Pediatrics

A STUDY OF THE CLINICAL OUTCOMES ASSOCIATED WITH FLUID OVERLOAD IN CRITICALLY ILL PEDIATRIC PATIENTS

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ABSTRACT:

BACKGROUND AND AIM: Intravenous fluid administration is one of the most frequently used therapies provided in hospitals. Daily fluid balance have been monitored to determine the incidence of fluid overload and its impact on the clinical outcome of the critically ill pediatric patients

METHODS: Over a 12 month period, all pediatric patients admitted to intensive care unit who completed more than 48 hours in the PICU were included. Data recorded for each patient: percentage fluid overload = (fluid in minus fluid out in liters)/ PICU admission weight in KG x 100 %, demographic and clinical data. Data were entered into SPSS and analyzed in terms of frequency and percentage.

RESULTS: 203 subjects were included in the study, median age 9 months, mortality rate 26.1 %, and were divided according to the peak positive fluid balance recorded during the admission into 3 groups: group A peak fluid overload (PFO) <5%, group B PFO 5-10% and group C PFO>10%. The incidence of fluid overload was 54(%), 82(%) and 67(%), in group A, B and C respectively. The incidence of PFO in survivors was 28% and was 47.1% among the non survivors (p=0.025*). PICU length of stay, mechanical ventilation days and the incidence of AKI differed significantly between the 3 groups (p= 0.002, 0.000 and 0.032 respectively). While vasoinotropic score, need for dialysis and diuretics revealed no statistically significant difference between the three groups (p=0.054, 0.537 and 0.109 respectively).

CONCLUSIONS: Fluid overload is a common problem in PICU, with PFO associated with respiratory morbidity, need for mechanicalventilation, PICU length of stay and mortality rates.

INTRODUCTION:-

Intravenous (I.V.) fluid administration is one of the most frequently used therapies provided in hospitals and plays a vital role in establishing and maintaining cellular homeostasis in hospitalized patients[1]. The requirement for ongoing fluid resuscitation in conditions associated with underlying endothelial dysfunction often leads to the development of significant fluid overload (FO) in the critically ill patient[2].

Recent data has underlined the detrimental effect positive fluid balance plays in the recovery phase after hemodynamic stabilization is reached by negatively impacting organ function.(3) This has been demonstrated in general pediatric ICUs[4] and in

specific clinical settings, such as acute respiratory distress syndrome (ARDS)[5] in patients undergoing major surgery,[6] cardiac surgery[7] and in septic patient.[8] Furthermore, fluid accumulation itself may be independently associated with an increased risk of developing acute kidney injury (AKI).[9,10]

In this prospective study we aim to evaluate the practice of fluid management in the PICU patients, and describe the relationship between FO and clinical parameters in terms of need for ventilation, duration of mechanical ventilation, vasopressors , need for dialysis and diuretics with a main objective to determine the incidence and degree of fluid overload in general PICU and as a secondary outcome to determine whether fluid balance throughout ICU stay affects the mortality of patients and respiratory morbidity .

SUBJECT AND METHODS

Patients :

This prospective observational study was conducted in Alexandria University Pediatric Intensive Care Unit (PICU). An informed consent was obtained from parents or legal guardians. All patients admitted to pediatric intensive care unit in time period from 1st of September 2016 till 30th of August 2017 were included in the study, except for those who were aged more than 16 years and less than 1 month, PICU stay less than 48 hours and all surgical and trauma patients.

Data collection:

Two hundred and three cases were included; patients' demographic data and anthropometric measurements were recorded: age, sex, weight and date of admission. All patients' admission and follow up data were recorded through history taking and clinical examination on admission using pediatric index of mortality II (PIM II) score(11) and daily follow up using the daily pediatric logistic organ dysfunction (PELOD) score to describe multiorgan dysfunction.(12)

Assessment of fluid overload:

For each patient, the daily fluid balance was calculated, and fluid overload was expressed as percentage and calculated as FO% = (fluid in minus fluid out in liters)/ PICU admission weight in KG x 100 %. The peak fluid overload (PFO) was considered to be the highest fluid balance received by the patient during the whole length of stay.

Patients were further categorized into 3 groups according to the PFO into: group A (<5%), group B (5-10%), group C (>10%). Different clinical and laboratory data were collected for each group and analyzed for being of statistical significance.

Clinical and laboratory data:

Hydration status for each patient on admission was recorded, and daily laboratory investigations, arterial blood gases were done. The need for ventilation, vasopressors/inotropes, diuretic or dialysis (either CRRT or peritoneal dialysis) was assessed daily.

Statistical methodology

Data were collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis (version 21).[10] Numerical data were described using median and inter-quartile range. Categorical variables were described using frequency and percentage.

RESULTS

Patients demographic and clinical characteristics charectestics

Two hundred and three patients met the inclusion criteria. Table (I) describes the demographic data of all included cases, with median age 9.00 (3-36) months, median weight of 8.3 (5.2-12.5) kg with a male to female ratio 1.01:1. As regard the PIM2 score, a median of 19.5 (6.7-35), meanwhile the lowest PELOD score recorded during the admission was ranging from 0.0-19 with a median 3 (1-6). Regarding the mortality rates, the median ICU length of stay 6 (4 to 10) days, and as regard the 28th day mortality, rates were 26.1%.

Patients were admitted with different diagnostic categories. The highest rates of admission were for septic patients (82%) followed by respiratory (72%) and cardiac respectively (60%) and the least was for burn category (2%) where each patient may have more than one diagnosis

Regarding the clinical fluid status on admission about 22.6% were overloaded on admission. Fifty five percent of admitted cases required mechanical ventilation at a point during the admission.

Relation between fluid overload groups and demographic data:

Cases were categorized according to the peak fluid overload during the whole admission into Group A (26.60%), Group B (40.40%), Group C (33.00%) (Figure 1). Results showed a statistically significant difference between the three groups as regard the age (p=0.000) (figure 2), worst PELOD 2 score recorded allover the days of admission(p=0.000) (figure 3), the need for mechanical ventillation (p=0.000) and the highest serum creatinine during the admission (p=0.003). Also the distribution of cases among the different diagnostic categories was statistically signifcant as regard cardiac (p=0.000), renal (p=0.000) and gasterointestinal (p=0.000) cases where these diagnosis had more tendency for higher fluid balances. (Table II)

As for the need for diuresis, dialysis or vasopressor/inotropes didn't differ statisticaly between the three groups with p values 0.109 ,0.537 and 0.938 respctively. (Table II)

Regarding the survival , mortality rates were significantly higher in group C while was lowest for group B (p=0.027). There was astatisticaly signofcant difference between the three groups as regard the length of ICU stay (p=0.000). (Figure 4) (Table II)

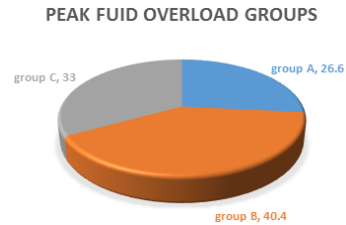### PEAK FUID OVERLOAD GROUPS

Figure (1): Pie chart illustrating peak fluid overload groups

Table (II): Demographic and clinical charectarestic of the PFO groups

Variables		A (n=54) (26.60%)	B (n=82) (40.39%)	C (n=67) (33.00%)	P value
Age (months)		43.5 (12,96)	9 (3,18)	6 (2,18)	0.000
Sex (%)	Male	50	57.3	43.3	0.245
	Female	50	42.7	56.7	
PIM2 score		20.0 (6.7,35)	13.5 (6,34)	23.4 (10,36)	0.192
PELOD score†		2 (0,4)	3 (1,6)	5 (3,8)	0.000
Diagnostic categories (%)	Sepsis	29.6	40.2	49.3	0.093
	Renal	24.1	13.4	43.3	0.000
	Cardiac	50.0	18.3	26.9	0.000
	Gastroenterology	5.6	12.2	32.8	0.000
	Respiratory	42.6	28.0	38.8	0.170
	Endocrinology	14.8	14.6	3.0	0.043
	Neurology	22.2	29.3	13.4	0.070
	Burns	0.0	3.6	0.0	0.106
	Hematology	9.3	7.3	16.4	0.188
Highest serum creatinine (mg/dl)		0.6 (0.4,0.9)	0.5 (0.3,0.7)	0.7 (0.5,1.4)	0.003
Need for mechanical ventilation (%)	Yes	31.5	58.8	71.6	0.000
	No	68.5	41.5	28.4	
Need for Vasopressor/ inotropes (%)	Yes	55.6	55.6	58.2	0.938
	No	44.4	44.4	34.2	
Diuretic drip (%)	Yes	33.3	18.3	20.9	0.109
	No	66.6	81.7	79.1	
Dialysis (%)	yes	١2.9	7.3	8.9	0.537
	No	87.1	92.7	91.0	
Length of stay		4 (3,7)	8 (4,11)	7 (4,12)	0.002
28 day mortality	Survivor	75.9	81.7	62.7	0.027
	Non survivor	24.1	18.3	37.8	

n : number of patients

IQR: Inter-quartile range

†PELOD: the worst PELOD

*Symptoms not mutually distributed

Table (I): demographic and clinical data of the whole group

Age: (months) • Median (IQR)	9.00 (3.00-36.00)
Sex • Male • Female	103 (50.74%) 100 (50.26%)
Weight on admission (kilograms) • Median (IQR)	8.30 (5.20-12.50)
Diagnosis categories • Sepsis • Renal • Cardiac • Gastroenterology • Respiratory • Endocrinology • Neurological • Burns • Hematological	82 (40.39%) 53 (26.11%) 60 (29.6%) 35 (17.2%) 72 (35.5%) 22 (10.8%) 45 (22.2%) 2 (1.0%) 22 (10.8%)
PIM2 (% of predicted mortality) • Median (IQR)	19.50 (6.70-35.00)
PELOD score (worst) • Median (IQR)	3.00 (1.00-6.00)
Clinical status on admission • Dehydrated • Overloaded • Euvolemic	21 (10.3%) 46 (22.7%) 136 (67%)
Need for mechanical ventilation • Not ventilated • Ventilated	90 (44.3%) 113 (55.7%)
Length of stay • Median (IQR)	6.00 (4.00-10.00)
28 Day Mortality • Deceased • Survived	53 (26.1%) 150 (73.9%)

PIM: pediatric index of mortality
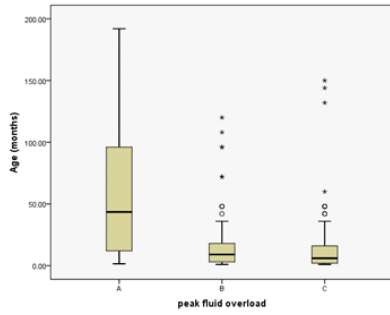**PELOD:** Pediatric Logistic Organ Dysfunction score

Figure (2): Comparison between the 3 studied groups as regard age (months), the thick line in the middle of the box represents the median, the box represents the inter-quartile range (from 25th to 75th percentiles), the whiskers represents the minimum and maximum after excluding outliers (black-filled circle) and extremes (black asterisks)
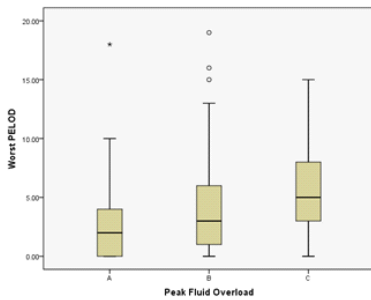

Figure (3): Comparison between the 3 studied groups as regard the worst PELOD score, the thick line in the middle of the box represents the median, the box represents the inter-quartile range (from 25th to 75th percentiles), the whiskers represents the minimum and maximum after excluding outliers (black-filled circle) and extremes (black asterisks)
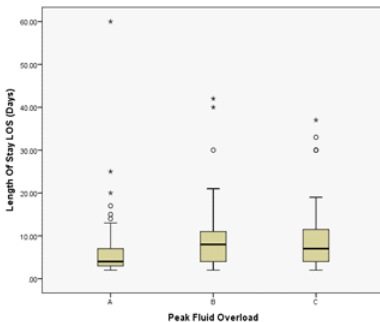

Figure (4): Comparison between the 3 studied groups as regard the length of stay in PICU, the thick line in the middle of the box represents the median, the box represents the inter-quartile range (from 25th to 75th percentiles), the whiskers represents the minimum and maximum after excluding outliers (black-filled circle) and extremes (black asterisks)

DISCUSSION

The present prospective observational study was conducted in the pediatric intensive care unit of the Alexandria Main University Hospital which is tertiary care hospital. This is a general PICU having 9 beds for a turnover rate of 300 admissions during the year. This is one of limited studies taking the setting in a general PICU, others included only septic patients[8,13], renal patients[9,14] and others included cardiac patients[7,15,16] only.

Patients were categorized according to the PFO, with cutoff points at 5% and 10% where the incidence of FO above 5% was 73.3% of all admitted cases and 33.3% of all studied cases were above 10% PFO.

A South African study had an incidence of 3% PFO above 10%[17], and Diaz et al. in Alabama united states[18] has taken the 10 and 20% as a cut off points with an incidence of 55.8% and 33.3% respectively showing that our strategy in fluid administration turned out to be more conservative regardless the diagnosis and patients' condition.

As regard the severity scores, a median PIM2 score wasn't significantly higher in the PFO>5% unlike Chen et al[19] who had a median PIM2 score of 16.2 which is significantly higher than those below 5% (3.3) with *p* value 0.000. Another study by Sinitsky et al[20] performed PICU at St Mary's Hospital, London, United Kingdom, where there was a significantly higher PIM2 score in the patients who received higher fluid balances. This difference in the results may be related to the diagnosis where patients of the present study and Sinitsky et al [20] were of different diagnostic categories while Chen et al [19] were concerned with the septic patients only.

As regard the organ dysfunction scores, PELOD score was assessed daily, the median worst PELOD was significantly lower in the PFO<5% and increased significantly as the PFO increased. Diaz F. et al[18] reported similar results, where number of organ failure increased with the peak FO, unlike Chen et al study for septic patients[19] where the multiorgan dysfunction was not correlating with the degree of FO. Another study in Children's Hospital of Soochow University in China[21] studying the effect of early FO in a general PICU, showed a lower values of multiorgan dysfunction scores at higher fluid balances. This may be related to the original disease requiring PICU admission rather than to the effect of FO.

The present study showed a significantly lower median age in the groups with higher FO >5% (6 months) in contrast to Chen al[19] who had no significant difference as regard the age all were about 6 months of age. Sinitsky et al[20] study showed a statistically significant lower age groups for the higher PFO groups, and a non-statistically significant difference was detected by Li et al[21] between ages of different PFO groups.

In the present study, renal and gastroenterological patients had the higher tendency for positive fluid balance, cardiac patients were of the least tendency to accumulate fluid overload. These results are not consistent with results of Li et al[21] which had the highest category for fluid overload patients with respiratory problems followed by the neurological patients. While as for Sinitsky et al[20] diagnostic categories didn't correlate with the degree of fluid overload, but linear regression showed that both FO and diagnostic category were independent predictor for mortality.

Seventy eight percent of patients with PFO >10% required mechanical ventilation at a point during their PICU stay, in contrast to the group<5% only 28% required ventilation. This is consistent with Ketharanathan et al[17] and the study conducted at the PICU of Texas Children's Hospital[2] who both showed that the degree of FO correlates significantly with the need of ventilation and also correlates with the parameters and days of ventilation.

As regard the renal morbidity, highest serum creatinine reached during the hospital stay was for the highest FO group>10%, this was consistent with results achieved by Lex et al [15] study coduct at cardiac ICU in Budapest, Hungary, and with Hassinger et al[7] study on post cardiac surgery patient in which both studies suggested that the FO preceded the AKI not in reverse. There was no significant difference in the need for dialysis or diuresis between the three groups in the present study, and this was consistent with the finding by Chen J. et al[19].in septic patients and by Li et al[21] in a general PICU, but not with results by Sinitsky et al[20] who had significantly higher needs for CRRT in patients with FO>15%

The need for vasopressor or inotropes was assessed daily in the present study, and there was no significant difference between the needs for vasopressors or inotropes at different degrees of FO. Sinitsky et al[20], reported significantly increased needs for vasoactive drugs at FO above 10%. Unlike Chen et al[19] in septic

patients who showed no difference in the needs of inotropes as regard different degrees of FO.

The PICU length of stay was much higher for those who had PFO >5% in the present study (p=0.003), but it didn't differ between >10% and 5-10% may be related to the initial disease or to the fact that mortality rates were higher in the >10% group. This is inconsistent with Chen et al(19) and may be attributed to his limited study conducted only on septic patients, but was consistent with post cardiac surgery PICU's studies as Hassinger et al(7) who showed prolonged PICU and hospital stay for those with higher fluid balances. General PICU studies showed a shorter length of stay for those with higher fluid balance may be due to the early death as with Ketharanathan et al(17), while LOS was longer in studies by Li et al[21] and by Arikan et al(2) who found that PFO is associated with prolonged PICU stay.

Twenty eight day survival remains the main goal of the present study, where results showed that PFO>10% has significantly higher mortality, but the PFO group<5% was not of the least mortality rates, this may be due to the contribution of the diagnostic category and other comorbidities as being cardiac or AKI patient to the probability of death. This is not consistent with Li et al(21) study which showed a significant higher mortality rates for those with PFO>5%, while Sinitsky et al(20) showed that the mortality rates were higher with higher FO bands but this difference wasn't significant. A single centered prospective observational study by Ralib et al(22), showed that a 48-hour actual cumulative fluid balance was independently predictive of mortality. A case-control study conducted at the PICU of Sanglah Hospital, Bali, reported that mortality rates in patients with fluid overload were 11.5 times higher than in patients without fluid overload (OR=11.5)(23).

CONCLUSIONS:

The present study concluded that the PFO has an association with PICU LOS, mortality rates, respiratory morbidity and the need for mechanical ventilation but PFO wasn't related to the need for diuresis or dialysis or the need for vasoactive inotropic drugs.

Conflict of Interest: None.

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