirds of the upper normal reference limit for serum LDH, However, this rule failed in determining the type of some effusions, especially in transudative effusions[7], which prompted many to test other indicators such as cholesterol, bilirubin, and the albumin gradient between serum and pleural fluid (SEAG) [8][9], The albumin gradient was used to differentiate between the two types of effusion with a cut-off value of 1.2, the effusion is consistent with an transudate when the gradient is greater than this value[10].

MATERIAL AND METHODS:

The study was took place at Tishreen University Hospital, the sample included patients from various departments of the hospital who had pleural effusion between 2021-2022, the sample was divided into the exudative effusion group and the transudative effusion group according to their known aetiology. The biochemical parameters were analyzed for the pleural fluid and blood samples of the patients in order to apply Light's criteria and albumin gradient, and compare their results with the real results to evaluate the usefulness of each one. Total protein, albumin, and LDH were calculated to all patients using Mindray BS-380 device in the biochemistry laboratory at Tishreen University Hospital, the reference value of LDH was 418 IU, therefore two-thirds of it is 278 IU, The required value for the third Light's criterion. Study type: prospective study, the numerical variables were expressed by the arithmetic mean ± standard deviation and the categorical variables by percentages, the efficiency of the studied indicators was investigated according to the reference values, and the confusion matrix was obtained to reach the values of sensitivity, specificity positive predictive value (PPV), negative predictive value (NPV) and total accuracy, considering the cases of exudative effusion are the positive ones. Inclusion criteria: Patients with clinically and radiologically proven pleural effusion with a diagnosed specific cause, Exclusion criteria: age less than 15, multiple disease and traumatic hemothorax.

RESULTS:

The study included 83 patients, 46 males and 37 females, They were divided into 45 patients with exudative effusion and 38 patients with transudative effusion, the most common cause was MPE in 22 patients, (Table 1) shows the distribution of different cases of exudative and transudative pleural effusions**.**

Table 1: the distribution of different cases of exudative and transudative pleural effusions

MPE	22	Exudate
CHF	17	Transudate
Nephrotic syndrome	14	Transudate
PPE	8	Exudate
Hepatic hydrothorax	7	Transudate
TPE	5	Exudate
Pulmonary embolism	4	Exudate
Post-CABG	4	Exudate
Rheumatoid Effusion	2	Exudate

(Table 2) and (Table 3) show the main statistical parameters of the numerical variables in the exudative and transudative effusion groups, respectively:

Table 2: the main statistical parameters of the numerical variables in the exudative effusion group

variable	n	min	max	median	mean	sd
Age in years	45	16	82	57.5	55.614	15.949
Pleural Fluid Albumin g/dl	45	1.21	4.91	3.5	3.357	0.953
Pleural Fluid LDH U/l	45	13.6	1417.7	589.2	640.107	369.619

Pleural Fluid LDH/Serum LDH	45	0.039	9.715	1.314	1.769	1.759
Pleural Fluid Protein g/dl	45	2.2	6.6	4.9	4.658	1.182
Pleural Fluid Protein/Serum Protein	45	0.379	0.904	0.7	0.681	0.139
SEAG g/dl	45	0.3	2.6	0.9	0.974	0.405
Serum Albumin g/dl	45	2.3	5.8	4.3	4.331	0.818
Serum LDH U/l	45	53.3	1008.9	477	520.513	250.703
Serum Protein g/dl	45	4.8	8.2	6.8	6.797	0.829

Table 3: the main statistical parameters of the numerical variables in the transudative effusion group

variable	n	min	Max	median	mean	sd
Age in years	38	23	85	67.5	63.974	13.389
Pleural Fluid Albumin g/dl	38	0.03	3.1	0.9	1.16	0.876
Pleural Fluid LDH U/l	38	14	457.7	101.5	143.018	116.422
Pleural Fluid LDH/Serum LDH	38	0.089	1.413	0.401	0.408	0.252
Pleural Fluid Protein g/dl	38	0.6	3.8	1.75	1.983	0.974
Pleural Fluid Protein/Serum Protein	38	0.096	0.691	0.272	0.319	0.16
SEAG g/dl	38	1	5.34	3.09	3.046	1.217
Serum Albumin g/dl	38	2.65	5.8	4.185	4.206	0.844
Serum LDH U/l	38	91.2	720.2	296.8	333.663	157.985
Serum Protein g/dl	38	5.1	8	6.115	6.297	0.646

The arithmetic mean of the albumin gradient in the transudative effusion sample was 3.046 ± 1.217, which is a statistically significant difference (P<0.0001) greater than the mean of the exudative sample 0.974 ± 0.405. After applying light's criteria rule on the sample, this rule succeeded in classifying 43 out of 45 patients with exudative effusion correctly and 28 out of 38 transudative ones, while SEAG succeeded in classifying 41 exudative and 35 transudative, (Table 4) shows the number of cases truly classified according to each indicator of the Light's criteria individually, Light's criteria rule and SEAG.

Table 4: the number of cases truly classified according to each indicator

Effusion type	Total number	pleural fluid/Serum protein	pleural fluid/ serum LDH	Pleural fluid LDH>278U/L	Light's criteria rule	SEAG
Exudate	45	37	31	38	43	41
Transudate	38	32	34	32	28	36

Based on the data obtained in (Table 4), the sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each of the previous indicators (Table 5).

Table 5: the sensitivity, specificity, ppv, npv and accuracy of each indicator

	pleural fluid/Serum protein	pleural fluid/ serum LDH	Pleural fluid LDH>278U/L	Light's criteria rule	SEAG
Sensitivity	86.05%	88.57%	84.44%	95.56%	91.11%
Specificity	80.00%	70.83%	84.21%	73.68%	94.74%
PPV	82.22%	68.89%	86.36%	81.13%	95.35%
NPV	84.21%	89.47%	82.05%	93.33%	90.00%
Overall Accuracy	83.13%	78.31%	84.34%	84.34%	92.77%

DISCUSSION:

MPE was the most common cause in our study contrary to international references that consider congestive heart failure as the commonest one[1], this may be due to the presence of a big oncology department in our center, as for the transudative effusions, congestive heart failure was the most frequent, the study was in line with the reference studies here. Light's criteria rule had the highest sensitivity for diagnosing exudative effusions, reaching 95.6%, and it is close to the reference results [11]. This high sensitivity explains the continued reliance on Light's criteria as a golden standard for differentiating until now to avoid a misdiagnosis of serious conditions (e.g., malignancy) or diseases urgently needing specific therapies (e.g., infections) [12], followed by SEAG with a sensitivity of 91.1%. As for the specificity, the results were different, Light's criteria rule had a relatively low quality of 73.68%, and this low value is one of the most important reasons that keep us searching for more effective indicators. The reason behind the lower specificity of light's criteria rule is because it combines three dichotomous tests into a decision rule that is considered positive if any one of the tests is positive, which will increase the chance of diagnosing exudative effusions and thus the chance of obtaining false positive results, while the specificity of SEAG was the highest 94.74%. Now we find ourselves in front of two balance scales, If we rely on Light's criteria rule, false positives will be increased and the result will be more costly and unnecessary invasive interventions such as pleural biopsy, thoracoscopy, and even thoracotomy. These interventions are not free of morbidity when they are performed in patients with a systemic disorder such as heart, renal, or hepatic failure[13], meanwhile relying on SEAG alone will allow a few cases to lose the chance of detect their important exudative diagnosis, The role of medical history and clinical examination may outweigh one side of this scale. A study by Sujatha conducted an analysis of a sample of 100 cases, 78 of them had exudative effusion and 22 had transudative, Light's criteria succeeded in classification for all the exudative cases (100% sensitivity) but failed in 5 transudative cases (77.3% specificity), while the albumin gradient obtained 97.4% sensitivity and 100% specificity [14]. In general, these results are consistent with the results of our study. In another study by Sandeesha, the albumin gradient had a sensitivity of 93.2% and a specificity of 90.1%, while Light's criteria had a sensitivity of 100% and a specificity of 70%[15]. Finally, in the most recent study that published in 2022 and included 97 cases, 57 exu and 42 trans, the albumin gradient significantly outperformed Light's criteria rule, as its sensitivity and specificity were 95.1% and 93.3%, respectively, compared to 78.3% and 75.6% % for Light's [16].

CONCLUSION:

The importance of SEAG stands out in the classification of transudative effusions, which are frequently diagnosed exudative according to Light's criteria. SEAG is also superior to each individual indicator of Light's criteria, while Light's criteria is still the best in detecting exudative effusions, in the end there is not yet any laboratory indicator capable of correct classification with 100% accuracy.

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