RESEARCH ARTICLE

CORRELATION OF B-LINES ON LUNG ULTRASOUND AND NT PRO BNP TO DIFFERENTIATE BETWEEN ACUTE HEART FAILURE FROM OTHER NON CARDIOGENIC CAUSES OF DYSPNEA- A PROSPECTIVE DIAGNOSTIC STUDY

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Manuscript Info

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Abstract

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Background: Dyspnea can be a manifestation of a variety of clinical conditions like acute heart failure (AHF), chronic obstructive pulmonary disease (COPD), pneumonia, pulmonary embolism and asthma. Dyspnea can prove to be life threatening and therefore it is immensely important to initiate the treatment at the earliest. It is not uncommon for patients to present as combination of various causes of breathing difficulty. In fact it is often almost impossible to discriminate between cardiogenic and non cardiogenic causes of dyspnea on initial presentation. A diagnostic aid which can be used at this very minute of presentation can prove to be boon for emergency physicians to accurately recognize the cause and initiate the treatment. We correlated the presence of B lines on lung USG and NT proBNP in cardiogenic pulmonary edema.

Methods: A diagnostic prospective study was done on patients of age more than 18 years presenting with acute dyspnea to the emergency department after obtaining informed consent. Lung ultrasound was done to look for B- lines and NT-Pro BNP samples were sent along with the other investigations. More than 3 B-lines in the anterior surface of the chest present bilaterally were taken as positive. NT pro BNP values above 900pg/ml were considered significantly positive. Final diagnosis made by Cardiologist/Intensivist/Pulmonologist was recorded.

Results: 65 patients presenting with symptoms of breathlessness were studied. 49 patients had presence of B-lines on the lung USG constituting about 75.4% of the patients. Based on history, clinical examination, initial diagnosis of cardiogenic dyspnea was made in 50.8% of 49 patients with B profile. Out of the 49 patients with positive B lines, 40 patients were finally diagnosed with cardiac failure by cardiologists/ intensivists with a sensitivity of B- lines to diagnose cardiac failure is 90.91%, specificity is 57.14%, Positive predictive value is 81.63% and Negative Predictive value is 75%. The data analysis showed that out of 49 subjects who had B profile of the lung, 44 patients had positive NT pro BNP values above 900pg/ml. However, A-profile of the lung was present in all the patients with NT proBNP values more

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than 900pg/ml. The mean NT-proBNP in the patients having B-profile was 8182. 47 while it was 251.69 in the patients having A-profile of the lung. We found good association and correlation between the two variables. Area under the curve suggested both lung USG and NT proBNP had good and similar diagnostic accuracy.

Conclusion: In acute onset of dyspnea, presence of B-lines on Lung Ultrasound has very good sensitivity to diagnose acute heart failure. The diagnostic accuracy increases if there are 4-5 B-lines present bilaterally on Lung Ultrasound. It has a strong correlation with raised NT- proBNP levels in diagnosis Acute Heart Failure. If the number of B-lines on Lung Ultrasound increases, the value of NT-pro BNP also increases.

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Introduction:-
Acute dyspnea is among the most common presentations to the Emergency Department (ED). Discriminating between cardiac and non-cardiac causes of dyspnea can sometimes be challenging.[1]

Point of care ultrasound (POCUS) is rapidly gaining an evidence base to support its use as an aid to traditional management techniques in the acutely ill patient. It has become firmly established in the acute and critical care settings (FAST, vascular access, echocardiography), and is now increasingly being used as an important tool in the assessment of lungs.[2]

Lung ultrasound has various advantages, as it is relatively easy-to-learn, quick to perform, portable, repeatable, non-ionizing and therefore suitable for evaluating patients in the Emergency Department for respiratory distress.[3] Previous studies have been done to explore the utility of lung ultrasound in differentiating the diagnosis of Acute Heart Failure with other causes of dyspnea. B lines – it is a subjective measure and assessment could vary with the individuals making these readings– hence a definitive objective measurement are needed for these tests.

Natriuretic peptides have been useful markers in differentiating acute dyspneic patients and has emerged as a potent prognostic marker for patients with congestive heart failure. NT-proBNP values are helpful in diagnosis of acute cardiogenic pulmonary oedema. Values of NT proBNP of 300pg/ml has been taken as the exclusionary limit in all ages. NT pro BNP values are depending on BMI, age and gender and laboratory method (assay sensitivity). The values of NT Pro BNP are also affected in conditions such as chronic renal failure sepsis and cardiac rhythm abnormalities.[4] Initial higher levels of NT-Pro BNP have been found have associated with poorer prognosis.[5]

Hence the study was taken up the to correlate the sensitivity of B lines on lung USG and compare the values of NT– pro BNP in differentiating cardiac and non-cardiac causes for dyspnea.

Methods:-
This prospective diagnostic study was conducted in a tertiary care hospital for a period of twelve months with an approval from institutional ethics committee. All patients enrolled for the study were provided the details of the study, risks of participating in the study and informed consent was taken. Patients of age more than eighteen years visiting the emergency room with complaints of acute onset of dyspnea were included in the study. Pregnant lactating women and patients of age less than eighteen years were excluded. Convenience sampling were performed, and the study included sixty-five patients. The primary objective was to correlate the sensitivity of B lines on lung USG and compare the values of NT proBNP to differentiate individuals with cardiac and non-cardiac causes of dyspnea.

Once the patients with acute onset of dyspnea arrived at the emergency department, complete history and examination of the patient was done. Lung ultrasound was done to look for B-lines and NT-Pro BNP samples were prescribed along with the other investigations (ABG, ECG, chest X-ray, echocardiography, complete blood count, urea and electrolytes and other relevant investigations).

The lung ultrasound was performed by those who are certified to perform ultrasound in emergency department. It was performed in the sitting posture using the convex probe of frequency 3-5MHz. Lung areas were assessed by moving the probe along the intercostals space in the anterior surface of the chest. With the probe application in two places in front of

the chest and the other more extended, evaluation of each intercostal space was done. It is basically used as B-Mode. B-Lines were looked for in both the lungs. The lung ultrasound images were saved in the USG machine for the review by the consultants. Presence of 3 or more B-lines in the anterior surface of the chest present bilaterally were taken as positive.

For NT-proBNP, blood samples were taken in plain vial before any pharmacological treatment and were performed at hospital laboratory. It is processed by electrochemiluminescence method by Cobas- 6000 machine. The age related threshold limit for positive NT-Pro BNP values are as follows:
1. Age <50years- 450pg/ml
2. Age 50-70years- 900pg/ml
3. Age >75years- 1800pg/ml.

Results were followed and values above 900pg/ml were considered significantly positive since the mean age of the subjects in our study was 70.5 years. The patients were stabilized and admitted in Intensive Care Unit or wards. The results of NT-Pro BNP were followed up. The patients were followed up till their discharge and final diagnosis made by cardiologist/intensivist/pulmonologist which was recorded.

Data analysis was done by using statistical software SPSS version16.0 and entered in microsoft excel spread sheet. All the continuous variables was assessed for the normality using Shapiro Wilk's test. If the variables were normally distributed, they were expressed as Mean+/-SD. All categorical variables were expressed either as percentage or proportions. Comparison of continuous variables was done by independent t test. Comparison of categorical variables was done by either chi-square test or Fischer's exact test based on number of observations.

Results And Discussion:-
In the current study we have studied sixty five patients presenting with symptoms of breathlessness, 49 patients had presence of B-lines on the lung USG constituting about 75.4% of the patients. Based on history, clinical examination, initial diagnosis of purely cardiogenic dyspnea was made in 50.8% of 49 patients with B profile. Out of the 49 patients with positive B-lines, 40 patients were finally diagnosed with cardiac failure by cardiologists/intensivists. In our study data analysis revealed that sensitivity of B-lines to diagnose cardiac failure is 90.91%, specificity is 57.14%, Positive predictive value is 81.63% and Negative Predictive value is 75%.

Blines categories

Frequency			Percent	Valid Percent	Cumulative Percent
Valid	B line+	49	75.4	75.4	75.4
	B lines -	16	24.6	24.6	100.0
	Total	65	100.0	100.0	

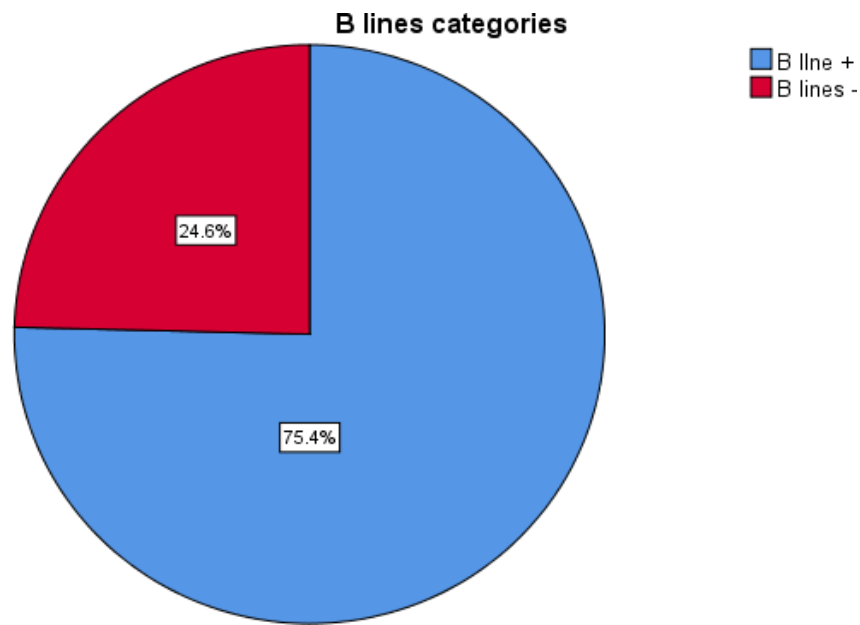**Table1:-** Showing B lines are present in 49 patients constituting 75.4% subjects.

B lines categories

Figure 1:-Pie diagram shows that 75.4% of the presenting with acute onset of dyspnea to ED had B-Profile of the lung.
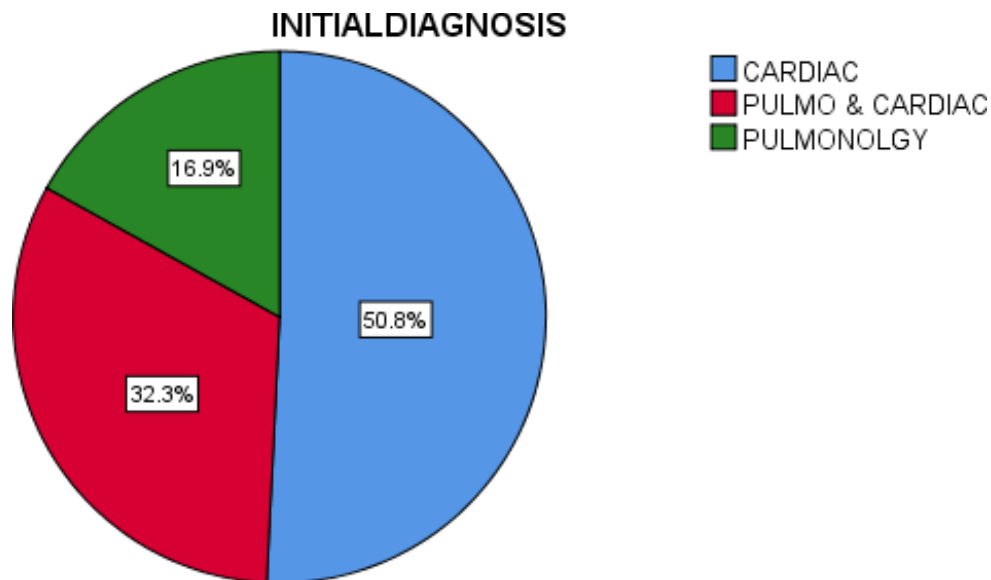
INITIALDIAGNOSIS

Figure 2:-Out of 49 patients who had B- profile, 50.8% were initially treated as cardiac failure alone, 32.3% were treated as cardiac failure with concomitant pulmonary disease.
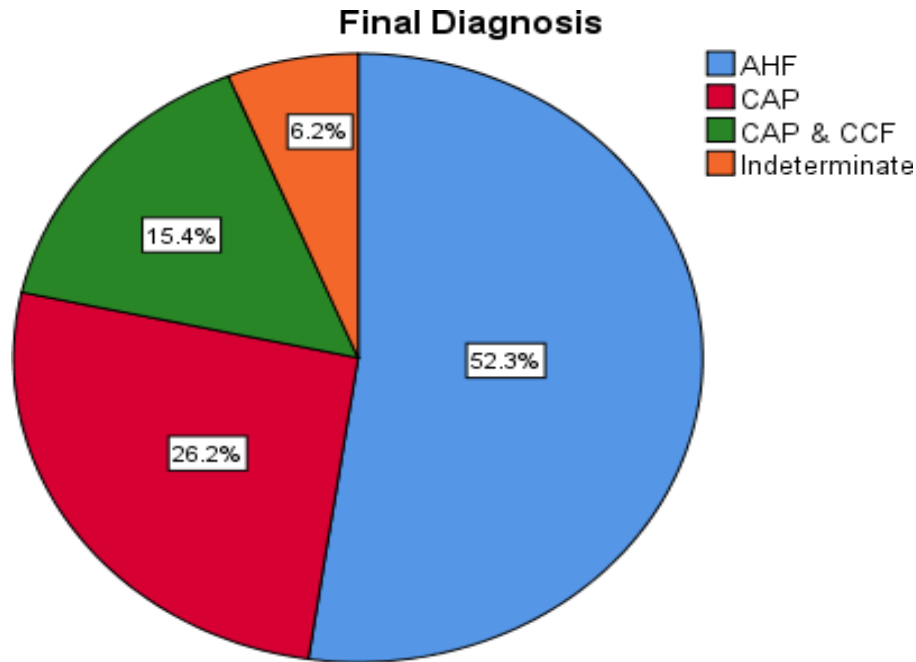
Figure3:- Final diagnosis of cardiac failure was present in 52.3% of cases as compared to the initial diagnosis in 50.8% of cases as shown in figure 2.

However, according to another study Zouheir Bitar, Ossama Mardaani et al[6], it was found that sensitivity of B-lines of 95%; specificity of 92% with NPV of 88% and PPV of 90%. While another study done by authors Siang-Hu Ang and Phillip Andrus[7] also found that sensitivity of 90%, specificity of 96%. Authors E Pivetta, M Tizzani et al[8] also found sensitivity of 85.3% and specificity of 90%. All three studies showed a higher specificity but similar sensitivity.

In our study we found that A-profile of the lung was present in all the patients with NT-proBNP values more than 900pg/ml. These results are also have similar findings found in different studies done by ZouheirBitar, Ossama Mardaani[6] et al and Gregor Preson, Petra Klemen et al[9].

The data analysis showed that out of 49 subjects who had B-profile of the lung, 44 patients had positive NT pro BNP values above 900pg/ml. The mean NT- pro BNP in the patients having B-profile was 8182.47pg/ml while it was 251.69pg/ml in the patients having A-profile of the lung. The distributions show significant differences in means in the two groups (MannWhitney U p value < 0.005, which is statistically significant). Authors Zouheir Bitar, Ossama Mardaani et al[6] also found the same.

Group Statistics

	B lines categories	N	Mean	Std. Deviation	Std .Error Mean
NT PROBNP	B line+	49	8182.47	9731.625	1390.232
	B lines -	16	251.69	252.234	63.058

Table2:-Out of 49 patients with B-profile, 44 patients had NT proBNP values >900pg/ml. Mean value- 8182.47pg/ml.
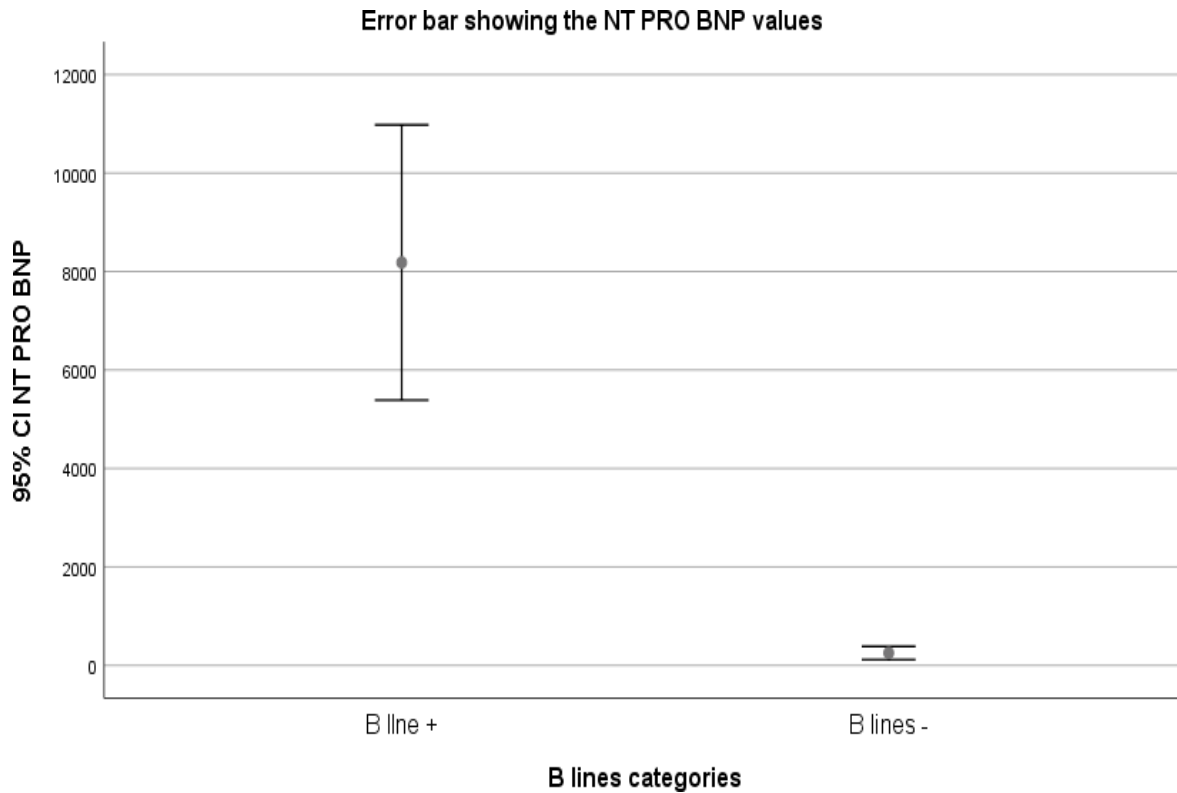
Figure 4:- Relationship between presence of B-lines and raised levels of NT-Pro BNP. If B-lines are present then, in 95%of the patients have higher NT-Pro BNP values.

Mann-WhitneyU	187.000
Wilcoxon W	418.000
Z	-3.858
Asymp. Sig. (2-tailed)	.001

Table3:-Mann- Whitney U test, showing significant difference in distribution.

Final diagnosis of cardiac failure was made by Intensivist/Cardiologist in 40 patients. Out of the 40 patients, 34 patients had NT- Pro BNP values above 900pg/ml.

	FINAL DIAGNOSIS	
	Cardiac	Non Cardiac
NT-ProBNP>900pg	34	6
NT-ProBNP<900pg	10	15

Table 4:- 40 patients who had NT- Pro BNP values above 900pg/ml, 34 patients were found to have cardiac failure on final diagnosis.
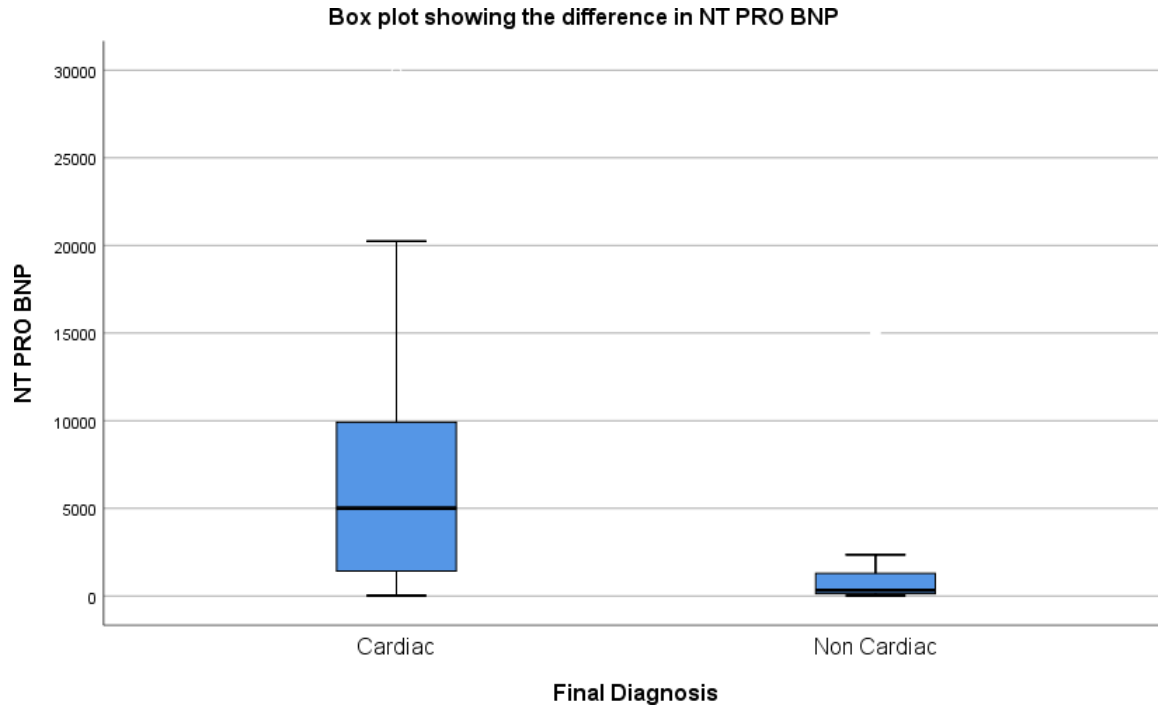
Figure5:- Box plot diagram, showing a strong association between NT-proBNP and Cardiac Failure.

Our study also found out that there is strong correlation between presence of B-lines on Lung USG and raised levels of NT-pro BNP. Authors Glöckner E, ChristM. Geier Fetal also concluded the same in their study.

B lines			NT PROBNP
B lines	Pearson Correlation	1	.848[**]
	Sig.(2-tailed)		.000
	N	51	51
NT PROBNP	Pearson Correlation	.848[**]	1
	Sig.(2-tailed)	.000	
	N	51	65

Table5:-Indicates strength of association between B lines and NT proBNP. And that the correlation coefficient is very highly significant different from zero (p< 0.001).

Value		Df	Asymptotic Significance(2-sided)	Exact Sig.(2-sided)	Exact Sig.(1-sided)
Pearson Chi-Square	17.689[a]	1	.000		
Continuity Correction[b]	15.194	1	.000		
Likelihood Ratio	17.059	1	.000		
Fisher's Exact Test				.000	.000
No of Valid Cases	65				

Table6:- Chi-square test, p value is 0.000;

From the above table since p value is 0.000; we can reject the null hypothesis and conclude that there is a relationship between presence of B lines and NT-Pro BNP levels at 5% significant levels.

In our study, the area under the curve for B-lines and NT-pro BNP is 0.752 and 0.757 respectively which is statistically significant. This suggests that both Lung USG and NT proBNP have good and similar diagnostic accuracy. In another study done by authors Gregor Preson, Petra Klemen et al[9] also had similar findings. Authors Katsuya Kajimota, Kelko Madeen et al[10] also found AUC for BNP as 0.75. In contrast, authors Marcello Pastrelli, Matteo Capecia V, Veronica Gialli et al did a study and found AUC for B-lines being 0.82 and that for NT-pro BNP was 0.75.

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In our study we found that there is a strong positive relationship between number of B-lines and increased levels NT-proBNP. The study also shows the significant association between two variables. Authors E. Glöckner E, Christ M, Geier F[11] also found strong association between the two variables(p=0.005).
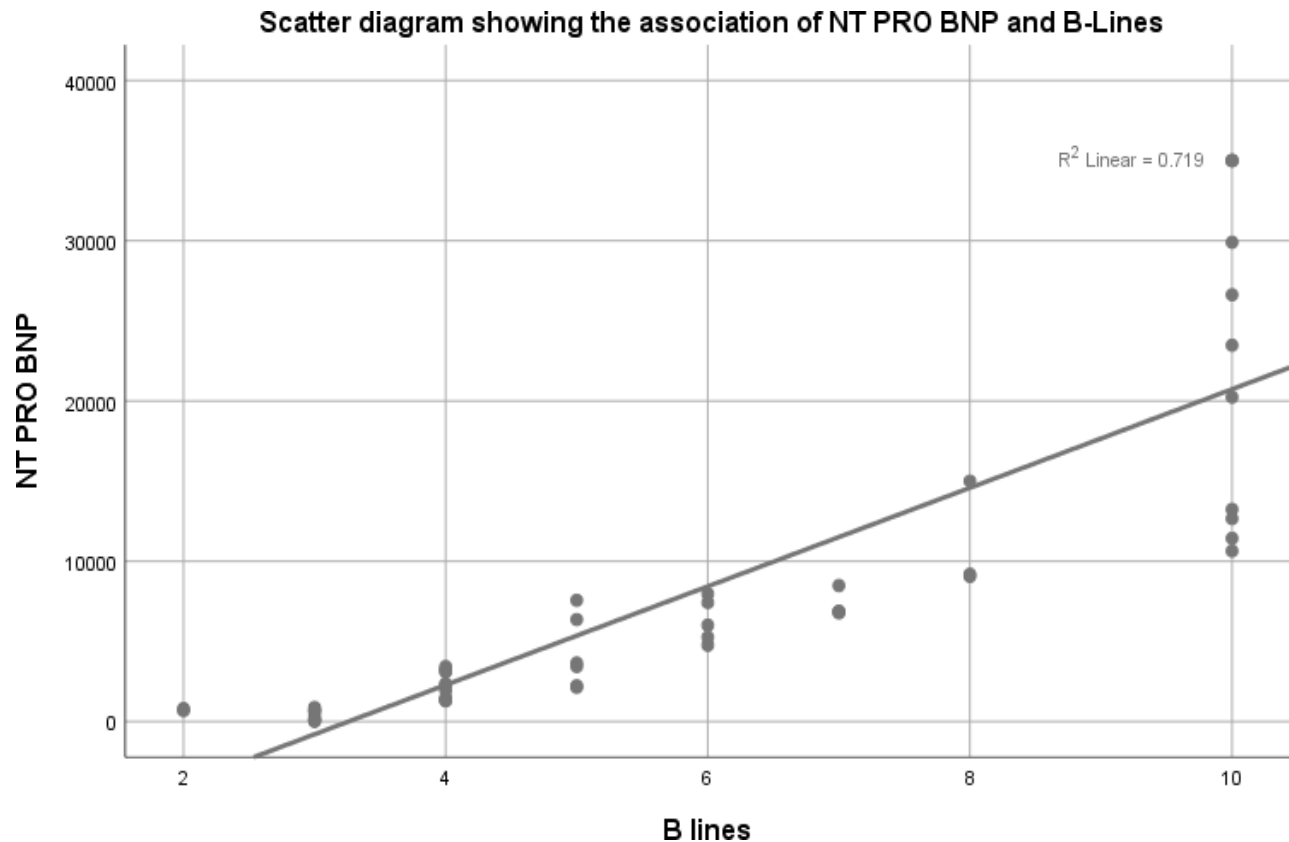

Figure6:-Illustrating a positive linear relationship and also strong strength of relationship indicating that more the number of B-lines seen on lung USG, higher the level of NT-proBNP.

Natriuretic peptides are atrial natriuretic peptide (ANP), B-type Natriuretic peptide (BNP), C-type natriuretic peptide and D- type natriurtic peptide. ANP and BNP have cardiovascular actions while C-type natriuretic peptide affects vascular endothelial system. DNP like activity has been found in myocardium and human plasma. ANP is stored in atrial granules and is released in a significant amount into blood even by a slight stimulus. However, it is not practical to measure ANP levels because it has a shorter half-life.[12]

BNP consists of 32 amino acids. It is secreted in response to the ventricular wall tension. Inactive NT-pro BNP and active molecule of BNP are secreted into blood in equal amounts; Hence both can be used to assess ventricular tension. In case of ventricular wall tension, NT-pro BNP is produced in both right and left ventricle causing smooth muscle proliferation of blood vessels and diuresis, vasodilatation, renin inhibition and aldosterone production.[13]

Ultrasound was first used in 1942 by Neurologist and psychiatrist Karl Theodore Dussik for medical diagnosis. He used it for detecting brain tumors. Since then, ultrasound has been used in various clinical applications and more advanced modes were also invented.[14] In healthy individuals, ultrasound shows homogenous, hyperechogenic pattern called as A-lines. They are present on pleural line and are formed due to reverberation between air in the alveoli and chest wall. The presence of lung sliding and A-lines signifies normal aerated healthy lung.[15]

Normally, due to the presence of air in the lungs, it is not possible to visualize organs in thoracic cavity. Air is in close contact with water in lung parenchyma and interaction of water and air leads to formation of artifacts and hence we can see the lung image. These artifacts can be static, dynamic or those used in assessment of inflammatory lesions and artifacts in pulmonary embolism.

While doing a longitudinal scan, acoustic shadows of two neighboring ribs are visible and a hyperechogenic line between them is seen, called as "bat sign".This line is pleural line, made up of the parietal pleura, the visceral pleura and a small amount of fluid between them.

Normally, it is smooth and around 2 mm thick, moving synchronously with respiration, characteristically called as, dynamic sign of lung sliding.

In case of fluid overload, there is an increase in pressure in pulmonary capillaries, resulting in formation of transudate in lung parenchyma and pulmonary alveoli causing disturbance in air and water balance. The result is appearance of B lines also called as comet-tail artifacts.

B lines appear due to presence of small amount of water under the visceral pleura, mostly in inter alveolar septa. B lines are vertical, hyperechogenic acoustic shadows arise from the pleural line, extend up to the bottom of the screen without fading and moves synchronously with lung sliding. The presence of one or two B-line artifacts is considered as normal.

Presence of 3 or more B lines bilaterally indicates increased extravascular lung water hence suggesting diagnosis of pulmonary oedema or acute respiratory distress syndrome.[3]

There are some limitation of this study. Small sample size of only 65 patients is major limitation of the study. The presence or absence of B-lines on lung ultrasound is also affected by any pre-hospital treatment with diuretics giving false negative results. The levels of NT-proBNP are affected by age, gender, rhythm abnormalities, chronic kidney disease. Our study did not take into account the difference in levels of NT-proBNP accordingly. Only one cutoff value was considered significantly positive.

Conclusion:-
1. In acute onset of dyspnea, presence of B-lines on Lung Ultrasound has very good sensitivity to diagnose acute heart failure.
2. The diagnostic accuracy increases if there are 4-5 B-lines present bilaterally on Lung ultrasound.
3. It has a strong correlation with raised NT- pro BNP levels in diagnosis Acute Heart failure.
4. If the number of B-lines on Lung Ultrasound increases, the value of NT-pro BNP also increases.

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