# Salt Based or BaLanced SolUtion–Trends Existing in Indian Intensive Care Units: A Multicenter Prospective Observational Cohort Study (SOLUTE Study)

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## Abstract

Introduction: Fluid administration is a commonly practiced intervention in the intensive care unit (ICU) with normal saline being the preferred fluid. We sought to understand the current practice of fluid administration and choice of fluids in Indian ICUs and its effect on renal outcomes. **Materials and methods:** The Indian Society of Critical Care Medicine (ISCCM)-endorsed multicenter prospective observational study was conducted on practice of fluid administration in critically ill patients between May 1, 2020, and January 31, 2023. SPSS software was used for statistical analysis.

**Results:** Private sector hospitals contributed 79.16% of data out of 144 ICUs. Around 961 patients belonged to the normal saline (NS) group, 672 to the Ringer's lactate (RL) group, and 891 to the balanced salt solution (BSS) group out of 2,452 patients. Patients with chronic obstructive pulmonary disease were more in the BSS and NS group as compared to RL group (p < 0.0001). Acute kidney injury (AKI) incidence was higher in the NS group, followed by RL and BSS (p < 0.0001). The serum creatinine rise was higher in the NS group on the first 2 days (p < 0.001). Daily fluid balance, urine output, and renal replacement therapy (RRT) needs were similar among the groups. The BSS group had shorter ICU and hospital length of stay (LOS) than the NS group (p < 0.001). The ICU survival was 63.3% in the NS group and 79.44% in the BSS group (p < 0.001). The AKI patients had higher survival in the BSS group (78.81%) as compared to the NS group (p < 0.001).

**Conclusion:** Balanced salt solution is the preferred intravenous fluid with a safe renal profile among critically ill patients. The AKI patients had shorter hospital and ICU LOS with BSS as compared to NS.

Keywords: Acute kidney injury, Balanced salt solution, ICU length of stay, Normal saline.

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## HIGHLIGHTS

- SOLUTE study highlights that the most preferred fluid given in ICU is normal saline in Indian ICUs.
- Balanced salt solution (BSS) is associated with reduced incidence of AKI as compared to normal saline in comparable groups.
- ICU and hospital length of stay is lower in the BSS group with lower mortality as shown by the study.

## INTRODUCTION

Fluid administration is one of the cornerstone therapies that is performed in intensive care units (ICUs) across the world. Historically, 0.9% normal saline (NS) has been the preferred fluid for most of the patients despite the risks of hyperchloremic metabolic acidosis<sup>1</sup> and acute kidney injury<sup>2</sup> (AKI), which are associated with large volume administration. Owing to these known side effects, the use of crystalloid solutions like Ringer's lactate and Plasma-Lyte A, which have a composition closer to human plasma, have increased and are considered as an alternative to saline therapy. These solutions are called BSS. The evidence regarding the superiority of BSS over NS is still not clear on various aspects of patient care like AKI, the need for renal replacement therapy (RRT), or death. <sup>1,3</sup>Department of Critical Care Medicine, Narayana Superspeciality Hospital, Gurugram, Haryana, India

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© The Author(s). 2024 Open Access. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons. org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated. The use of fluids in our country has been very varied, and there has been no data to date regarding the practices in ICUs in India. To study the practice pattern of administering intravenous fluids in India, we conducted this multicentric observational study and looked at various outcomes between the NS and BSS groups. This is the first Indian study capturing the aspect of fluid administration in ICUs of our country.

## **MATERIALS AND METHODS**

The Indian Society of Critical Care Medicine (ISCCM)-endorsed this study. The National Principal Investigator (PI) was responsible for conducting the study nationwide. Ethics approval was not mandatory from the participating centers as no patient intervention was done, and only data about the intravenous fluids used in the patient care and patient laboratory tests were captured. Still, each center had to follow their respective hospital norms. The study received clearance from the Institutional Ethics Committee (IEC) bearing the registration number ECR/226/INST/DL/2013/ RR-22 with ethics approval number 35. Consent waiver for data capture was obtained from the Institutional Ethics Committee of the Principal Investigator but other hospitals had to follow their institutional protocol. The study was registered with CTRI with REF/2020/05/033965. The data were captured on an online case record form (CRF). The CRF was divided into three domains covering: (a) baseline characteristics of the patient; (b) intervention details; and (c) outcome details. The participating ICUs had to complete an ICU registration form, following which they were provided a unique username and password to fill out the online CRF. Each participating ICU had one designated principal investigator (PI) and one Co-PI, and they were responsible for data capturing and data uploading on the online CRF. The study duration was from May 2020 to January 2023. The data regarding the type and volume of fluid administered to all ICU patients who were admitted for at least 3 days in the ICU were captured. The entire data were scrutinized and analyzed by the National PI and the steering committee of the study.

All sections of the CRF were mandatory. Section I captured the patient demographics, comorbidities, and the indication of admission to the ICU. Scores like Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) were also captured along with baseline serum creatinine.

The intervention-related data included the type and volume of various intravenous fluids administered before ICU admission. In the ICU, data were captured for the first 3 days like fluid administered as a bolus, maintenance and replacement to all patients, daily urine output and fluid balance, and worst laboratory values and arterial blood gas (ABG) values. SOFA scores were also captured for the first 3 days. Any evidence of sepsis was defined as per the SEPSIS-3 definition. Bolus fluid administration was defined as fluid given was more than 5 mL/kg within 1 h. Maintenance fluid was defined as a fluid that is given continuously to meet daily fluid requirements. Replacement fluid was defined as fluid that is given for the replacement of losses like drain losses, gastric loss, or dilution for antibiotics and other medications.

The outcome-related data captured indications of RRT. Renal outcome was defined both as Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) and Kidney Disease Improving Global Outcomes (KDIGO) criteria for the first 3 days. The ICU and hospital length of stay (LOS) was captured along with the survival status from ICU and hospital up to day 28. <sup>20,21</sup>Department of Critical Care, Royal Care Superspeciality Hospital, Coimbatore, Tamil Nadu, India

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The data were divided into various crystalloid groups like Ringer lactate, normal saline, and balanced salt solutions and were then analyzed.

#### **Statistical Analysis**

The analysis included profiling of patients on different demographic, clinical, severity scores, types and volume of various fluids administered, kidney function test, complication, and outcome parameters. The quantitative data have been shown as mean and standard deviation, whereas qualitative/categorical data have been shown as absolute numbers and proportions. Cross tables were generated and Chi-square test was used for the testing of association. The quantitative outcome parameters were compared using the independent Student t test. *P*-value < 0.05 was considered statistically significant. The statistical analysis was carried out on IBM SPSS statistics software for Windows (Version 24.0, Armonk, NY: IBM Corp).

### RESULTS

The total enrolled ICUs were 192, out of which 144 (75%) contributed data. The rest of the ICUs could not either get ethics approval or waiver from the institute or they were unable to upload data during the COVID era. The data of 2,758 patients were uploaded via the eCRF, and after cleansing the incomplete data and removing patients who received colloids, analysis was done for 2,452 patients.

The data were majorly contributed by private hospitals as compared to public hospitals (79.2 vs 20.8%), and most of them were mixed medical-surgical ICUs (81.25%). Hospitals from across the country contributed the data as shown in Table 1.

The patients were divided into three groups based on the fluid that they received during the study period: NS group; RL group; and BSS group. There was no difference in the age (p = 0.915) and

weight (p = 0.679) of the patients between the groups. There were more male patients enrolled in the study as compared to female patients (p < 0.00001).

Most of the patients did not have any comorbidities (n = 1162, 47.4%). Among the remaining patients, there was uneven

Variables	n = 144	Percentage
Type of hospital		
Public	30	20.8
Private	114	79.2
Type of ICU		
Medical	19	13.2
Surgical	8	5.5
Medical + Surgical	117	81.25
Zones		
North	22	15.27
South	36	25
East	26	18.05
West	34	23.6
Central	26	18.05

distribution in terms of comorbidities between the groups. The NS and BSS groups had more chronic pulmonary disease (p < 0.00001), chronic cardiac disease (p = 0.014), and chronic liver disease patients (p = 0.028) as compared to the RL group. There were fewer patients suffering from malignancy in the BSS group (p = 0.0004). Most of the patients enrolled in the study were admitted directly from the emergency room but had no statistical difference across the groups (p = 0.06).

The severity scores of APACHE II and SOFA were similar in all three groups (p = 0.080 and p = 0.949, respectively). All three groups had no statistical difference in baseline mean serum creatinine (p = 0.956) (Table 2).

The incidence of AKI was calculated on the basis of the KDIGO and/or RIFLE criteria for the first 3 days of ICU admission and was correlated with the type of fluid administered during these 3 days. Patients who received different types of fluids on any day were allocated to the fluid group based on the higher volume of fluid that was administered on that particular day. This was done to counteract any effect of cross-over due to more than one type of fluid administration. Table 3 depicts the incidence of AKI during the first 3 days of ICU stay based on the type of fluid received. All the patients who received NS as compared to RL or BSS on all the

#### Table 2: Patient demographics

	NS group	RL group	BSS group	
Variables	(n = 961)	(n = 672)	(n = 819)	p-value
Age				
<50 years	48	46	49	0.915
>50 years	68	67	64	
Weight (mean $\pm$ SD)	$66.3 \pm 2.3$	$64.3 \pm 5.03$	$52.6 \pm 0.577$	0.679
Gender				
Female	301	270	251	<0.00001*
Male	660	402	568	
Comorbidities				
Chronic pulmonary disease	162 (16.16%)	45 (7 %)	141 (17.21%)	<0.00001*
Chronic cardiac disease	126 (12.92%)	100 (14.89%)	154 (18.80%)	0.014*
Chronic liver disease	178 (18.25%)	112 (16.66%)	128 (15.62%)	0.028*
Malignancy	40 (4.10%)	40 (4.10%)	25 (3.05%)	0.0004*
Immunosuppression	17 (1.74%)	10 (1.48%)	26 (3.17%)	0.060
Source of admission				
Emergency	708	436	617	0.06
Operation theater	132	106	133	0.14
Hospital floor	121	130	75	<0.00001*
APACHE II (mean)	17	16	18	0.080
SOFA score (mean)	6.86	6.94	7.21	0.949
Baseline serum creatinine (mean)	1.42	1.54	1.46	0.956

\*p < 0.05

#### Table 3: AKI and fluid type

		AKI	Day 1			AKI	Day 2			AKI	Day 3	
Fluid	Yes	No	Chi-sq	p-value	Yes	No	Chi-sq	p-value	Yes	No	Chi-sq	p-value
NS	360	601	120.05	<0.0001*	344	617	128.24	<0.0001*	312	649	147.83	<0.0001*
RL	112	560			132	540			126	546		
BSS	153	666			112	707			85	744		
NS vs RL			83.214	<0.0001*			49.96	<0.0001*			37.90	<0.0001*
NS vs BSS			76.017	<0.0001*			113.55	<0.0001*			141.19	<0.0001*
RL vs BSS			1.025	0.3113			9.60	0.002*			22.18	<0.0001*
*n < 0.0E												



days had a higher incidence of AKI (p < 0.00001). By the third day, the BSS group had fewer AKI patients as compared to other groups. The groups were also compared with one another independently, and the incidence of AKI was higher in the NS group as compared to the RL (p < 0.00001) and BSS groups (p < 0.00001) on all 3 days. On comparing RL with BSS, the AKI incidence was lower in the BSS group, as shown in Figure 1.

Other indicators of AKI like urine output and serum creatinine were also analyzed during the study period. The daily urine output was lower in the NS group on all the study days although it was statistically significant only on day 1 (p < 0.001) (Fig. 2). On days 2 and 3, the BSS group had higher urine output on days 2 and 3 but

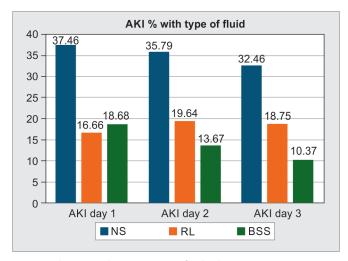


Fig. 1: Daily AKI incidence in various fluid subsets

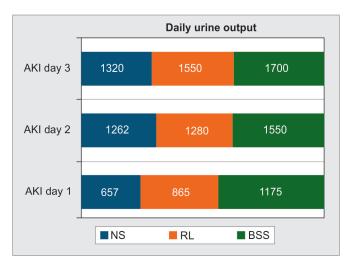


Fig. 2: Daily mean urine output on AKI days in various subsets

Table 4: Dail	y urine	output	and <i>I</i>	AKI	incidence
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not reaching statistical significance (p = 0.059; p = 0.055 respectively) (Table 4).

Table 5 shows the trend of serum creatinine associated with all three groups. The serum creatinine was higher in the NS group as compared to others on days 1 and 2 (p < 0.001). This trend was not significant on day 3, although on all days, the lowest mean serum creatinine was seen with the BSS group, followed by the RL group and then with the NS group (Fig. 3).

Tables 6A to C represent the relationship of daily fluid balance and incidence of AKI across the various fluid groups. Daily fluid balance was similar in all the groups (p > 0.05). The AKI patients had higher fluid balance in the NS group as compared to other groups (p < 0.00001) (Fig. 4). On comparing mean fluid balance between two groups, BSS had the least cumulative fluid balance on comparison to both RL and NS separately (p < 0.0001).

RRT therapy was needed in only 190 patients during the hospital stay. Table 7 displays the RRT incidence across the various treatment groups, and it was similar among all the groups (p = 0.775). The length of stay of the patients was analyzed both in the ICU and hospitals. Tables 8A and B depict the ICU LOS among the various treatment groups. BSS had the lowest ICU LOS, followed by RL and NS (p < 0.001). The mean ICU LOS for the BSS group was 6.13 days as compared to 8.96 days in the NS group. When each group was independently compared with each other, NS had higher ICU LOS to the RL (0.9 days) and BSS groups (2.8 days). Hospital LOS was also compared between the groups, as shown in Tables 9A and B. The trend was similar to ICU LOS, and the BSS group had the lowest stay in the hospital as compared to the NS group (9.9 vs 14.1 days). On comparing each group with one another, NS had higher LOS than the RL and BSS groups (Fig. 5).

The mortality of patients was analyzed both for the ICU and hospitals. Among 2,452 patients, 579 patients died in the ICU and 623 patients died in hospitals (Tables 10A and B and 11A and B). There was statistically higher mortality in the NS followed by the RL and BSS groups. On comparing the groups independently, there was no difference between the RL and BSS groups (p = 0.228), whereas the NS group had higher ICU mortality as compared to other groups (p < 0.001). Hospital mortality was higher in the NS group as compared to other groups (p < 0.001) (Fig. 6).

#### DISCUSSION

We conducted this multicenter prospective data collection to understand the practices of intravenous fluid therapy in Indian ICUs and compare the effect of normal saline with a BSS on renal parameters and overall outcomes in critically ill patients. The nationwide representation from 144 ICUs contributed to 2,452 cases, and out of these, 961 patients were given NS, 672 patients were given RL, and 819 patients were given BSS during the study period. The patients who received colloid were excluded from the data analysis. These data show that both NS and BSS are the

AKI incidence day	NS	RL	BSS	Chi-sq	p-value
1	657.5 (345–1082.5)	865 (250–1905)	1175 (700–1827.5)	38.011	<0.001*
2	1262.5 (750–1720)	1280 (715–1980)	1550 (1001–2100)	13.57	0.059
3	1320 (800–1845)	1550 (1015–2160)	1700 (725–2200)	13.777	0.055

\*p < 0.05

Table 5: Mean seru	ım creatinii	ne and AKI	incidence		
AKI incidence day	NS	RL	BSS	Chi-sq	p-value
1	2.1 (1.3–3.4)	1.7 (0.8–2.7)	1.1 (0.8–1.6)	43.862	<0.001*
2	1.9 (0.8–3.2)	1.4 (0.8–2)	1 (0.8–1.5)	29.021	<0.001*
3	1.4 (0.8–2.9)	1 (0.8–1.4)	1 (0.8–1.4)	12.328	0.09

\*p < 0.05

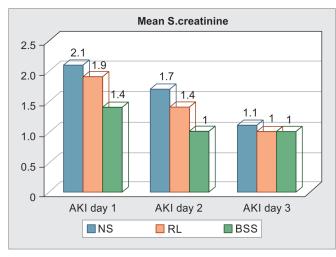


Fig. 3: Daily mean serum creatinine in different fluid subgroups

Table 6A: Daily f	luid balanc	e and type	of fluid		
Day of study	NS	RL	BSS	Chi-sq	p-value
1	1225	1180	1210	0.44	0.50
2	1040	1060	1010	0.63	0.43
3	960	890	910	1.45	0.22

 Table 6B: Fluid balance in different fluid groups and AKI incidence

AKI incidence day	NS	RL	BSS	Chi-sq	p-value
1	1040	860	660	43.12	<0.0001*
2	990	750	495	85.01	<0.0001*
3	910	736	480	69.51	<0.0001*
*p < 0.05					

Table 6C: Mean fluid balance in AKI in various groups

	3	
Fluid group	Ch-SQ	p-value
NS vs RL	10.40	<0.0001*
NS vs BSS	63.58	<0.0001*
RL vs BSS	22.87	<0.0001*
*p < 0.05		

preferred fluids by the clinicians for their critically ill patients. The same finding was observed in a meta-analysis conducted by Zayed et al.,<sup>3</sup> where the retrospective studies had a similar distribution of patients between NS and BSS. The INDICAPS<sup>4</sup> study showed that 23.2% of patients received NS during the study days, but they did not capture the data of BSS. Mixed medical-surgical ICUs from the private sector contributed the maximum data, as also seen in INDICAPS.<sup>4</sup> This is one of the largest data sets analyzing the fluid

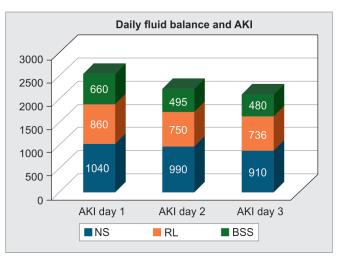


Fig. 4: Daily mean fluid balance and AKI in different fluid groups

 Table 7: RRT incidence across the various treatment groups

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RRT	NS	RL	BSS	Chi-sq	p-value
Yes	65	62	63	0.082	0.775
No	558	561	560		

administration practices in India and also comparing NS with BSS for our country.

We found that around 53% of patients in our study had one or more comorbidities with chronic liver disease and chronic cardiac disease forming the majority of them. This has nothing to do with the type of fluid administration and probably is due to the distribution of patients in the participating ICUs. The APACHE II and SOFA scores in our study were similar to the presentation as seen in INDICAPS<sup>4</sup> study. The baseline serum creatinine was not different among the three groups in our study and a similar finding was there in the SPLIT trial,<sup>5</sup> which compared buffered crystalloid solution with normal saline and also in a study conducted by Finfer et al.<sup>6</sup>

There have been many trials that have looked at the incidence of new-onset AKI with the type of fluid administered. We found that patients who received NS during the study period had a higher incidence of AKI as compared to both RL and BSS. This is contrary to the findings of various randomized trials,<sup>7,8</sup> which compared NS with Plasma-Lyte 148, where they did not find any difference in AKI. In a systematic review and meta-analysis<sup>9</sup> comparing balanced crystalloids and saline, there was no difference in the incidence of AKI (p = 0.37) between the groups, but the quality of evidence was very low; hence, the interpretation of the results cannot be extrapolated.

The PLUS investigators<sup>10</sup> found no difference in serum creatinine change between the balanced multielectrolyte solution and normal saline patients, but this was opposite to what we found in our study. The plausible explanation for this could be that our study looked at patients only during the first 3 days of ICU admission, whereas the PLUS trial analyzed the data for the first 7 days. Even in our study, the creatinine rise started settling around the 3rd day and hence it could have been possible that by the 7th day, there would have been no difference in creatinine change. The SALT-ED trial<sup>11</sup> found a higher incidence of hyperchloremic metabolic acidosis in non-critically ill patients when they were given normal saline as compared to other crystalloids. They also concluded that patients



#### Table 8A: Comparison of ICU LOS across different treatment groups

NS	RL	BSS		
(mean ± SD)	(mean ± SD)	(mean ± SD)	Chi-sq	p-value
8.6 ± 5.9	9.8 ± 6.4	6.2 ± 5.8	23.633	<0.001*
$8.4 \pm 5.8$	$7.4 \pm 6.8$	$6.3 \pm 4.3$	32.835	<0.001*
$9.9 \pm 9.3$	7.1 ± 7.3	$5.9 \pm 4.6$	54.981	<0.001*
	$(mean \pm SD)$ 8.6 ± 5.9 8.4 ± 5.8	(mean $\pm$ SD)         (mean $\pm$ SD) $8.6 \pm 5.9$ $9.8 \pm 6.4$ $8.4 \pm 5.8$ $7.4 \pm 6.8$	(mean $\pm$ SD)(mean $\pm$ SD)(mean $\pm$ SD) $8.6 \pm 5.9$ $9.8 \pm 6.4$ $6.2 \pm 5.8$ $8.4 \pm 5.8$ $7.4 \pm 6.8$ $6.3 \pm 4.3$	(mean $\pm$ SD)(mean $\pm$ SD)(mean $\pm$ SD)Chi-sq $8.6 \pm 5.9$ $9.8 \pm 6.4$ $6.2 \pm 5.8$ $23.633$ $8.4 \pm 5.8$ $7.4 \pm 6.8$ $6.3 \pm 4.3$ $32.835$

Table 8B: Comparison of ICU LOS across two different groups

Groups	95% Cl	p-value
NS vs RL	–1.539 to –0.1804	0.013*
NS vs BSS	-3.401 to -2.258	<0.0001*
RL vs BSS	-2.503 to -1.436	<0.0001*
*p < 0.05		

#### Table 9A: Comparison of hospital LOS across two different groups

AKI incidence	e NS	RL	BSS		
day	(mean ± SD)	(mean ± SD)	(mean ± SD)	Chi-sq	p-value
1	$14.7\pm0.6$	17.8 ± 15.7	10.6 ± 17.2	19.005	< 0.001*
2	$14.8 \pm 0.5$	11.8 ± 9.8	$9.5 \pm 8.2$	19.633	< 0.001*
3	$13 \pm 8.1$	10.1 ± 7.4	$9.6 \pm 6.3$	44.937	< 0.001*
*p < 0.05					

 Table 9B: Comparison of hospital LOS across two different groups

Groups	95% CI	p-value
NS vs RL	-1.6610 to -0.1990	0.012*
NS vs BSS	-4.9602 to -3.5598	<0.001*
RL vs BSS	-4.4267 to -2.2333	<0.001*

\*p < 0.05 significant

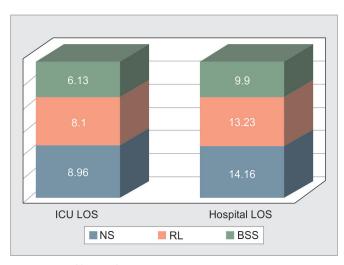


Fig. 5: ICU and hospital LOS

have a higher incidence of persistent renal dysfunction and new renal replacement therapy in the saline group. This is due to the effect of chloride-rich fluid resuscitation in both critical and non-critically ill patients.<sup>12</sup>

None of the studies have analyzed the type of fluid that affect the daily fluid balance and its effect on the incidence of AKI. The study by Wang et al.<sup>13</sup> looked at the correlation of fluid balance on mortality and AKI. They concluded that patients with AKI had higher

 Table 10A: ICU survival of AKI patients

Event	NS	RL	BSS	Chi-sq	p-value
Death	212	136	119	43.12	<0.0001*
Alive	367	443	460		
*	au if an ut				

\**p* < 0.05 significant

## Table 10B: Comparison of ICU mortality of AKI patients between treatment groups

Groups	Chi-sq	p-value
NS vs RL	23.71	<0.001*
NS vs BSS	36.58	<0.001*
RL vs BSS	1.45	0.228

\*p < 0.05 significant

#### Table 11A: Hospital mortality of AKI patients

Event	NS	RL	BSS	Chi-sq	p-value
Death	230	149	132	44.31	<0.0001*
Alive	393	474	491		
*n < 0.05 significant					

\**p* < 0.05 significant

Table 11B: Comparison of hospital mortality of AKI patients between
treatment groups

Groups	Chi-sq	p-value
NS vs RL	24.88	<0.001*
NS vs BSS	37.39	<0.001*
RL vs BSS	1.32	0.25
*		

\*p < 0.05 significant

fluid balance as compared to non-AKI patients, but they did not differentiate between any specific fluid types. Other studies have also found similar results.<sup>14</sup> Our study also had similar findings with higher fluid balance in patients with AKI. In comparison, the NS group had a higher fluid balance and hence higher AKI (p < 0.0001).

The incidence of RRT did not differ between BSS and NS in our study. The meta-analysis by Wang et al.<sup>15</sup> and Hammond et al.<sup>16</sup> did not find any difference in RRT between saline and other crystalloids. Another study<sup>17</sup> comparing the choice of intravenous fluid on hospital mortality also concluded that the need for RRT is not affected by the type of fluid.

Intensive care unit and hospital LOS are affected by many factors, and among them, the presence of AKI plays a major role. Our study found that patients who received NS had higher ICU and hospital length of stay as compared to other fluids. The SPLIT study<sup>5</sup> did not show any difference in the LOS between the groups, which probably could be due to the longer duration of protocolized fluid administration. The meta-analysis by Liu et al.<sup>18</sup> also could not show any difference in LOS between the studied groups. The explanation

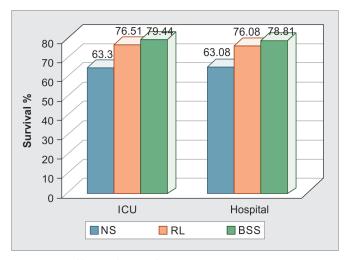


Fig. 6: ICU and hospital survival

of higher LOS in our study could be due to the shorter study period and also due to heterogenous data from various ICUs.

Our study documented higher mortality and AKI in the NS group. Chloride-rich fluids when given in larger volumes can cause metabolic acidosis, leading to AKI and higher mortality.<sup>19</sup> Neyra et al.<sup>20</sup> and Yessayan et al.<sup>21</sup> showed that hyperchloremia is associated with increased all-cause mortality, and these associations were not dependent on other factors like cumulative fluid balance and or other critical illness parameters. In our study, we also measured the worst arterial blood analysis parameters on all 3 days, but due to incomplete and non-consistent data, we did not include this in our analysis. The available data showed higher chloride levels in patients who received NS and hence could have contributed in higher mortality. A similar study<sup>22</sup> conducted in children did not find any difference in mortality between the NS and BSS groups. This could be due to the use of these fluids only as maintenance fluids and not as resuscitation fluids, and hence, the volume of fluid administration was less. Barhight et al.<sup>23</sup> found that an increase in serum chloride levels on the first day of ICU admission was associated with increased hospital mortality. In the study by Trepatchayakorn et al.,<sup>24</sup> the researchers did not find any difference in the incidence of AKI or mortality between the groups but concluded that patients who received a balanced solution had

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a significant reduction in the renal biomarker, urinary neutrophil gelatinase-associated lipocalin (uNGAL) levels and hence was thought to be renal protective.

The major limitation of our study was that we had to extend the study for 3 years as there was a COVID pandemic during the study period. Hence, the data capturing was almost stopped. The other limitation was that we could not analyze certain renal outcome data, which could have contributed further to understanding the reason for the increased incidence of AKI in the NS group. Secondly, our study period was very precisely defined, and the entire intervention was only to be done during the first 3 days of ICU admission. Hence, the result of the study was totally dependent on the data collected in these days only. Most of the other studies had the intervention done for almost a week, but with time, most of the parameters related to AKI had settled down. We assumed that the data uploaded are correct as per the inclusion criteria, as there was no means of source data validation.

The strengths of this study include the largest database from Indian ICUs spread across the country. We removed the data pertaining to COVID patients as it would have created a bias and the quality of data would have not been very good. Our findings were different from a couple of randomized trials and that could be due to a local practice pattern. It is clear from our study that intensivists are divided when it comes to the use of normal saline or balanced salt solutions in the ICU and the use of NS can be associated with worse renal outcomes. This is the first study worldwide that looked at the fluid balance of different fluids and correlation with AKI. This could form the basis of a much bigger and randomized trial to validate the findings.

#### CONCLUSION

This multicenter, prospective data collected from 2,452 patients from 144 ICUs across the country is a snapshot of the practice pattern of the use of intravenous fluids in critically ill patients and the effect of various crystalloids on renal outcome and length of stay. The highlights of the study are that normal saline is still the most preferred fluid used in Indian ICUs but its use has shown an increase in the incidence of AKI, ICU and hospital length of stay. The renal safety profile is better with the balanced salt solution as compared to saline in this study. The study supports the use of a balanced salt solution over normal saline as resuscitation and maintenance fluid in ICUs.

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