# The Effect of Limiting Fluid Intake on Clinical, Biochemical and Functional Parameters in Compensated Heart Failure Patients at a North Indian Hospital

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# ABSTRACT

# BACKGROUND

Restriction of fluid is widely adopted as a strategic non-pharmacological therapy for patients with heart failure (HF). However, insufficient fluid leads to intravascular volume contraction further causing hypoperfusion of vital organs. Renal dysfunction and cardiac ischemia caused by hypoperfusion can further aggravate heart failure. Therefore, the authors decided to study the effect of fluid intake on various functional and cardiac parameters of patients of HF.

### METHODS

50 patients with a diagnosis of heart failure with reduced ejection fraction who had been discharged from the hospital since last 6 months and who were on restricted fluid therapy were included in the study. Patients were advised to visit the OPD once every 4 weeks and provide a record of their fluid intake. All patients irrespective of functional class were advised a fluid intake of 30 mL / day / Kg body weight. Functional status, biochemical parameters and clinical parameters were measured regularly until the end of 12 weeks.

### RESULTS

There was marked improvement in the functional status of patients and statistically significant number was shifted from NYHA III and IV to NYHA I and II. PFI (Prescribed Fluid Intake) was associated with improvement of exercise tolerance in all NYHA Classes. Creatinine levels declined in all NYHA Classes with very high drop from 2.32 to 1.0 in NYHA Class IV.

# CONCLUSIONS

Compensated HF patients should be prescribed physiologically correct dietary fluid intake based on body weight. This improves their functional capacity, biochemical parameters and left ventricular ejection fraction.

### **KEYWORDS**

Heart Failure, Diet, Sodium-Restricted, Diuretics, Exercise Tolerance

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# BACKGROUND

India faces a major challenge from the epidemic of noncommunicable lifestyle diseases. Chaturvedi et al found that prevalence of heart failure (HF) in a rural community as well as tertiary care hospital in North India was 1.2 / 1000.<sup>1</sup> According to the Trivandrum Heart Failure Registry,<sup>2</sup> India accounts for 25 % of the world HF patients with an estimated 1.3 to 23 million persons. Compared to western countries, Indian patients suffer from HF at a younger age.<sup>3</sup>

Initially HF was considered a "Cardio-Renal Model" caused by excessive intake of salt leading to water retention and abnormalities of renal blood flow.<sup>4</sup> This has been the reason that dietary fluid intake became a prime adjunct in management of HF. Later haemodynamic measurements associated HF to reduced cardiac output and excessive peripheral vasoconstriction. Thus the "cardio circulatory" or "haemodynamic" model of HF was considered as a result of abnormalities of the pumping capacity of the heart and excessive peripheral vasoconstriction.<sup>5</sup>

For a healthy person, the physiological fluid requirement is 30 - 35 mL / day / Kg body weight. Physiologically, fluid deficit of 2 % of the body weight or more has been linked to decline in mental functions and reduced capacity to physical exercise. Therefore, restricted fluid intake in CHF (Congestive Heart Failure) patients may deteriorate normal physiological functions, cause dryness of skin and itching and damage kidneys and heart due to hypoperfusion.

In addition, the last two decades have witnessed development of drugs that can improve the cardiac function, reduce preload and afterload on the heart, counteract neuro-hormonal activation and drive out surplus fluid.<sup>6</sup>

Therefore, the authors decided to study the effect of fluid intake on various functional and cardiac parameters of patients of HF.

#### METHODS

This study was carried out at the Army Hospital Research & Referral, New Delhi (AHRR). Patients with a diagnosis of heart failure with reduced ejection fraction, LVEF (Left Ventricular Ejection Fraction) < 40 % on 2-Dimensional echocardiography who had been discharged from the hospital since last 6 months and were on restricted fluid therapy were included in the study. 150 such patients were individually contacted over telephone and requested to voluntarily report in person. Chronic kidney disease patients with creatinine clearance < 30 mL / min, chronic liver disease and patients having grade 3 and grade 4 pedal oedema were excluded. Out of the 150 patients, 50 were followed up every 4 weeks for a total of 12 weeks in Cardiology OPD. On their first visit patients were divided into 4 groups depending upon their functional class as follows and their average voluntary fluid intake (VFI) being taken pre-treatment was noted.

2,300 mL or 37 mL / Kg in NYHA Class I; 2,426 mL or 36 mL / Kg in NYHA Class II; 2,066 mL or 31 mL / Kg in NYHA Class III and 1,466 mL or 23 mL / Kg in NYHA Class IV.

After their acceptance to join this study, all patients irrespective of functional class were advised a fluid intake of 30 mL / day / Kg body weight. Patients were examined and their medical history, symptoms of HF and medications were recorded. Baseline 2D echocardiography was done. Functional assessment was done with modified Bruce TMT protocol. Blood samples were taken at every visit and analysed for sodium, potassium, blood urea nitrogen (BUN), creatinine and haemoglobin and compared against the normal values. (Sodium: 135 - 145 mEq / L, Potassium: 3.5 - 5.5 mEq / L, Creatinine: 0.8 - 1.2 mg / dL, haemoglobin: male > 13 gm / dL and for female > 12 g / dL). Patients were advised to visit the OPD Clinic once every 4 weeks and provide a record of their fluid intake. Weight and waist circumference were measured until the end of 12 week period.

#### **Statistical Analysis**

Pre-treatment parameters were obtained from patients when they were on voluntary fluid intake (VFI). The posttreatment parameters were taken after the patients were on prescribed fluid intake (PFI) for at least 12 weeks. The pre and post-treatment parameters were recorded and analysed separately using SPSS software.

#### RESULTS

50 heart failure patients were enrolled in this study. 60 % had ischemic aetiology while 40 % were non-ischemic. 7 patients (13 %) had CRT device (Cardiac Resynchronization Therapy) and 13 patients (25 %) had AICD's (Automated Intracardiac Defibrillator Device). Out of 50 patients in this study 24 % (12) were females and 76 % (38) were males. All baselines parameters were well balanced in the two groups except serum creatinine and LVESD. Mean serum creatinine was 1.5 mg / dL in males. LVEF was 33 % in both groups. (Table 1). After 12 weeks of prescribed fluid intake mean serum creatinine decreased to 1.04 mg. There was significant increase (p value < .05) in exercise capacity in female group from 4.2 to 6.3 METS (Metabolic Equivalent of Task) and from 4.9 to 5.5 METS in males.

This study cohort of 50 patients was divided into 5 age groups. 3 patients were less than 40 years; 4 were between 41 - 50 years; 9 were between 51 – 60 years; 17 were between 61 - 70 years and 17 were above 70 years (Table 2). Age group differences for most parameters were nonsignificant. Lower K + levels were observed for less than 40 years age group. LVEF was minimal in < 40 years age group and maximum of 35 % in > 70 years at baseline. Among all groups exercise tolerance was best among 41 - 50 years (6.42 METS) at base line and least (4.67 METS) in 51 - 60 years age group. Post treatment after 12 weeks there was significant increase in exercise capacity in majority age groups; best improvement was seen in > 70 years age group where exercise capacity increase from 4.8 to 6.3 METS; followed by 61 - 70 years age group where increase was from 4.67 to 6 METS.

No. of Patier	nts Fe	emale - 12	Male -	· 38 C	verall - 50							
Parameters												
	Volunta	ry Fluid Inta	ke (Pre-Trea	itment)	2 22 4 2 26							
HD	1.	$1.83 \pm 0.40$	12.47 ±	0.32 1	$2.32 \pm 0.26$							
Creatinine	12	$.82^{-} \pm 0.11$	1.50° ±	0.18 1	$1.34 \pm 0.14$							
K +	4	$54 \pm 0.18$	4 44 +	0.09 1	1 46 + 0 08							
I VEE	33	333 + 216	33 16 +	138 3	$320 \pm 116$							
LVESD	49	$5.35 \pm 2.10$ 5 75 <sup>b</sup> + 2 09	51.08° +	1.30 3	$9.80 \pm 1.10$							
LVEDD	57	$7.50 \pm 1.94$	61.34 ±	1.58 6	$0.42 \pm 1.30$							
TMT	4	$.20 \pm 0.47$	4.99 ±	0.24 4	$1.79^{B} \pm 0.22$							
Prescribed Fluid Intake (Post-Treatment)												
Hb	12	2.56 ± 0.30	12.79 ±	0.23 1	2.73 <sup>A</sup> ± 0.18							
Creatinine	1	.42ª ± 0.36	1.04 <sup>b</sup> ±	0.05	1.13 ± 0.09							
Na +	13	7.83 ± 1.36	136.50 ±	0.55 13	$36.82 \pm 0.53$							
K +	4	.58 ± 0.15	4.32 ±	0.12 4	1.38 ± 0.10							
LVEF	33	3.33 ± 2.07	34.08 ±	1.80 3	3.90 ± 1.45							
LVESD	49.08 ± 4.47		49.24 ± 1.65		49.20 ± 1.63							
LVEDD	VEDD 58.58 ± 4.66		61.24 ±	1.62 6	$60.60 \pm 1.64$							
TMT	6	.33 ± 0.94	5.53 ±	0.23 5	$1.73^{A} \pm 0.30$							
Table 1.	Sex Wise	e Average a	nd Standard	d Error of	Various							
Parameters	in Patien	ts on Volun	tary and Pr	escribed F	luid Intake							
Means bearing	g different su	perscripts diffe	r significantly (	o < 0.05) fror	n each other							
			Ago in Yoars									
	< 40	41 - 50	51 - 60	61 - 70	> 70							
No. of				47	47							
Patients	3	4	9	17	17							
Parameter	Volumba	or Fluid Take	ke (Dre Tree									
	13.23	12 38	12 06	12 37	12 23							
Hb	±	±	±	±	±							
	0.48	1.57	0.42	0.52	0.41							
	2.17	1.01	1.47	1.13	1.40							
Creatinine	±	±	±	±	±							
	135.33	139.25	139.22	137.06	139.41							
Na +	±	±	±	±	±							
	4.67	1.11	1.38	0.82	1.20							
	3.83 <sup>b</sup>	4.15 <sup>ab</sup>	4.71ª	4.38 <sup>ab</sup>	4.61ª							
К +	± 0.23	± 0.14	± 0 10	± 0.13	± 0.15							
	30.00	33.75	33.89	31.18	35.29							
LVEF	±	±	±	±	±							
	5.00	6.25	3.38	1.80	1.99							
	48.00	51.50	47.89	49.41	51.12							
LVESD	± 473	± 4 37	± 3 35	± 139	± 233							
	59.00	63.00	59.44	59.29	61.71							
LVEDD	±	±	±	±	±							
	3.21	5.21	2.96	2.14	2.57							
тмт	4.63	6.42°	4.14	4.6/**	4.8/**							
	1.89	1.25	0.46	0.28	0.31							
	Prescribe	ed Fluid Inta	ke (Post-Tre	atment)								
	12.70	12.53	12.28	12.93	12.84							
HD	± 0.85	± 0.8.0	± 0.38	± 0 3 2	± 0.35							
	1.07	1.05	1.21	0.52	1.29							
Creatinine	±	±	±	±	±							
	0.09	0.13	0.09	0.06	0.26							
No ±	138.33	137.00	137.00	137.47 ±	135.76							
ina +	2.03	2.86	1.55	0.80	0.80							
	3.83 <sup>b</sup>	4.88ª	4.07 <sup>ab</sup>	4.50 <sup>ab</sup>	4.41 <sup>ab</sup>							
K +	±	±	±	±	±							
	0.15	0.38	0.37	0.16	0.11							
LVFF	но.00 ±	51.25 ±	/ە.ەر ±	52.04 ±	55.24 ±							
	5.77	5.91	12.50	2.27	2.42							
	32.00 <sup>b</sup>	55.00ª	50.89ª	49.53ª	49.65ª							
LVESD	±	±	±	±	±							
	3.46 42.67 <sup>b</sup>	4.04 65 75ª	3.54 60.67ª	2.45 60 Q/a	3.11 62 19ª							
LVEDD	±.07	±	±	±	±							
	2.40	4.29	3.61	2.17	3.33							
_	3.90 <sup>c</sup>	7.27ª	4.04 <sup>bc</sup>	6.00 <sup>abc</sup>	6.33 <sup>ab</sup>							
TMT	±	±	±	±	±							
Table 2		0.9/	0.49	0.40	Various							
Parameters	in Pation	ts on Volum	tary and P	escribed E	luid Inteko							
Means bearing	different su	perscripts diffe	r significantly (	p < 0.05) from	m each other							

# **Original Research Article**

There was a significant decrease in both left ventricular end systolic dimension (LVESD) and left ventricular end diastolic dimension (LVEDD) amongst the patients below 40 years on prescribed fluid intake. Differences for other age groups were not significant for these parameters. Post prescribed fluid intake treatment, left ventricular ejection fraction (LVEF) increased in all group of patients except in > 70 years age group; best improvement was seen in < 40 years age group where ejection fraction (EF) increased from 30 % to 40 %.

	NYHA Class												
	I		11	I	11	I	v						
Parameter													
NYHA Class Average and Standard Error of Various Parameters in													
Patients on Voluntary Fluid Intake													
No. of Patients	12		23	12		3							
Hb	13.46 ± 0.57	$11.88 \pm 0.36$		11.99 ± 0.40		12.53 ± 1.38							
Creatinine	$1.43^{ab} \pm 0.35$	$1.01^{b} \pm 0.07$		$1.62^{ab} \pm 0.35$		2.32ª ± 1.24							
Na +	139.08 ± 0.76 1		3.48 ± 0.90	136.83 ± 1.70		140.00 ± 2.31							
K +	4.52 ± 0.17		51 ± 0.13	4.42 ± 0.16		4.13 ± 0.47							
LVEF	35.83ª ± 2.12	36.	.52ª ± 1.39	27.08 <sup>b</sup> ± 1.79		$21.67^{b} \pm 4.41$							
LVESD	48.58 <sup>b</sup> ± 2.44	48.	.39 <sup>b</sup> ± 1.79	51.50 <sup>ab</sup> ± 1.76		58.67 <sup>a</sup> ± 4.37							
LVEDD	61.17 <sup>ab</sup> ± 2.49 5		.83 <sup>b</sup> ± 2.16	62.25 <sup>ab</sup> ± 1.59		70.00 <sup>a</sup> ± 5.29							
TMT	5.94ª ± 0.49	4.8	$32^{ab} \pm 0.27$	3.65 <sup>b</sup> ± 0.30		$3.20^{ab} \pm 0.20$							
NYHA Class Average and Standard Error of Various Parameters in													
Patients on Prescribed Fluid Intake													
No. of Patients	12 00 + 0 20		21	12.2	4		12.00						
HD	12.80 ± 0.28	12	2.70 ± 0.29	$12.20 \pm 0.59$		13.90							
Creatinine	$1.19 \pm 0.19$	1	$.12 \pm 0.05$	$0.95 \pm 0.06$		1.00							
Na +	$136.92 \pm 0.71$	13	6.57 ± 0.89	$136.50 \pm 2.10$		141.00							
K +	$4.40 \pm 0.18$	4	.32 ± 0.12	$4.60 \pm 0.23$		4.10							
LVEF	34.79 ± 2.10	34	1.76 ± 2.30	$27.50 \pm 10.05$		20.00							
LVESD	47.88 ± 2.49	50	).29 ± 2.29	48.00 ± 7.07		63.00							
LVEDD	59.25 ± 2.48	61.81 ± 2.07		59.50 ± 10.05		72.00							
TMT	$6.38 \pm 0.50$	6.38 ± 0.50 5.01 ± 0		5.93	± 0.81	3.40							
Table 3. I	NYHA Class A	vera	ge and St	andard	l Error d	of Vari	ous						
Parameters	in Patients of	1 Vo	oluntary a	nd Pres	scribed	Fluid 1	ntake						
Means bearing	different supersci	ripts	differ signific	antly (p	< 0.05) fi	rom eac	h other						
NY			Unit	T	TT	TTT	τv						
Patients on Voluntary Fluid Inta		ake	Number	12	23	12	3						
No. of Patients on Prescribed Flui Intake			Number	24	21	4	1						
Average Voluntary Fluid Intake			mL / Kg BW	37	36	31	23						
Average Prescribed Fluid Intake			mL / Kg BW	35	35	35	35						
Pre-Treatment Creatinine				1.43	1.01	1.62	2.32						
Pre-Treatment LVEF			%	35,83	36,52	27.08	21.67						
Post-Tre	Post-Treatment LVEF		%	34.79	34.76	27.5	20						
Pre-Treatment TMT			METS	5.94	4.82	3.65	4.4						
Table 4. Impact of Eluid Intake on Select Parameters													
Table	Table 4. Impact of Fluid Intake on Select Parameters before and after Treatment												

Among 50 patients in this study patients were grouped according to NYHA Class (Table 3). Serum creatinine was highest in NYHA IV group (2.32 mg / dL). LVEF was maximum in NYHA Class II (36.5 %) and minimum in Class IV group (21 %). Class IV group had maximally dilated left ventricle with LVESD of 58.6 mm and LVEDD of 70 mm. Exercise tolerance was maximum in NYHA Class I group (5.9 METS) and least in NYHA Class III (3.65 METS). Although, LVEF and TMT were higher in NYHA Class I & II in

comparison to NYHA Class III & IV, these differences were statistically non-significant because of large variation.

After 12 weeks of Prescribed Fluid Intake NYHA Class differences were non-significant for all the parameters. This may be attributed to the significant improvement observed in NYHA Class through PFI. For example, there were 3 patients in NYHA Stage IV when on VFI but on PFI only 1 remained in Stage IV. The corresponding reduction of patients in NYHA III and NYHA II were 12 to 4 and 23 to 21. This improvement has led to increase in number of patients in NYHA I heart failure condition from 12 pre-treatment to 24 post-treatment. This may be attributed to the PFI.

# DISCUSSION

Fluid overload in patients with heart dysfunction is detrimental and can precipitate acute decompensation. Therefore, restriction of fluid is widely adopted as a strategic non-pharmacological therapy for patients with HF. However, insufficient fluid volume as a result of fluid restriction can cause hypoperfusion of vital organs. Renal dysfunction and cardiac ischemia caused by hypoperfusion can further aggravate heart failure.

In this study, we investigated the effect of a weight based fluid intake on various parameters of HF patients. Pre -treatment parameters were those recorded while the patients were on their wilful and uncompelled fluid intake. The post-treatment parameters were taken after the patients were prescribed fluid intake (PFI) of 30 mL / Kg / day continued for the study period of at least 12 weeks. This is one of the first studies to apply a uniform weight based fluid intake for comparison of results. The results of this study raise an interrogation point on the conventional approach of restricting the fluid intake universally for all patients of HF. The observed impact of fluid intake on important HF indicators is presented in Table 4.

#### **Effect of PFI on NYHA Class**

Within the 12 week's period, the number of patients that shifted from NYHA III and IV to NYHA I and II were large enough to justify our prescription. In contrast to our study Philipson et al.<sup>7</sup> restricted the intake of fluid to 1.5 L / day and that of sodium to 135 mg / dL / day. In their study, the number of patients in NYHA III came down from 35 to 28. Of these, one patient was upgraded to Class I and 6 upgraded to Class II.

### Effect of PFI on Serum Creatinine Level

Creatinine levels declined in all NYHA Classes with very high drop from 2.32 to 1.0 in NYHA Class IV. There was no significant variation in creatinine in other studies.<sup>8,9,10</sup> In a trial conducted by Albert et al<sup>9</sup> creatinine had increased almost by 50 percent in the group that was given water at 2 litre / day with low dose of diuretics and salt restricted diet as compared to the group given 1 I / day and high dose of diuretics.

#### Effect of PFI on LVEF

In our study, the PFI improved the LVEF of all NYHA Classes even though the increase in LVEF was non-significant.

## **Effect of PFI on Exercise Tolerance**

PFI was associated with improvement of exercise tolerance in all NYHA Classes. In fact, the improvement was very noteworthy and significant in NYHA Class III. Our results are contrary to intervention comparison on 6-minute walk test between a fluid intake of 1.5 l / day and 30 mL / Kg per day intake.<sup>11</sup>

#### **Effect of PFI on Biochemical Parameters**

We noted that with PFI, there were no significant difference in biochemical parameters such as sodium and potassium. Our results confirmed the findings of obtained in other studies.<sup>7,12</sup> As in our study fluid restriction did not improve outcomes in a number of other studies,<sup>8,10</sup> Only in those subsets of patients who have hyponatremia and fluid overload; fluid restriction has been found to be useful.<sup>9,12,13</sup> It has been shown that beneficial effect of fluid restriction is short lived, as contraction of intravascular volume leads to increase in anti-diuretic hormone which increases the absorption of water from distal renal tubules and nullifies the effect of fluid restriction.<sup>13,14</sup>

# CONCLUSIONS

Compensated HF patients should be prescribed physiologically correct dietary fluid intake based on body weight of the patient. Such a prescription on fluid intake improves their functional capacity, biochemical parameters and LVEF. It is therefore submitted that dietary fluid restriction should not routinely be recommended to all HF patients. Their condition with regard decompensated HF and / or hyponatremia must be assessed and fluid restriction based on body weight should be recommended.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

### REFERENCES

- Chaturvedi V, Parakh N, Seth S, et al. Heart failure in India: The INDUS (INDia Ukieri Study) study. J Pract Cardiovasc Sci 2016;2(1):28-35.
- [2] Harikrishnan S, Sanjay G, Anees T, et al. Clinical presentation, management, in-hospital and 90-day outcomes of heart failure patients in Trivandrum, Kerala, India: the Trivandrum Heart Failure Registry. Eur J Heart Fail 2015;17(8):794-800.

- [3] Pillai HS, Ganapathi S. Heart failure in South Asia. Curr Cardiol Rev 2013;9(2):102-111.
- [4] Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380(9859):2095-2128.
- [5] Packer M. The neurohormonal hypothesis: a theory to explain the mechanism of disease progression in heart failure. J Am Coll Cardiol 1992;20(1):248-254.
- [6] Holst M, Strömberg A, Lindholm M, et al. Fluid restriction in heart failure patients: is it useful? The design of a prospective, randomised study. Eur J Cardiovasc Nurs 2003;2(3):237-242.
- [7] Philipson H, Ekman I, Forslund HB, et al. Salt and fluid restriction is effective in patients with chronic heart failure. Eur J Heart Fail 2013;15(11):1304-1310.
- [8] Paterna S, Parrinello G, Cannizzaro S, et al. Medium term effects of different dosage of diuretic, sodium, and fluid administration on neurohormonal and clinical outcome in patients with recently compensated heart failure. Am J Cardiol 2009;103(1):93-102.
- [9] Albert NM, Nutter B, Forney J, et al. A randomized controlled pilot study of outcomes of strict allowance of fluid therapy in hyponatremic heart failure (SALT-HF). J

# Original Research Article

Card Fail 2013;19(1):1-9. http://dx.doi.org/10.1016/j.cardfail.2012.11.007.

- [10] Aliti GB, Rabelo ER, Clausell N, et al. Aggressive fluid and sodium restriction in acute decompensated heart failure: a randomized clinical trial. JAMA Intern Med 2013;173(12):1058-1064.
- [11] Holst M, Strömberg A, Lindholm M, et al. Liberal versus restricted fluid prescription in stabilised patients with chronic heart failure: result of a randomised cross-over study of the effects on health-related quality of life, physical capacity, thirst and morbidity. Scand Cardiovasc J 2008;42(5):316-322.
- [12] Travers B, O'Loughlin C, Murphy NF, et al. Fluid restriction in the management of decompensated heart failure: no impact on time to clinical stability. J Card Fail 2007;13(2):128-132.
- [13] De Vecchis R, Baldi C, Cioppa C, et al. Effects of limiting fluid intake on clinical and laboratory outcomes in patients with heart failure: results of a meta-analysis of randomized controlled trials. Herz 2016;41(1):63-75.
- [14] Li Y, Fu B, Qian X. Liberal versus restricted fluid administration in heart failure patients. A systematic review and meta-analysis of randomized trials. Int Heart J 2015;56(2):192-195.