Original Article

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Ability of Passive Leg Raising Test in Predicting Positive Fluid Response in Paediatric Patients with Shock: A Prospective Observational Study

Paediatrics Section

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ABSTRACT

Introduction: Shock is an acute syndrome in which the circulatory system is unable to provide adequate oxygen and nutrients to meet the metabolic demands of vital organs. Fluid replacement is often necessary to optimise the cardiovascular function by maintaining adequate cardiac preload and output. It's a reversible manoeuvre that simulates a rapid fluid bolus by shifting blood from the lower extremities and abdominal compartment into the central circulation.

Aim: To evaluate the Passive Leg Raising (PLR) test as a simple bedside tool to assess volume responsiveness in children with shock aged less than eight years.

Materials and Methods: The present prospective observational study was conducted in Paediatric Ward and Paediatric Intensive Care Unit of a tertiary level teaching hospital between November 2020 to October 2022. Total 42 children between one month to eight years of age diagnosed with shock were included in the study. Bedside echocardiography was done to calculate stroke volume combining Velocity Time Integral (VTI) at aortic root with the Cross-sectional Area (CSA) of the aortic root. VTI was measured at baseline, after PLR and after giving a fluid bolus of 10 mL/kg of crystalloid fluid. Change in VTI was compared between PLR and fluid bolus interventions. Cut-off for positive test was kept as ≥12% increase in VTI from baseline for both PLR and fluid bolus.

Results: Mean age of study population was 55 months (SD-50), out of which 27 (64.3%) were below four years of age. A total of 29 (69%) of patients were male. Overall sensitivity of passive leg raise test was 76.7%, specificity of 85.7% when cut-off value was taken as >12% for change in VTI post-PLR. Negative predictive value of PLR was 37.5% and positive predictive value of 97.1%. The Area Under the Receiver Operating Characteristic (AUROC) curve was 0.855 with significance of 0.021.

Conclusion: The study found that the PLR test is a reasonably accurate tool for predicting fluid responsiveness in children younger than eight-year-old. When an increase in cardiac index of more than 12% is used as the indicator of a positive test, the PLR manoeuvre correctly identifies about 77% of fluid-responsive children and correctly identifies about 86% of children who are not fluid responsive.

Keywords: Cardiac index, Echocardiography, Fluid bolus, Stroke volume, Velocity time integral

INTRODUCTION

Shock is an acute syndrome in which the circulatory system is unable to provide adequate oxygen and nutrients to meet the metabolic demands of vital organs [1]. Fluid replacement is often necessary to optimise the cardiovascular function by maintaining adequate cardiac preload and output providing enough tissue oxygen delivery, which is essential in the management of critically ill patients. Intravascular volume status assessment is an essential component in the diagnosis and management of critically ill patients [2].

Assessment of intravascular volume status can sometimes be challenging in the Emergency Department. One of the important tasks for the clinician is to determine whether the patient will respond to fluid bolus or not. Optimal fluid management is crucial to avoid the deleterious effect of over, under, or inappropriate resuscitation. Non-optimised fluid administration, cardiovascular derangements, as well as aggressive uncontrolled infection are the main causes of Multiple Organ Dysfunction Syndrome (MODS), which is a significant cause of mortality in the intensive care units worldwide [3].

The PLR test has been proposed as a simple bedside method to assess fluid responsiveness, which is similar to an "auto-fluid challenge" without external fluid [4,5]. It acts as an alternative preload-modifying manoeuvre: when inferior limbs are raised, an amount of blood is "auto-transfused" into the central circulation. The PLR test is in fact a reversible "preload challenge" of blood that can be repeated as frequently as required without infusing a drop of fluid.

Paediatric patients are unique in terms of limb size compared to rest of the body. Adult studies have shown good prediction for leg raising in shock [6,7]. The smaller lower body size in children makes this reservoir less functioning as compared to adults [7]. Thus, PLR evaluation in children is more challenging. Only three studies have been identified which evaluate the role of PLR as a marker of fluid responsiveness in children [7-9]. As very limited data is available in literature, therefore, this study was planned to evaluate the PLR test as a simple bedside tool to assess volume responsiveness in children with shock.

MATERIALS AND METHODS

The present prospective observational study was conducted in paediatric emergency room and Inpatient Department of Jawaharlal Nehru Medical College, Aligarh, Uttar Pradesh, India, from November 2020 to October 2022. Institutional Ethical Committee approval was obtained prior to patient recruitment (No IECJNMC/549 dated 02.11.2021).

Inclusion criteria: Children between one month to eight years of age diagnosed with shock based on the American Heart Association -Paediatric Advanced life Support (PALS) 2020 guidelines were included [10].

Exclusion criteria: Increased abdominal or intracranial pressure patients who require urgent fluid bolus or inotrope adjustments, patients with suspected lower limb infections and suspected lower limb deep venous thrombosis, patients requiring Positive End Expiratory Pressure (PEEP) >5 cm of water during invasive or non-invasive ventilation, Failure to obtain adequate ultrasonography windows. Presence of congenital heart defects was excluded.

Sample size selection: Evaluation of past three year medical records at our hospital revealed that yearly 150 paediatric patients were diagnosed with shock. Out of this approximately 50 patients were between one month to eight years of age. Based on this data and accommodating to 20% attrition rate, a convenient sample size of minimum 40 cases was kept for this study.

Study Procedure

Patients demographic variables like age, gender, primary disease, etc., were recorded. Bedside Portable Echocardiography Machine (GE VIVID S6/ VIVID E95) were used. Echocardiography was performed by a single operator after receiving adequate training in basic Echocardiography (ECHO). All images and measurements were saved on the system reviewed by a Paediatric Cardiologist within 24 hours who was blinded to the clinical condition of the studied patients. The Left Ventricle Outflow Tract (LVOT) diameter (D) was measured at the aortic root at the insertion of two aortic cusps in left parasternal short axis (PLAX) view LVOT CSA was calculated as LVOT CSA=3.14 × $(D/2)^2$.

LVOT VTI was obtained by tracing the envelope of the doppler spectrum of LVOT systolic flow from the apical five chamber view using Pulsed-Wave Doppler (PWD), with the sample volume placed within the LVOT, approximately at 1 cm distance to the aortic valve. An average of 3-5 VTI measurements in an expiratory phase was recorded as VTI. Cardiac output and cardiac index was calculated during all measurements as per the formulas

Cardiac output [7,8] (cc/min) **=** VTI (cm/contraction) × LVOT Area (cm^2) × Heart rate (beats/min).

Cardiac index [8] ($l/min/m^2$)=Cardiac output (L/min)/Body Surface Area (BSA) (Kg/m^2).

The VTI measurements and vitals were taken in a semi-recumbent position (baseline I). Then, the patient's lower limbs were elevated 45 from the horizontal passively by the automatic raising of the bed's leg while simultaneously lowering the bed's head to the horizontal position (PLR). Re-measurement of all haemodynamic variables was done after one minute. Change in VTI (delta VTI) was compared to baseline I. Patient was replaced in semi recumbent position and baseline II vitals were recorded. Fluid bolus of 10 mL/kg of isotonic saline was given over 10 minutes and delta VTI post bolus was compared to baseline II. Ventilator settings and inotropic/vasopressor support was constant. Fluid responsiveness was considered positive when delta VTI was more than 12 % from the baseline after the fluid challenge [10,11].

PLR was done for one minute and VTI was calculated pre and post PLR in all patients. On the basis of response to PLR test patients were categorised to be responders (delta VTI >12%) and non-responders (delta VTI ≤12%). Fluid bolus was taken as gold standard method for assessing fluid responsiveness in patients with shock and PLR test was taken as bedside screening tool for determining fluid responsiveness.

STATISTICAL ANALYSIS

Data analysis was done with descriptive statistics, coefficient of correlation was calculated. Receiver Operator Characteristics (ROC) was plotted as appropriate. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) for windows software (version 26). Statistical significance was set at 0.05.

RESULTS

During study period 60 patients satisfied the inclusion criteria, 18 were excluded. Out of excluded cases six patients had congenital heart disease, three patients had raised intracranial pressure, five patients required urgent fluid bolus and inotropic adjustment two patients had lower limb infection and guardians of two patients did not give consent.

[Table/Fig-1] shows the baseline characteristics. Mean age of study population was 55.33±50.77 months, out of which 27 (64.3%) were below four years of age. Of study population 18 (42.9%) were severely thinned and 10 (23.8%) were found to be having haemoglobin level <10 g/dL, 16 (38.1 %) patients were on invasive mechanical ventilation and 20(46.5%) were already on inotropic support. Of 42 patients, 33 patients (78.6%) showed positive response (>12%) to PLR test while nine patients (21.4%) did not responded to PLR hence comprised the non-responder group [Table/Fig-2].

Demographic variables	All cases (n=42)
Age in months (mean±SD)	55.33±50.77
Gender	
Male n (%)	29 (69%)
Female n (%)	13 (31%)
Weight (Kg±SD)	12.57±10.11
Height (cm±SD)	89.41±32.89
Overall built	
Haemoglobin (<10 g/dL) (n,%)	10 (23.8)
Severe thinness n (%)	18 (42.9)
Thinness	12
Normal	9
Overweight	3
Invasive mechanical ventilation n (%)	16 (37.2)
Ionotropic support n (%)	20 (46.5)
Primary condition n (%)	
Pneumonia	16 (38.1)
Sepsis	15 (35.7)
Encephalitis	5 (11.9)
Others (hepatic, cardiac)	6 (14.3)

[Table/Fig-1]: Baseline characteristics of study participants.

Outcome of PLR and fluid bolus (cut- off change in CO>12%)		
	Frequency (n)	Percentage
PLR responder	33	78.6
PLR non responder	9	21.4
Fluid responder	38	90.5
Fluid non responder	4	9.5

[Table/Fig-2]: Volume responsiveness to PLR and fluid bolus.
Cut-off change in CO>12%

[Table/Fig-3] shows the haemodynamic parameters at baseline and post PLR (after one minute) and Fluid bolus (after 10 minutes). There was no statistically significant change in haemodynamic parameters like heart rate, cardiac output and cardiac index among responders and non-responders. Subsequent to PLR, patients were again shifted to semi recumbent position, after one minutes fluid bolus of 10 mL/kg of isotonic saline was given over 10 minutes and VTI was calculated. [Table/Fig-4] shows the scatter plot of variation of heart rate, cardiac output and cardiac index during pre and post-intervention. A total of 38 patients (90.5%) were responders having delta VTI >12% post-fluid bolus and four patients were non-responders with delta VTI ≤12% and comprise about 9.5% of all patients.

Regression analysis showed statistically significant positive correlation ($p<0.0001$) between ΔVTI post PLR and ΔVTI post FB was present with Pearson coefficient (r) of 0.868 [Table/Fig-5].

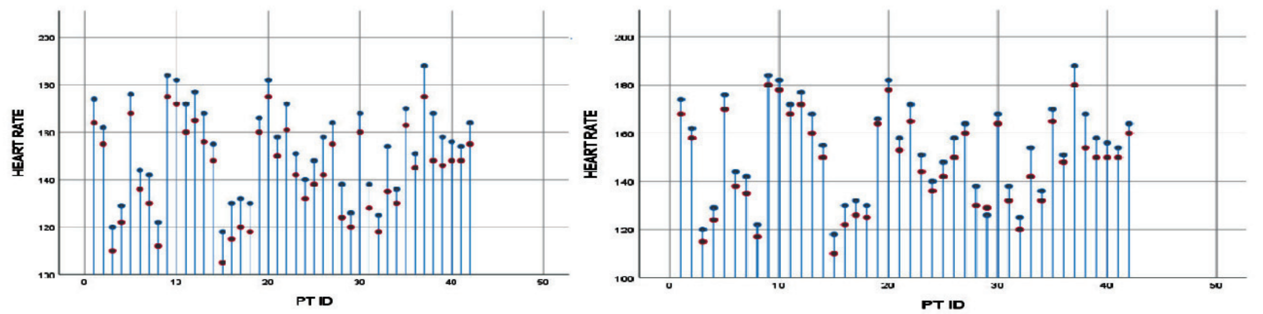
Haemodynamic Parameters	Baseline Responder n=38 Non-responder = 4	Post PLR Responder n=33 Non-responder = 9	Post fluid bolus Responder n=38 Non-responder = 4
Heart rate (bpm)			
Responders	152 (131-169)	143 (128-164)	140 (121-160)
Non-responders	161 (154-169)	152 (150-163)	148 (146-161)
p-value	p(MW)*=0.157	p(MW)*=0.177	p(MW)*=0.167
Cardiac output (l/min)			
Responders	1.18 (0.57-1.89)	1.66 (0.75-2.43)	1.74 (0.80-2.78)
Non-responders	1.00 (0.70-1.18)	1.05 (0.72-1.26)	1.14 (0.74-1.32)
p-value	p(MW)*=0.519	p(MW)*=0.147	p(MW)*=0.093
Cardiac index (l/min/m²)			
Responders	2.13 (1.64-3.19)	2.79 (2.16-4.19)	2.96 (2.33-4.40)
Non-responders	2.88 (1.94-4.24)	2.91 (2.07-4.49)	3.02 (2.19-4.63)
p-value	p(MW)*=0.093	p(MW)*=0.838	p(MW)*=0.694

[Table/Fig-3]: Haemodynamic parameters at baseline and post PLR and post fluid bolus.
(*$p_{(MW)}$- p-value of Mann-Whitney U test, Data is presented in median with interquartile range. PLR: Passive leg raise.

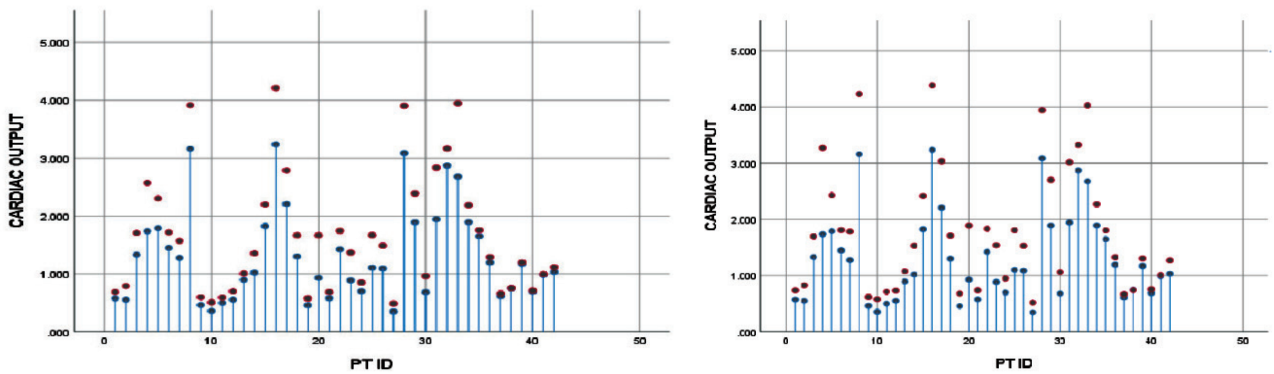
Fluid bolus was taken as gold standard method for assessing fluid responsiveness in patients with shock and PLR test was taken as bedside screening tool for determining fluid responsiveness. Receiver Operating Curve (ROC) was obtained for percentage change in left ventricular outflow tract- VTI after PLR test. Area under ROC curve is 0.855 with significance of 0.021. Cut-off of %change of VTI. When taken as 12% has sensitivity of 76.7% and specificity of 85.7%. This curve showed that best cut-off of % change in VTI post PLR is around 9.6% with sensitivity of 97.4% and specificity of 75% [Table/Fig-6,7].

DISCUSSION

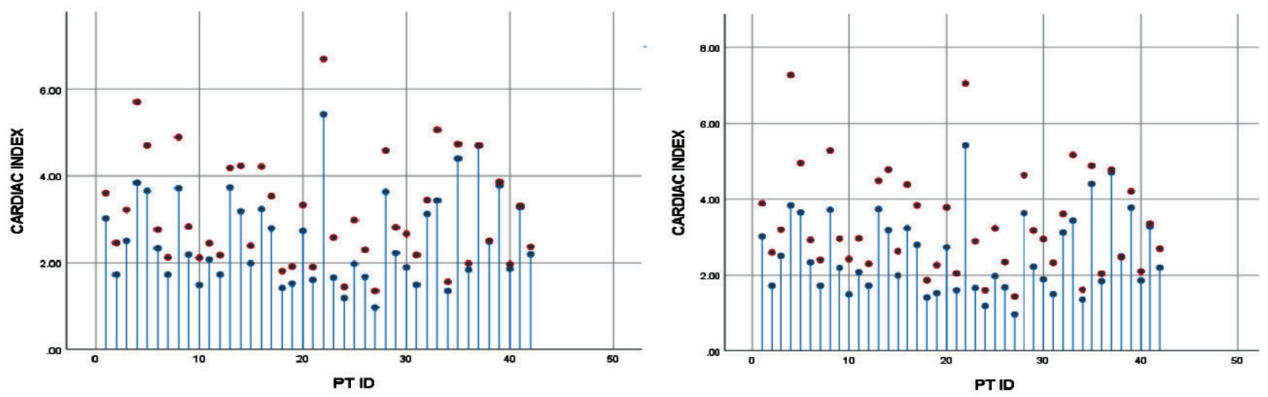
Shock is a prominent cause of morbidity and mortality in critically ill patients. Fluid bolus is the mainstay of treatment of shock since uncorrected hypervolaemia contributes to mortality. However, over administration of fluids also results in increased mortality and morbidity. Therefore, it is essential to assess the intravascular status with accuracy in each patient. No gold standard test available. Simple bedside auto fluid challenge (PLR test) can be used to assess the response to fluid bolus along



a(i) HR variation Pre and post PLR: a(ii) HR Variation Pre and post-Fluid Bolus.

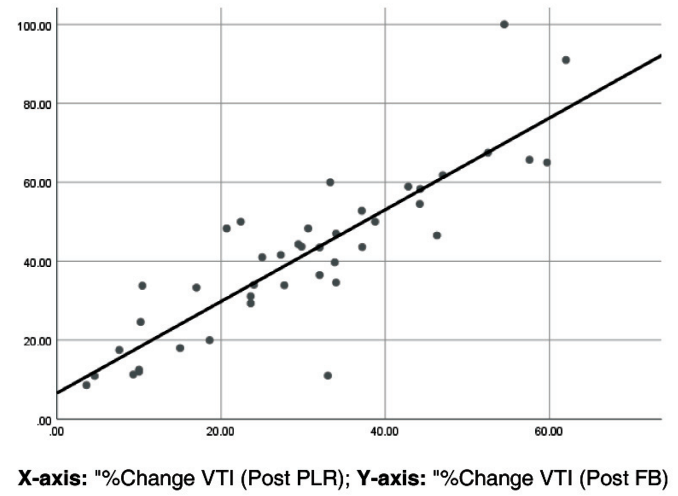


b(i)CO variation Pre and post PLR b(ii) CO variation Pre and post Fluid Bolus.



C(i) CI variation Pre and post PLR c(ii) CI variation Pre and post Fluid Bolus.

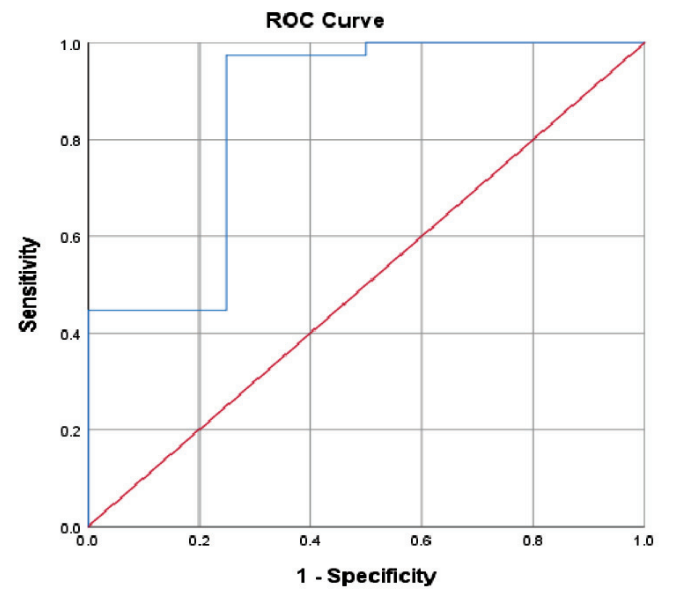
[Table/Fig-4]: Scatter plot showing (a) heart rate; (b) cardiac output; (c) Cardiac Index variations .
(Blue dots represent pre and Red dots represent post).



[Table/Fig-5]: Regression plot for ΔVTI for post PLR and post Fluid bolus.

Senstivity	Specificity	PPV	NPV
76.7%	85.7%	97.1%	37.5%

[Table/Fig-6]: Showing sensitivity and specificity of Passive Leg Raising (PLR) test for predicting a positive fluid response.



[Table/Fig-7]: ROC obtained for percentage change in left ventricular outflow tract- Velocity Time Integral (VTI) after Passive Leg Raising (PLR) test.

with real time cardiac output monitoring. The present study included about 42 patients who met the inclusion criteria which is comparable to other studies, done by Lu GP et al., and El Nawawy AA et al., [7,8].

The present study included children aged from one month to 96 months. With mean age of 55.33 months while other study included children aged from one month to 12 years.

The mean weight and height of patients in study by Lu GP et al., was 22 kg and 101cm while in the present study mean weight and height of study population was 12.5 kg and 89.41 cm [7]. PLR manoeuvre was done in all patients after taking baseline haemodynamic parameters. In study by Lu GP et al., various haemodynamic parameters including heart rate, stroke volume and cardiac output were evaluated (measured non-invasively by NICOM), while in study by El Nawawy AA et al., similar to our study cardiac output was calculated by using left ventricular outflow tract VTI and expressed in form of cardiac index [7,8]. Studies such as those by Lu GP et al., and El Nawawy AA et al. (the latter citing 10%), used a 7.5-10% cutoff for positive response to a Passive Leg Raise (PLR) and fluid bolus [7,8]. Our study, however, set the cutoff higher at 12%.

Present study showed that 78.6 % patients were responder to PLR manoeuvre which is comparable to what El Nawawy AA et al., have found in their study [8]. The comparison was done among responders and non-responders of PLR test as done by El Nawawy AA et al., [8]. Our study showed no significant difference in change of HR cardiac output and cardiac index among responders and non-responders in contrast to this study El Nawawy AA et al., have found significant difference in change in haemodynamic parameters from baseline after PLR and fluid bolus [8]. Area under the ROC curve was obtained as done by El Nawawy AA et al., [8]. In study by El Nawawy AA et al., delta Stroke volume of >10% after PLR was an excellent discriminator of fluid responsiveness with AUC ROC of 0.81 [8], sensitivity was 65.88% and specificity was 100%. In the current study, delta VTI >12% showed AUC of 0.855 with sensitivity of 76.7% and specificity of 85.7%. The present study revealed that delta VTI when taken as >9.6% is a best predictor of fluid responsiveness with sensitivity of 97.6% and specificity of 75%.

Limitation(s)

Majority of the patients included in the study were infants which may have affected the outcome of the study. Advanced haemodynamic monitoring like PiCCO and LiDCO were not used in the study. Furthermore the study duration coincided with the COVID-19 pandemic and cases managed in COVID ICU were not included in the study.

CONCLUSION(S)

The present study showed that PLR test can be used in paediatric population (<8 years) to predict fluid responsiveness with a sensitivity of 76.7% and specificity of 85.7% when cut-off for change in cardiac index was taken as 12%. This simple bedside procedure is valuable in resource poor settings where access to advanced haemodynamic monitoring or ultrasonography is not available. Future studies are needed to determine utility of PLR as a reversible fluid bolus is management of children with shock.

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