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STUDY OF LIVER FUNCTION AND SERUM ELECTROLYTES (SODIUM, POTASSIUM, MAGNESIUM AND CALCIUM) IN PATIENTS OF CONGESTIVE HEART FAILURE

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ABSTRACT Congestive Heart Failure (CHF) is a burgeoning problem worldwide with more than 20 million people affected. It is defined as a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood. The present study is to evaluate liver function and level of serum electrolytes (sodium, potassium, magnesium and calcium) in patients of congestive heart failure attending a tertiary care hospital of Tripura. **Aims And Objectives:** To evaluate Liver function and level of serum electrolytes (sodium, potassium, magnesium and calcium) in patients of CHF admitted in Medicine ward of AGMC & GBP Hospital. **Materials And Methods:** 45 (Forty five) patients of diagnosed CHF who were admitted in the Medicine ward of AGMC & GBPH during the study period. **Results:** Except in case of total protein and albumin, all the other parameters of Liver Function like total bilirubin, direct bilirubin, SGPT, SGOT, ALP shows negative correlation with ejection fraction .Serum electrolytes are showing positive correlation with ejection fraction and significance level are <0.001. **Conclusion:** Early diagnosis of liver function abnormalities and electrolyte imbalances can be used to prevent complications in patients with CHF.

KEYWORDS : Serum electrolytes, Congestive heart failure

INTRODUCTION:

Congestive Heart Failure (CHF) is a burgeoning problem worldwide with more than 20 million people affected. The current American College of Cardiology Foundation (ACCF) / American Heart Association guidelines define CHF as a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood which in turn leads to cardinal clinical symptoms of dyspnoea, fatigue, wheezing, cough, arrhythmias, angina, heart attacks, gastrointestinal symptoms, impaired liver function, impaired kidney function, pulmonary edema, abnormal heart rhythms, central sleep apnoea, loss of muscle mass.[1]

Rheumatic Heart Disease remains a major cause of CHF in Asia, especially in young. Not surprisingly, 'Anemia' is a frequent concomitant factor in CHF in developing nations. As developing nations undergo socioeconomic development, the epidemiology of CHF is becoming similar to that of western Europe and North America with Coronary Artery Disease emerging as the single most common cause of CHF. Although the contribution of Diabetes Mellitus to CHF is not well understood, diabetes accelerates atherosclerosis & often is associated with hypertension. Despite many recent advances in the evaluation & management of CHF, the development of symptomatic CHF still carries a poor prognosis. Community based studies indicate that 30% - 40% of patients die within one year of diagnosis & 60% - 70% die within five years, mainly from worsening CHF or as a sudden event (probably because of a ventricular arrhythmia). Patients with symptoms at rest (New York Heart Association, class IV) have a 30% - 70% annual mortality rate, whereas symptomatic patients with moderate activity (NYHA class II) have a annual mortality rate of 5% - 10%.

According to the study conducted by **Hajouli S et al**,[2] three main phenotypes describe HF according to the measurement of the left ventricle ejection fraction (EF), and the differentiation between these types is important due to different demographics, co-morbidities, and response to therapies:

- Heart failure with reduced ejection fraction (HFrEF): EF less than or equal to 40%
- Heart failure with preserved EF (HFpEF): EF is greater than or equal to 50%
- Heart failure with mid-range EF (HFmrEF) (other names are: HFpEF-borderline and HFpEF-improved when EF in HFrEF improves to greater than 40%): EF is 41% to 49% per European guidelines and 40 to 49% per the US guidelines.[3][4]new reference page. A new class of HF that introduced by the 2016 European Society of Cardiology (ESC) guidelines for diagnosis and management of HF. This class was known as the grey area between the HFpEF and HFrEF and now has its distinct entity by giving it a name as HFmrEF.

All patients with HFrEF have concomitant diastolic dysfunction; in contrast, diastolic dysfunction may occur in the absence of systolic dysfunction.[3]

From this perspective, we would like to conduct a study to assess Liver Function Test & serum sodium, potassium, magnesium and calcium in CHF patients attending Agartala Government Medical College & Gobinda Ballabh Pant Hospital. The study may throw some light for early detection of these complications of CHF & may be of helpful to reduce the mortality by some modification of management.

AIMS AND OBJECTIVE

Aim:

To evaluate Liver function and level of serum electrolytes (sodium, potassium, magnesium and calcium) in patients of Congestive Heart Failure admitted in medicine ward of AGMC & GBP Hospital.

Objectives:-

1) To estimate Liver Function among the patients with congestive Heart Failure.

2) To estimate level of Serum Electrolytes (sodium, potassium,

magnesium and calcium) among the Congestive Heart Failure patients admitted in the Department of Medicine, AGMC & GBP Hospital.

MATERIAL AND METHODS:

This is a cross-sectional, hospital based Observational study. Sample size includes 45 (Forty five) patients of diagnosed Congestive Heart Failure who were admitted in the medicine ward of AGMC & GBPH.

- Inclusion criteria: Subjects with evidence of congestive heart failure due to various etiologies.
- Exclusion criteria: Chronic liver disease, chronic renal disease, any other chronic illnesses,pregnancy, patients unwilling to participate in the study.

Sample Collection:

Under aseptic measures 5 ml of blood drawn preferably from the antecubital vein using a sterile needle and syringe. Blood sample kept in container were allowed to clot at room temperature and then serum was separated by centrifugation. Whenever possible the analysis was done immediately. In case, there is a possibility of delay the serum aliquots was stored at 2-8 degree celcius until analysis.

Biochemical Analysis:

Serum total and direct bilirubin estimation by Diazo method, Serum SGPT/ALT and SGOT/AST estimation by ALT reagent based on the recommendation of IFCC without PLP, Serum ALP estimation by ALP-AMP method, total protein estimation by Biuret method, Serum albumin estimation by BCG method, estimation of serum sodium, potassium by ISE method, Estimation of serum magnesium by Calmagite method, Estimation of serum calcium by Arsenazo method. All the Liver parameters are estimated by using autoanalyzer.

RESULTS:

Table I- Descriptive Statistics (mean, Standard Deviation) Of Ejection Fraction, Duration Of Disease In Years, Systolic And Diastolic Blood Pressure, Body Mass Index.

Descriptive Statistics			
	Mean	Std. Deviation	N
Ejection fraction	44.65	4.239	46
DOD	6.28	2.770	46
SBP	181.52	26.033	46
DBP	106.74	10.468	46
BMI	16.041	1.23082	46

Table II - Mean And Standard Deviation Of Ejection Fraction, Total Bilirubin, Direct Bilirubin, SGPT, SGOT, ALP, Total Protein, Albumin.

	Mean	Std. Deviation	N
Ejection fraction	44.65	4.239	46
Total Bilirubin	0.7163	0.47871	46
Direct Bilirubin	0.5357	0.36299	46
SGPT	69.24	31.567	46
SGOT	71.28	33.086	46
ALP	213.20	75.020	46
Total Protein	6.6748	1.08260	46
Albumin	4.0248	0.76763	46

Table III - Mean And Standard Deviation Of Ejection Fraction, Sodium, Potassium, Calcium And Magnesium.

	Mean	Std. Deviation
Ejection fraction	44.65	4.239
Sodium	135.98	7.912
Potassium	3.8200	0.83119
Calcium	9.6207	1.04800
Magnesium	1.5963	.41025

Table IV (showing Pearson Correlation Of Ejection Fraction With Total Bilirubin, Direct Bilirubin, SGPT, SGOT, ALP, Total Protein, Albumin.)

	Pearson Correlations						
	Total Bilirubin	Direct Bilirubin	SGPT	SGOT	ALP	Total Protein	Albumin
Ejection fraction	-.783**	-.718**	-.767**	-.799**	-.919**	.979**	.843**
Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001	<.001

** Correlation is significant at the 0.01 level (2-tailed).

Table V- Anova In Between Groups And Within Groups Of Liver Parameters And Their Significance Level.

ANOVA						
		Sum of Squares	Df	Mean Square	F	Sig.
Total Bilirubin	Between Groups	7.751	2	3.875	65.059	<.001
	Within Groups	2.561	43	0.060		
	Total	10.312	45			
Direct Bilirubin	Between Groups	4.785	2	2.393	89.954	<.001
	Within Groups	1.144	43	0.027		
	Total	5.929	45			
SGPT	Between Groups	27697.284	2	13848.642	34.737	<.001
	Within Groups	17143.086	43	398.676		
	Total	44840.370	45			
SGOT	Between Groups	29531.021	2	14765.511	32.183	<.001
	Within Groups	19728.305	43	458.798		
	Total	49259.326	45			
ALP	Between Groups	166512.920	2	83256.460	41.269	<.001
	Within Groups	86748.319	43	2017.403		
	Total	253261.239	45			
Total Protein	Between Groups	28.500	2	14.250	25.276	<.001
	Within Groups	24.242	43	.564		
	Total	52.741	45			
Albumin	Between Groups	18.959	2	9.479	53.932	<.001
	Within Groups	7.558	43	0.176		
	Total	26.516	45			

Table no. V – Anova study in between groups in case of liver parameters shows p value<0.001.

Table VI - Linear Regression Parameter Estimates Of Liver Parameters With Ejection Fraction.

Linear Regression Parameter Estimates							
Dependent Variable	Parameter	B	Std. Error	T	Sig.	99% Confidence Interval	
						Lower Bound	Upper Bound
Total Bilirubin	Intercept	4.667	.475	9.830	<.001	3.388	5.945
	Ejectionfraction	-.088	0.011	-8.358	<.001	-.117	-.060
Direct Bilirubin	P	3.280	0.403	8.135	<.001	2.195	4.366
	Ejectionfraction	-.061	0.009	-6.837	<.001	-.086	-.037
SGPT	Intercept	324.425	32.288	10.048	<.001	237.497	411.352
	Ejectionfraction	-5.715	0.720	-7.938	<.001	-7.653	-3.777
SGOT	Intercept	349.683	31.755	11.012	<.001	264.190	435.175

	Ejectionfraction	-6.235	0.708	-8.806	<.001	-8.141	-4.329
ALP	Intercept	939.280	47.259	19.875	<.001	812.045	1066.514
	Ejectionfraction	-16.261	1.054	-15.431	<.001	-19.098	-13.424
Total Protein	Intercept	-4.490	0.353	-12.729	<.001	-5.439	-3.540
	Ejectionfraction	.250	0.008	31.792	<.001	0.229	0.271
Albumin	Intercept	-2.791	0.659	-4.234	<.001	-4.565	-1.016
	Ejectionfraction	.153	.015	10.387	<.001	0.113	.192

Table VI shows Linear regression parameter estimates of all the liver parameters with ejection fraction which are statistically significant($p<0.001$).

Table Vii – Descriptive Statistics Of Serum Electrolytes With Reduced, Midrange, Preserved Ejection Fraction And Total.

		N	Mean	SD	99% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Sodium	HFrEF	6	118.17	5.845	108.54	127.79	110	125
	HFmrEF	35	137.89	2.918	136.54	139.23	131	143
	HFpEF	5	144.00	1.000	141.94	146.06	143	145
	Total	46	135.98	7.912	132.84	139.12	110	145
Potassium	HFrEF	6	2.5500	.18708	2.2420	2.8580	2.30	2.80
	HFmrEF	35	3.8463	.59069	3.5739	4.1187	2.90	4.70
	HFpEF	5	5.1600	.30496	4.5321	5.7879	4.80	5.50
	Total	46	3.8200	.83119	3.4904	4.1496	2.30	5.50
Calcium	HFrEF	6	7.9500	.18708	7.6420	8.2580	7.70	8.20
	HFmrEF	35	9.6929	.78010	9.3331	10.0526	8.30	10.70
	HFpEF	5	11.120	.31145	10.4787	11.7613	10.80	11.50
	Total	46	9.6207	1.0480	9.2051	10.0362	7.70	11.50
Magnesium	HFrEF	6	1.0500	.05477	.9598	1.1402	1.00	1.10
	HFmrEF	35	1.5809	.28447	1.4497	1.7121	1.10	2.10
	HFpEF	5	2.3600	.15166	2.0477	2.6723	2.20	2.50
	Total	46	1.5963	.41025	1.4336	1.7590	1.00	2.50

Table VIII- Anova In Between Groups And Within Groups In Case Of Serum Electrolytes Along With Their Significance Level

ANOVA						
		Sum of Squares	Df	Mean Square	F	Sig.
Sodium	Between Groups	2352.602	2	1176.301	108.922	<.001
	Within Groups	464.376	43	10.799		
	Total	2816.978	45			
Potassium	Between Groups	18.680	2	9.340	32.361	<.001
	Within Groups	12.410	43	0.289		
	Total	31.090	45			
Calcium	Between Groups	28.169	2	14.085	28.495	<.001
	Within Groups	21.254	43	0.494		
	Total	49.423	45			
Magnesium	Between Groups	4.715	2	2.358	35.465	<.001
	Within Groups	2.858	43	0.066		
	Total	7.574	45			

ANOVA study in between groups in case of sodium, potassium, calcium and magnesium shows statistically significant result ($p<0.001$).

Table IX - Linear Regression Parameter Estimates Of The Serum Electrolytes With Ejection Fraction And Their Significance Level.

Linear Regression Parameter Estimates							
Dependent Variable	Parameter	B	Std. Error	T	Sig.	99% Confidence Interval	
						Lower Bound	Upper Bound
Sodium	Intercept	71.099	7.923	8.973	<.001	49.767	92.430
	Ejectionfraction	1.453	.177	8.225	<.001	0.977	1.929
Potassium	Intercept	-4.662	0.330	-14.142	<.001	-5.549	-3.774
	Ejectionfraction	0.190	0.007	25.844	<.001	0.170	0.210
Calcium	Intercept	-.780	0.561	-1.390	00.172	-2.290	0.730
	Ejectionfraction	0.233	0.013	18.623	<.001	0.199	0.267
Magnesium	Intercept	-2.668	0.106	-25.121	<.001	-2.954	-2.382
	Ejectionfraction	0.096	0.002	40.326	<.001	0.089	0.102

General Linear Model

Linear regression parameter estimates of sodium, potassium, calcium, magnesium with ejection fraction shows statistically significant result($p<0.001$).

DISCUSSION:

Except in case of total protein and albumin, all the other parameters of liver function like total bilirubin, direct bilirubin, SGPT, SGOT, ALP shows negative correlation with ejection fraction and pearson correlation showing significant level because of increased central venous pressure results in congestive hepatopathy and also because of low protein diet. Anova features in between groups of all the above mentioned liver parameters are significant ($p< 0.001$).

Serum electrolytes (sodium, potassium, magnesium, calcium) are showing positive correlation with ejection fraction and significance level are <0.001. Anova features in between groups of sodium, potassium, magnesium and calcium are significant as decrease in cardiac output leads directly to a reduction in renal blood flow, with impairment of renal excretion of water and electrolytes.

With increase in mean of above electrolytes – heart failure controlled. In regression coefficient analysis, magnesium shows significant correlation ($p<0.001$) with ejection fraction due to activation of the renin – angiotensin – aldosterone and sympathoadrenergic system.

Oertel (1910) named this condition "multiple non-inflammatory necrosis of the liver with jaundice in chronic cyanosis" and ascribed to the liver the chief role in the production of the jaundice.[4] Fishberg (1923) emphasized the serious prognostic import of jaundice in heart failure and attributed it to increased red cell destruction.[5] Jolliffe (1930) reported a 5 per cent incidence of visible jaundice in 231 cases, there being no apparent relation to the severity of heart failure.[6] Keefer and Resnik (1926) found jaundice most commonly in rheumatic patients with auricular fibrillation and long-standing failure.[7] Boland and Willius (1938) noted icterus in 14.6 per cent of 75 patients and emphasized the fact that repeated bouts of cardiac failure contributed to the incidence of jaundice.[8] Halsted and Bauer, Meakins, Chavez, Sepulveda and Ortega all report elevated bilirubin values in from 37 to 84 per cent of their patients and again correlate degree and duration of failure

with the incidence of jaundice.[9,10]

Vyskocilova et al. (2015) found that ALT and AST pattern predominated in the left-sided forward AHF (more likely presented by reduced EF), while cholestatic profile occurred mainly in the bilateral and right-sided AHF.[11]

Japanese Acute Decompensated Heart Failure Syndrome Registry reported 11.6% hyponatremics, Korean heart failure Registry (KorHF) reported 18%, Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) reported 19.7%, Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheter Effectiveness (ESCAPE) trial reported 24%, and Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) trial reported 27% hyponatremia.[12-16]

In heart failure subjects, there is evidence that the serum potassium level should be maintained above 4.5 mEq/L to minimize the risk of SCD. A mild hypokalemia may be corrected by the use of aldosterone receptor antagonists such as spironolactone or eplerenone, while a more severe hypokalemia should preferably be corrected using K^+ supplement.[17] However, potassium replacement should be routinely considered in patients with CHF, even if the initial potassium determination appears to be normal.[18]

The prognostic significance of serum magnesium concentration in CHF subjects is currently under investigation, although in a retrospective study of subjects with moderate-to-severe CHF, an inverse correlation was noted between mortality and plasma magnesium. [19]

Hypocalcemia (total serum calcium concentration <8.6 mg/dL or ionized calcium concentration < 1.1 mmol/L) is less investigated in HF subjects even though not of minor importance. Despite the pivotal role of calcium ions in contraction of cardiac muscle, few cases of hypocalcemia in CHF have been reported and these are often in association with hypomagnesemia.[20,21]

SUMMARY AND CONCLUSION:

In our study, it has been observed that patients with congestive heart failure had liver function abnormalities and electrolyte imbalance. In conclusion, it is to be stated that the differences found in the liver parameters and serum electrolyte levels in patients with congestive heart failure can be used as a diagnostic tool in our daily practices. Early diagnosis of liver function abnormalities and electrolyte imbalances can also be used to prevent complications in patients with congestive heart failure.

Limitation:

In this study, sample size is small. So, there is need of bigger sample size to correlate the different parameters very sophistically.

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