



ORIGINAL ARTICLE

Wernovsky-Inotropic Score and it's Relation to Outcome of Critically Ill Patients in Pediatric Intensive Care Unit

⁽¹⁾Mohamed Mahmud Romih, ⁽¹⁾Dalia Abdellatif Abdalrahman, and ⁽²⁾Samer Anwar Mubarek

⁽¹⁾Department of Pediatrics Faculty of Medicine –ZagazigUniversity,Egypt.

⁽²⁾Department of Pediatrics, Faculty of Medicine - Al-Zawia University, Libya

Corresponding author:

Dr. Samer Anwar Mubarek.
MBBCH – Faculty of Medicine
– Zawia University - Libya.
*Resident of Pediatrics Faculty
of Medicine - Zagazig
University.*

*Postgraduate student(master
degree)- Faculty of Medicine –
Zagazig University.*

Tripoli, Libya.

e-mail:

samermubarek86@gmail.com

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ABSTRACT

Background: Hemodynamic instability is defined as any instability in blood pressure which can lead to inadequate arterial blood flow to organs. Wernovsky-inotropic score (WIS), a measure of post-operative cardiovascular support, has been associated with morbidity and mortality after infant cardiac surgery in prior center studies.

Objectives: This study aimed to determine the association of Wernovsky-inotropic score (WIS) with clinical outcome of critically ill children with hemodynamic instability in PICU and to use it as a predictor of the outcome of the critically ill patients.

Patients & Methods: This study was prospective analytical study which conducted at pediatric intensive care unit (PICU) at Pediatric Department, Zagazig University Hospital on 102 patients during the period of 10 months from April 2018 to January 2019.

Results: On studying relationship between WIS score over time and patient outcome, WIS didn't statistically significantly differ between dead or discharge patients at baseline, 6 and 12 hours. While there is significant difference between both groups at 24 and 48 hours.

Conclusions: Wernovssky-inotrpic score (WIS) is an easily calculated clinical score. It is useful as an independent predictor of clinical outcomes of critically ill pediatric patients with hemodynamic instability in PICU.WIS is a reliable marker of cardiovascular support that may be used as a surrogate outcome for research studies and provide additive value to existing pediatric acuity scores in this population.

Keywords: Wernovesky Score; instability ; outcome ; marker ; monitoring

INTRODUCTION

Hemodynamic instability is defined as any instability in blood pressure which can lead to inadequate arterial blood flow to organs. It is also a state where there is a requirement for physiological and mechanical support to ensure there is adequate cardiac input and output or blood pressure ^[1].

Hemodynamic monitoring represents a cornerstone in the management of the critically ill patient, as it is used to identify cardiovascular insufficiency, its probable

cause, and response to therapy. It needs to be used with the perspective of tailoring treatment to physiology and the underlying disease process ^[2]. So it represents an ongoing challenge in the management of critically ill infants and neonates ^[3]. Inotropes are agents used to increase myocardial contractility, while vasopressors are administered to increase vascular tone ^[4]. Their use is mostly confined to critically ill patients whose hemodynamic impairment is such that tissue

perfusion is insufficient to meet metabolic requirements^[5].

Patients in need of inotropic or vasopressor support are often presented with septic or cardiogenic shock and severe heart failure, and are victims of major trauma or undergoing major surgery^[6].

Wernovsky-inotropic score (WIS), a measure of post-operative cardiovascular support, has been associated with morbidity and mortality after infant cardiac surgery in prior single center studies^[7].

One candidate scoring system was proposed by **Gaies et al.**,^[7] for use in infant cardiac surgery. The WIS, expanded from the previously described inotropic Score, quantifies the amount of cardiovascular support required by infants postoperatively and includes dopamine, dobutamine, epinephrine, milrinone, vasopressin, and norepinephrine. WIS has been shown to correlate with worse short-term clinical outcomes in infants following cardiac surgery^{[8], [9]}.

The amount of cardiovascular support after hemodynamic instability predicts eventual morbidity and mortality in young infants. The degree of support is best characterized by a maximum WIS obtained during this period. The usefulness of WIS as an independent predictor of clinical outcome in infants after hemodynamic impairment may have important implications for future cardiothoracic intensive care unit research^[9].

After controlling for diagnosis, high maximum WIS was strongly associated with a poor outcome as compared with patients with low maximum WIS^[8]. High WIS was also associated with prolonged cardiothoracic ICU stay, duration of the mechanical ventilation, and time to negative fluid balance. The amount of cardiovascular support in the first 48 hours after hemodynamic impairment predicts eventual morbidity and mortality in young infants. The degree of support is best characterized by a maximum WIS obtained during this period^[7].

PATIENTS AND METHODS

This study was prospective analytical study (cohort) which was conducted at pediatric intensive care unit (PICU) at

Pediatric Department, Zagazig University Hospital on 102 patients during the period of 10 months from April 2018 to January 2019.

Inclusion criteria: Children older than one month and younger than 18 years, critically ill patients admitted to the Pediatric Intensive Care Unit (PICU). Children presented with hemodynamic impairment and under hemodynamic monitoring and all cases in need for vasoactive or inotropic support.

Exclusion criteria: Children age less than one month or greater than 18 years. Children with chronic renal failure Children with known chronic cardiac diseases. Children with metabolic syndromes. Children refused to be enrolled in the study. Children of long term cardiac support medication. Children need surgery in the 1st 48 hours of admission. Cardiac arrest in the 1st 48 hours will not be included after post arrest support.

Wernovsky formula:

Wernovsky IS = dopamine dose ($\mu\text{g}/\text{kg}/\text{min}$) + dobutamine dose ($\mu\text{g}/\text{kg}/\text{min}$) + $100 \times$ epinephrine dose ($\mu\text{g}/\text{kg}/\text{min}$)^[10].

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean \pm SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (χ^2). Differences between quantitative independent groups by t test or Mann Whitney, correlation by Pearson's correlation or Spearman's. P value was set at <0.05 for significant results & <0.001 for high significant result.

Data were collected and submitted to statistical analysis

Written informed consent was obtained from all participants parents and the study was approved by the research ethical committee of faculty of medicine, Zagazig university.

the work has been carried out in accordance with the code of code of ethics of the world medical association (Declaration of Helsinki) for studies involving humans.

RESULTS

(Table 1) On studying relationship between WIS score over time and patient outcome, WIS didn't statistically significantly differ between dead or discharge patients at baseline, 6 and 12 hours. While there is significant difference between both groups at 24 and 48 hours.

(Table 2) There is statistically significant differences between WIS values over time within patients who died by the end of the study, with the difference started to be significant at 24 and 48 hours. Within the group of discharged patients, no statistically significant difference was noticed.

(Table 3) On studying relationship between ICU stay and ventilation days in relation to patient outcome, there were statistically significant differences between both groups.

On studying correlation between WIS and VIS over time, there are highly significant positive correlation between both scores values.

(Table 4) On assessing correlations between ICU stay of the studied patients and their WIS score over time, there were significant positive correlations between Length of ICU stay and WIS score at baseline, 6, 12, 24 and 48 hours. On assessing correlations between duration of ventilation of the studied patients and their WIS score over time, there were non-significant positive correlations between it, and WIS score at baseline, 6 and 12 hours while there are significant positive correlation between duration of ventilation and WIS score at 24 and 48 hours.

(Table 5)(Figure 1) The best cutoff of WIS at 24 hours in prediction of mortality was ≥ 12.5 with area under curve 0.682 at sensitivity 79.2%, specificity 51%, PPV 63.6%, NPV 69.4%, +LR 1.62, -LR 0.41 and accuracy 65.7% ($p < 0.05$).

(Table 6)(Figure 2) The best cutoff of WIS at 48 hours in prediction of mortality was ≥ 12.5 with area under curve 0.772 at sensitivity 86.8%, specificity 51%, PPV 65.7%, NPV 78.1%, +LR 1.77, -LR 0.26 and accuracy 69.6% ($p < 0.05$).

Table (1) Comparison of WIS in studied patients in relation to outcome:

	Death	Discharged	MW	p
	Mean \pm SD	Mean \pm SD		
Baseline	13.58 \pm 7.1	14.39 \pm 5.56	-0.298	0.766
At 6 hours	13.68 \pm 7.08	14.39 \pm 5.56	-0.208	0.835
At 12 hours	13.58 \pm 7.1	14.49 \pm 5.42	-0.374	0.709
At 24 hours	19.72 \pm 9.92	14.9 \pm 5.82	-3.324	0.001**
At 48 hours	22.64 \pm 10.54	14.69 \pm 5.44	-4.943	<0.001**
P(fr)	<0.001**	0.075		

MW Mann Whitney test FrFrideman test P \leq 0.001 is highly significant

Table (2) Comparison of WIS in studied patients on inotropes in relation to icu stay and ventilation days:

	Death	Discharged	MW	p
	Mean \pm SD	Mean \pm SD		
ICU stay	11.25 \pm 4.89	8.41 \pm 2.61	-7.362	<0.001**
Ventilation days	8.49 \pm 5.04	5.18 \pm 2.69	-7.599	<0.001**

MW Mann Whitney test P \leq 0.001 is highly significant

Table (3) Correlation between WIS over time and VIS:

WIS		VIS									
		base		6hr		12hr		24hr		48hr	
		r	p	r	p	r	p	r	p	r	p
	Base	0.731	<0.001	0.997	<0.001	0.997	<0.001	0.742	<0.001	0.717	<0.001
	6hr	0.997	<0.001	0.732	<0.001	0.993	<0.001	0.747	<0.001	0.726	<0.001
	12hr	0.726	<0.001	0.992	<0.001	1		0.740	<0.001	0.714	<0.001
	24hr	0.514	<0.001	0.772	<0.001	0.766	<0.001	0.998	<0.001	0.890	<0.001
	48hr	0.488	<0.001	0.748	<0.001	0.738	<0.001	0.886	<0.001	0.991	<0.001

P ≤0.001 is highly significant

Table (4) Correlation between WIS over time and ICU stay, duration of ventilation:

WIS		ICU stay		Duration of ventilation	
		r	p	r	p
		Base	0.249	0.012	0.178
6hr	0.250	0.011	0.186	0.061	
12hr	0.243	0.014	0.169	0.089	
24hr	0.305	0.002	0.329	0.001	
48hr	0.298	0.002	0.363	<0.001	

P<0.05 is statistically significant

P ≤0.001 is highly significant

Table (5) Performance of WIS score at 24 hours in prediction of mortality in studied patients:

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	+LR	-LR	Accuracy	p
≥12.5	0.682	79.2	51	63.6	69.4	1.62	0.41	65.7	0.002

P<0.05 is statistically significant

P ≤0.001 is highly significant

Table (6) Performance of WIS score at 48 hours in prediction of mortality in studied patients:

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	+LR	-LR	Accuracy	p
≥12.5	0.772	86.8	51	65.7	78.1	1.77	0.26	69.6	<0.001

P<0.05 is statistically significant

P ≤0.001 is highly significant

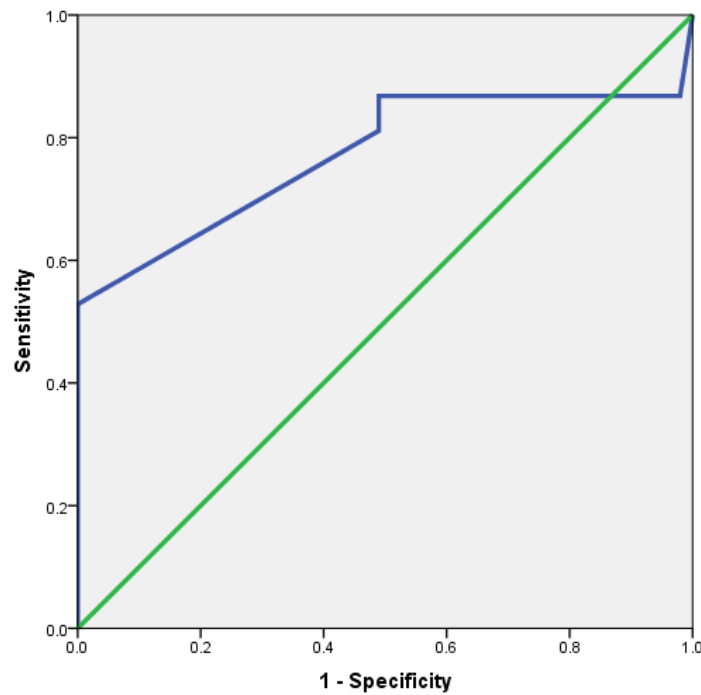


Figure (2) ROC curve showing performance of WIS score at 48 hours in prediction of mortality in studied patients

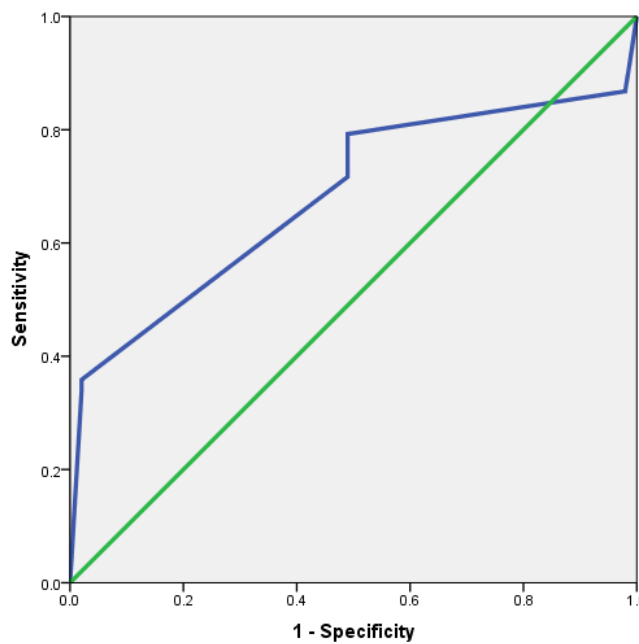


Figure (1) ROC curve showing performance of WIS score at 24 hours in prediction of mortality in studied patients

DISCUSSION

The focus on the quality and safety of medical care is increasing because of the high cost of healthcare and potential for harm. There are many evaluations of mortality and incidence of complications, such as

nasocomial infections in the ICUs, with an increased emphasis on the quality improvement efforts and evaluation of outcomes. [11].

Vasoactive and inotropic medications are standardly used to treat hypotension and

cardiovascular dysfunction associated with pediatric Septic shock ^[12]. Currently, no uniform, validated measure or scoring system exists to describe the magnitude of hemodynamic support required in pediatric sepsis. In adult sepsis, clinical measures that both objectively describe illness severity and correlate with important outcomes such as mortality are being increasingly recognized as necessary to identify which patients are most at risk for poor outcomes ^[13].

A validated score that accurately describes cardiovascular dysfunction and correlates with other clinically relevant outcomes such as duration of mechanical ventilation and ICU stay could be used to identify high-risk patients and as an outcome in research and quality improvement.

One candidate scoring system was proposed by **Gaies et al.**, ^[14] for use in infant cardiac surgery. The Vasoactive-Inotropic Score (VIS), expanded from the previously described Inotropic Score ^[15], quantifies the amount of cardiovascular support required by infants postoperatively and includes dopamine, dobutamine, epinephrine, milrinone, vasopressin, and norepinephrine. VIS has been shown to correlate with worse short-term clinical outcomes in infants following cardiac surgery ^[16].

Few studies have used VIS in pediatric sepsis to describe inotropic and vasopressor support in their population. However, to our knowledge, only one previous study by **Haque et al.**, ^[17] has shown an association between VIS and mortality in pediatric sepsis.

This study aimed to determine the association of Wernovsky-inotropic score (WIS) with clinical outcome of critically ill children with hemodynamic instability in PICU and to use it as a predictor of the outcome of the critically ill patients.

This study was prospective analytical study which conducted at pediatric intensive care unit (PICU) at Pediatric Department, Zagazig University Hospital on 102 patients during the study from april of 2018. outcome, WIS didn't statistically significantly differ between dead or discharge patients at baseline, 6 and 12 hours while mean value of WIS score at 24 and 48 hours were

significantly higher among death than discharged cases ($P < 0.05$). There is statistically significant differences between WIS values over time within patients who died by the end of the study, with the difference started to be significant at 24 and 48 hours. Within the group of discharged patients, no statistically significant difference was noticed.

McIntosh et al., ^[18] who aimed to assess the validity of Vasoactive-Inotropic Score as a scoring system for cardiovascular support and surrogate outcome in pediatric sepsis. Children greater than 60 days and less than 18 years with sepsis identified in the emergency department between January 2012 and June 2015 treated with at least one vasoactive medication within 48 hours of admission to the PICU. Vasoactive-Inotropic Score was abstracted at 6, 12, 24, and 48 hours post PICU admission. They found that, vasoactive-Inotropic Score may be a useful surrogate outcome in pediatric sepsis. Previous studies of VIS in infant cardiac surgery ^[7] and the study by **Haque et al.**, ^[17] of VIS in pediatric sepsis, find a strong correlation between maximal VIS and outcomes of interest. Early aggressive resuscitation is associated with improved outcomes and shock reversal in pediatric sepsis ^[12], and it is possible that early and maximal VIS may reflect attentive support of reversible pathophysiology compared with VIS at later time points. This study showed that, mean value of Ventilation days was significantly higher among death than discharged cases ($P < 0.05$). This is in agreement with **Mukhtar et al.**, ^[19].

This study showed that, on assessing correlations between ICU stay of the studied patients and their WIS score over time, there were significant positive correlations between Length of ICU stay sand WIS score at baseline, 6, 12, 24 and 48 hours. On assessing correlations between duration of ventilation of the studied patients and their WIS score over time, there were non-significant positive correlations between it, and WIS score at baseline, 6 and 12 hours while there are significant positive correlation between duration of ventilation and WIS

score at 24 and 48 hours. This is in agreement with **McIntosh et al.**,^[18]

This study showed that, on assessing correlations between ICU stay of the studied patients and their WIS score over time, there were significant positive correlations between Length of ICU stay and WIS score at baseline, 6, 12, 24 and 48 hours. This is in agreement with **Davidson et al.**,^[9] who reported striking association between WIS48 and several important short term outcomes including length of hospital stay. Overall in their study WIS48 outperformed WIS48max, suggesting that duration of intensive cardiovascular support may be more important than maximal intensity of therapy as a predictor of these short term outcomes.

The strong association between WIS and length of mechanical ventilation makes intuitive sense. Positive pressure ventilation decreases the energy expended by the patient for breathing. In a critically ill post-operative infant who already requires high levels of inotropic and vasoactive support, clinicians are less likely to extubate and thereby transfer the work of breathing exclusively to the patient. So while we agree with the general idea that high VIS is largely a surrogate marker for poor outcomes and WIS should not be targeted as a primary intervention to improve outcomes, it is likely that therapies capable of improving post-operative WIS would directly improve intubation times as well. High WIS is simply a marker for poor physiology in the immediate post-operative period. This poor physiology may in turn lead to prolonged therapies, more frequent complications, and borderline cardiac and pulmonary function that impair convalescence, particularly feeding. Conversely, in the face of conflicting data in the literature concerning the risk/benefit of specific medications for cardiovascular support^[20]. **McIntosh et al.**,^[18] reported that, WIS at 48 hours had the strongest correlation with the primary outcomes (LOS and ventilator days). Our study complements the study by **Haque et al.**,^[17] done in a resource-poor setting, by showing that in a resource-rich setting with a medically complex, low-mortality cohort of children with septic shock,

WIS at 48 hours after ICU arrival is independently associated with short-term outcomes including ICU LOS and ventilator days. On assessing correlations between PIM-2 score, there are significant positive correlation between them and WIS score at 48 hours. This is in agreement with **Gandhi et al.**,^[21] The best cutoff of WIS at 24 hours in prediction of mortality was ≥ 12.5 with area under curve 0.682 at sensitivity 79.2%, specificity 51 %, PPV 63.6%, NPV 69.4%, +LR 1.62, -LR 0.41 and accuracy 65.7% ($p < 0.05$). This agrees with **McIntosh et al.**,^[18] who found that, WIS is a reliable marker that may be used as a surrogate outcome for research studies and provide additive value to existing pediatric acuity scores in this population.

CONCLUSION

Wernovssky-inotropic score (WIS) is an easily calculated clinical score. It is useful as an independent predictor of clinical outcomes of critically ill pediatric patients with hemodynamic instability in PICU. WIS is a reliable marker of cardiovascular support that may be used as a surrogate outcome for research studies and provide additive value to existing pediatric acuity scores in this population.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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