International Journal of Community Medicine and Public Health
Althagafi TH et al. Int J Community Med Public Health. 2022 Oct;9(10):3960-3964
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20222387

Review Article

Adverse effects of fluid overload in different paediatric age groups

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Received: 01 September 2022
Accepted: 15 September 2022

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ABSTRACT

Fluid resuscitation is a routine procedure in the treatment of critically ill patients especially in paediatric intensive care units. Fluid overload can result from instability in fluid homeostasis caused by the administration of excessive fluids. Fluid overload can have a wide range of adverse impacts on paediatric critical care patients, including increased mortality risk. Fluid overload increases the length of hospital stay and ventilation time also elevates requirement for renal replacement treatment. The purpose of this research is to review the available information about adverse effects of fluid overload in different paediatric age groups. Literature suggests that fluid overload is associated with significant morbidity and mortality among children. Fluid overload percentage greater than 10% is linked to higher mortality rates among children. Respiratory failure can be triggered by pulmonary alveolar and interstitial edema caused by hypervolemia. Children suffering from acute kidney injury or other renal diseases experience more worsened conditions in presence of fluid overload. Fluid overload can impair organ performance, which can impact disease and fatality. Excessive fluid may alter the efficiency of the heart and perhaps impair cardiac function by considerably moving ventricular compliance to the right on the Frank-Starling curve. The negative effects of fluid overload make patients more susceptible to an elevated risk of morbidity and death even if fluid overload itself is not a direct indicator of mortality. Further research can in aid in developing preventive and management strategies for the fluid balance in paediatric settings.

Keywords: Fluid, Overload, Morbidity, Children

INTRODUCTION

The foundation of resuscitation in critically ill children is fluid treatment. It may be possible to save a life by restoring an adequate intravascular volume with early, intensive fluid delivery. However, in addition to fluid treatment for resuscitation, children with severe illnesses frequently get varying amounts of obligatory fluid intake as part of their care which includes nutrition, medications, and maintenance fluid. A net positive fluid balance results when cumulative fluid delivery surpasses cumulative fluid loss. There is mounting circumstantial evidence that implies fluid build-up following initial resuscitation may pose a serious risk for morbidity and mortality.[1] Fluid overload refers to a condition when there is positive fluid balance in the body which is probably the result of extensive fluid administration and can further lead to several adverse effects.[2]

Patients who are brought to an intensive care unit are vulnerable to cumulative fluid overload and are

administered intravenous fluids as part of the vigorous resuscitation advised for treating septic shock, in addition to other fluid sources related to various medication and nutritional support. Higher morbidity and mortality have been linked to the liberal fluid supply. The endothelial glycocalyx is harmed during systemic inflammatory response syndrome, promoting fluid extravasation and producing interstitial edema. In addition to other alterations, extravasation to the third space prolongs mechanical ventilation, necessitates more renal replacement treatment, and lengthens stays in the intensive care unit and hospital.[3] Fluid management is one of the routine parts of care in the paediatric intensive care unit (PICU) setting, and earlier studies have emphasized its significance. Prior studies demonstrated that early aggressive fluid resuscitation may enhance prognosis in critical illness, particularly in situations linked with endothelial dysfunction. Fluid resuscitation may be required to maintain intravascular volume as part of fluid management. Unfortunately, this routine maintenance frequently causes fluid overload and positive fluid balance to develop. Numerous studies have shown that administering children with large volumes or quantities of fluid who were sent to PICU is directly related to having unfavourable impacts. It is recognized that fluid overload increases the risk of morbidity, mortality, length of time spent on mechanical ventilation, length of stay in the hospital, and requirement for renal replacement treatment.[4]

There is still debate over the clinical effects of fluid overload and how to treat it in the literature on paediatric critical care. In critical care, resuscitation using intravenous fluids is frequently required to maintain perfusion during shock or hypovolemic conditions. In an effort to improve outcomes, a recent shift toward early sepsis detection has advocated quick and early fluid administration at the time of illness presentation. Therefore, in the context of a severe disease, intensive early fluid resuscitation might cause fluid overload situations. Fluid excess in critical illness may have adverse effects and contribute to morbidity and death, as per the recent studies in both adult and paediatric patients.[5] The purpose of this research is to review the available information about adverse effects of fluid overload in different paediatric age groups**.**

METHODS

This study is based on a comprehensive literature search conducted on 26 August 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about adverse effects of fluid overload in different paediatric age groups**.** There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

It is possible for the fluid administered to seriously harm and affect children during the resuscitation phase and build up, which can later result in fluid overload that can have negative effects. This inverse relationship has been shown to be positive in a number of clinical contexts, including children needing continuous renal replacement therapy, having heart surgery, and children with severe sepsis. There is limited data available on how fluid overload affects mortality in a general PICU population. The majority of studies emphasized the negative impact of fluid unbalance. However, there is still disagreement on whether fluid overload is a standalone risk factor for a worse prognosis in critically ill paediatric patients or whether the adverse outcome is merely due to the severity of the underlying illness.[6] Fluid overload management among severely ill children is challenging and fraught with certain complications. Management is difficult because there is not a solid consensus on how to calculate fluid overload and majority of input and output estimates have considerable uncertainties. The negative effects of fluid overload make patients more susceptible to an elevated risk of morbidity and death even if fluid overload itself is not a direct indicator of mortality. Fluid overload increases the chance of underdiagnosis of acute kidney injury, delays therapy, lengthens hospital and intensive care unit stays, and increases the need for ventilator support in the critically ill population. Further research is needed since there is lack of knowledge regarding fluid overload.[2] The pathogenesis and adverse effects of fluid overload are illustrated in (Figure 1).

Evidence from literature for adverse effects of fluid overload

Findings of a retrospective cohort study conducted on 165 patients showed that with a median age of 3.2 years (interquartile range 0.7-9.9), a death rate of 45.5% was observed, 64 (38.8%) patients had acute kidney injury, while 73(44.2%) patients had severe paediatric acute respiratory distress syndrome. Acute kidney injury and the rate to peak cumulative fluid overload were linked to mortality (odds ratio (OR) 3.19, 95% confidence interval (CI) 1.43-7.09, p=0.004) and death (OR 1.23, 95% CI 1.07-1.42). Reduced ventilation free days and intensive unit free days were related to acute kidney injury and peak cumulative fluid overload. Peak chronic fluid overload was linked to lower ventilation free days and intensive unit free days, and the rate to peak chronic fluid overload throughout the first 14 days of paediatric acute respiratory distress was linked to death.[7] Findings of another retrospective cohort study revealed that 132 (18%) participants died while non-survivors showed greater overall fluid balance beginning on day 3 as per the unadjusted analyses. A positive overall fluid balance on days 5 through 7 was linked, in a multivariable analysis, to higher mortality. Lower probability of extubation was associated with higher cumulative fluid balance on days 4 to 7. Fluid overload more than or equal to 10% was

anticipated by raised angiopoietin-2 on day 1 and predicted by elevated angiopoietin-2 on day 3, which occurred between days 4 and 7. Poorer outcomes were linked to fluid overload after day 4 of acute respiratory distress syndrome but not before. Angiopoietin-2 levels were a predictor of ensuing fluid overload.[8] Results of a cohort study showed that among 263 patients with the mean age of 8±3 years old death rates were 33%. The only linked outcome measure was fluid overload percentage of 10.1% accumulated at 96 hours and fluid overload percentage greater than 10.1% was associated with a greater mortality rate.[9]

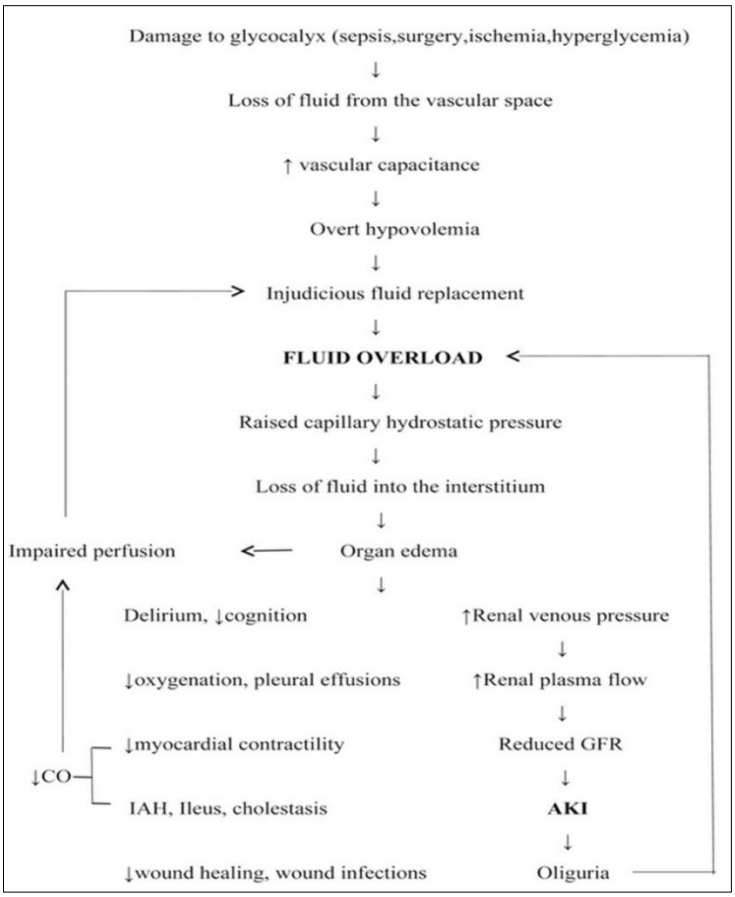

Figure 1: The pathogenesis and adverse effects of fluid overload 2.

*CO: Cardiac output; ** AKI: acute kidney injury

Results of a multicentre retrospective cohort study showed that peak fluid overload during extracorporeal membrane oxygenation (ECMO) predicted mortality on ECMO; peak fluid overload during ECMO (OR 1.13; 95% CI, 1.05–1.22) and hospital mortality (OR, 1.18; 95% CI 1.12-1.24). In a large paediatric ECMO population, fluid overload happens often and is independently linked to unfavourable outcomes including higher mortality and prolonged ECMO. Author further stated that these findings imply that fluid overload is a target for intervention that could enhance the outcomes for children receiving ECMO.[10] Mallory reported in his study findings that there was an approximately 1.2-fold increase in the likelihood of hospital death for every 10% rise in peak fluid overload during ECMO. The duration of ECMO hours changed significantly related by a factor of 1.08 for every 10% rise in peak fluid overload during ECMO. For hospital survivors, there was a substantial relative change in the number of hours spent on mechanical ventilation by a factor of 1.13 for every 10% rise in peak fluid overload level during ECMO. Acute kidney injury and fluid overload should be targeted for medical therapies such as prudent fluid control, the use of diuretics, and renal replacement therapy because they are linked to higher mortality in this patient population.[11]

Results of a prospective study revealed that patients who had greater or equal 20% fluid overload at the start of continuous renal replacement therapy had substantially higher mortality (61/93; 65.6%) than those who did not (22/51; 43.1%), and those who did (45/153; 29.4%). Even after accounting for intergroup differences and the severity of the illness, the correlation between the degree of fluid overflow and mortality persisted. A 3% increase in mortality is predicted for every 1% rise in the severity of fluid overload, according to the adjusted mortality OR of 1.03 (95% CI, 1.01-1.05). Patients with greater or equal 20% fluid overload had an adjusted mortality OR of 8.5 (95% CI, 2.8-25.7) when fluid overload was dichotomized as greater or equal 20%. Children with critical illnesses

who have greater fluid overload before beginning of continuous renal replacement therapy had higher fatality rates than those who experience less fluid overload.[12] Results of another prospective study reported that 74 (62.7%) children were found to have cumulative fluid overload of greater or equal 15%. Within the first five days of their hospitalization in the PICU, about half of these children experienced cumulative fluid overload of more than 15% within 5 days of PICU. In comparison to the rest, those with overall fluid overload greater than 15% cumulative fluid; mortality was 40.5% [OR (95% CI): 1.02 (0.97, 1.07]. After controlling for confounders, multivariate analysis revealed that cumulative fluid overload greater than 15% was linked to longer median durations of mechanical ventilation (10 versus 4 d; p<0.0001) and PICU stays (13.5 versus 6 d; p<0.0001), as well as higher maximum paediatric logistic organ dysfunction scores (median: 21 versus 12; p=0.03). Fluid overload did not significantly affect oxygenation index (p=0.32). Overloading on fluids has no connection to mortality. However, in children who are critically ill and on mechanical ventilation, it is linked to poor organ function, a longer time spent in the PICU, and a longer duration of mechanical ventilation.[13]

Another prospective study demonstrated that 64 (17.3%) of the patients experienced early fluid overload within the first 24 hours of hospitalization. The PICU mortality rate of the overall group was 4.9%. Age, acute kidney injury, PRISM III, and blood bicarbonate level were the independent variables that were substantially linked with early fluid overload. Acute kidney injury and death were linked to the early fluid overload (OR 1.34, p<0.001; and OR=1.36, p<0.001). After adjusting for potential variables such acute kidney injury and illness severity, the link between early fluid overload and death remained significant. Acute renal injury and mortality in critically ill children are independently linked to acute fluid overload in the first 24 hours following PICU admission.[14] Ketharanath stated that various tools have been devised to quantify fluid overload and link it to morbidity. In this regard, fluid overload percent with a severity cut-off of 10% has shown to be useful in demonstrating an independent association with morbidity markers such as higher oxygenation index, prolonged mechanical ventilation, acute kidney injury requiring renal replacement therapy, and ultimately longer admission to the PICU and hospital. Furthermore, fluid overload has been linked to a higher death rate in paediatric patients who experience renal failure as a result of an acute illness.[15]

Lawati described in his study findings that on day 3, fluid exposure consistently surpassed maintenance requirements, despite the fact that resuscitation fluids were more of a contributor to fluid exposure on day 1 than on day 3. Fluid overload is frequent in PICUs and has been linked to higher morbidity and mortality rates. It is still unknown if fluid overload is an iatrogenic modifiable risk factor, an indication of oliguria, or a substitute signal for the severity of disease and the need for greater assistance. There has not been enough research done on the percentages of different fluid consumption that contribute to fluid overload and how to identify it also PICU professionals do not always notice fluid overload.[16]

Ker stated that the states of fluid overload can affect how well organ's function, which can affect morbidity and mortality. By significantly shifting ventricular compliance to the right on the Frank-Starling curve, excessive fluid might change the heart's efficiency and potentially damage cardiac function. Respiratory failure can be triggered by pulmonary alveolar and interstitial edema brought on by hypervolemia. Particularly, pulmonary edema worsening will impair lung compliance, exacerbate V/Q mismatch, and thus compromise ventilation and oxygenation. Finally, renal perfusion may be compromised, especially under stressful situations, leading to the development of acute kidney injury, which makes it more difficult for the kidneys to maintain euvolemia.[17]

Hayes described in his study that in children with end-stage kidney disease, dysregulation of intravascular fluid volume leads to cardiovascular morbidity and eventually mortality. The most frequent cause of death in children receiving dialysis is cardiovascular problems. A significant risk factor for cardiovascular problems in children, such as left ventricular hypertrophy, is chronic intravascular volume overload. To reduce chronic fluid overload, it is essential that children's dialysis prescriptions include enough dialysis frequency and ultrafiltration. On the other hand, excessive ultrafiltration can cause intradialytic symptoms and is toxic to children's myocardium.[18]

Carlisle stated that acute kidney injury and fluid overload show how bidirectional risk is physiologically exhibited. The kidney is susceptible to interstitial space expansion and elevated venous pressure, which causes an increase in renal subcapsular pressure, a decrease in renal blood flow, and a slower rate of glomerular filtration. Acute kidney injury concurrently predisposes patients to volume retention and fluid build-up due to reduced glomerular filtration rate and tubular dysfunction. Patient outcomes suffer when fluid overload is present either by itself or in combination with acute kidney injury. It is linked to a lengthier hospital stay, a longer time spent on ventilator support, and a higher risk of infection. In the intensive care unit, higher fluid overload at the start of renal replacement treatment has been linked to an increased risk of death in both adults and children.[19]

Studies in literature elaborately discusses the impact and adverse effects of fluid overload among children generally although very limited studies are stratified into various age groups further research can be beneficial in studying the effects of fluid overload in children of different ages and develop management strategies for fluid balance so fluid overload phenomena can be prevented. Also, clinical trials in future can effectively evaluate the relationship of fluid overload with mortality.

CONCLUSION

Fluid overload is subject of concern and worry especially in paediatric settings as it is a significant contributor of morbidity and mortality. Effective guidelines, strategies and their practical implication for the management of fluid resuscitation among children is need of time.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Althagafi TH, Qartali AA, Alasmari NH, Alasmree AD, Alahmadi AS, Alharbi OA. Adverse effects of fluid overload in different paediatric age groups. Int J Community Med Public Health 2022;9:3960-4.