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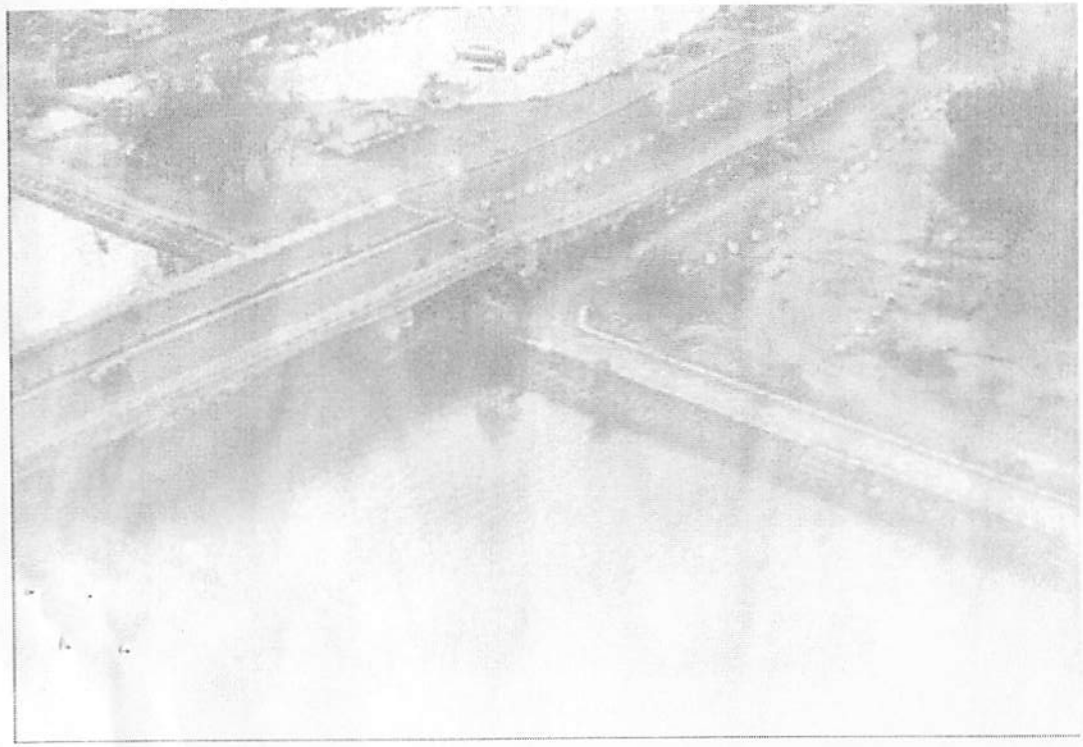

Medical and Health Care Improvement Through Innovative Research and Interdiciplinary Collaboration

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Conference Program and Abstract Book

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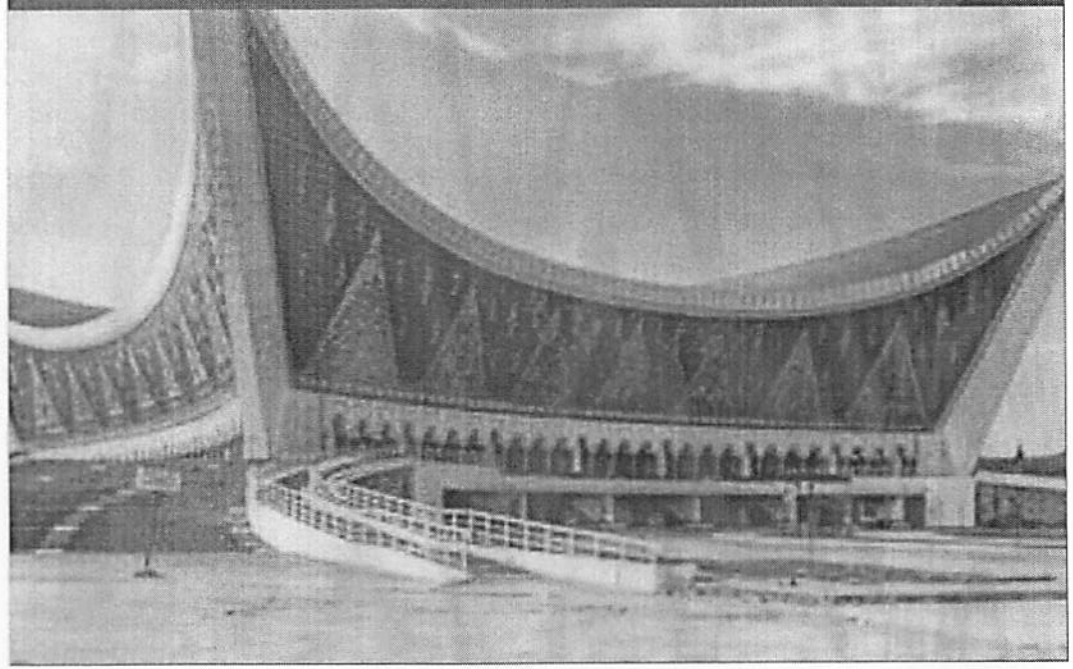

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CD64 Index as a predictor of outcome for children with systemic inflammatory response syndrome (SIRS)

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Introduction

- Sepsis is the prominent causal of morbidity and mortality in children worldwide including developing countries [Kissoon et al., 2015].
- Sepsis is defined as life-threatening organ dysfunction or systemic inflammatory response syndrome (SIRS) caused by dysregulated host response to infection [Singer et al., 2016: Goldstein et al., 2005].
- Symptom are similar to SIRS without infection [Hassuna et al., 2016].
- The disease could progress to severe sepsis or septic shock and mortality.

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- ✓ Biomakers to predict severity and/or sepsis outcome such as Procalcitonin, TNF, LPS, IL-6. IL-8, CD64 [Djordjevic et al., 2016; Livaditi et al., 2005; Oda et al., 2005].
- ✓ However, IL-6; PCT and CRP were not the ideal predictor of prognosis [Oda et al., 2005; Clec'h et al., 2004].
- ✓ Biomarker that is widely assess is CD64 (FcγR1) → is a membrane glycoprotein, which is expressed mainly on monocytes and macrophages with low concentration on the surface of non-activated neutrophils.
- ✓ Neutrophil CD64 (nCD64) expression can be distinctly elevated at the onset of sepsis, and is superior to standard laboratory tests (neutrophilia, band forms, etc.) for early detection of sepsis [Godnic et al., 2015; Davis, 1996].
- ✓ Nevertheles, the prognostic value of CD64 in children with SIRS is still uncertain, so the aim of the study was to know the role of CD64 netrofil index to predict sepsis outcome in children with SIRS.

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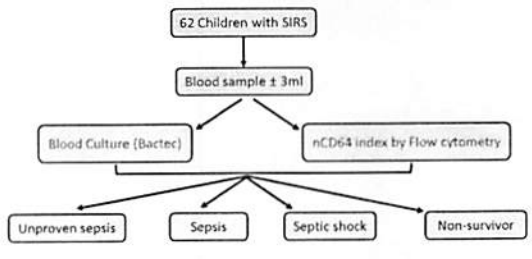
Materials and Methods



Results

Table 1. Demographic and clinical characteristics of patients with sepsis according to outcome

Variable	All patients (n= 62)	Survivors (n= %)	Nonsurvivors (n= %)	*P* value
Sex, n (%)				
Male	31 (50%)	26 (83,9%)	5 (16,1%)	0,362
Female	31 (50%)	22 (71,0%)	9(29,0%)	
Age				
1 month – 1 year	22 (35.5%)	16 (72,7%)	6 (27,3%)	0,660
2 – 5 years	26 (41.9%)	20 (76,9%)	6 (23,1%)	
6-12 years	14 (22.6%)	12 (85,7%)	2 (14,3%)	
Long of hospital stay, days, median (min-max)	7 (1-18)	8 (5- 18)	2 (1 – 17)	0,000
Disease grade				
Unproven sepsis	38 (61.3%)	31 (81.58%)	7 (18.42%)	0,000
Sepsis	6 (9.68%)	6 (100%)	0 (0%)	
Septic shock	18(29.03%)	11(61.11%)	7 (38.9%)	
Laboratory results				
Hemoglobin g/L, mean (SD)	10.55 ± 1.71	10,8 ± 1,56	9,68 ± 1,95	0,029
WBC x 10^9/L, mean (SD)	14.978 ± 8217	13.390 ± 7061	20.422 ± 9763	0,004
CD64 index, mean (SD)	1.78 ± 0.96	1.47 ± 0.64	2.86 ± 1.1	0,000

Table 2. Performance of CD64 index in predicting mortality

Predictor	AUC	*P* value	Cut-off point	OR	95% CI	Sensitivity (%)	Specificity (%)
CD64 index	0.863	0.005	1.705	6.7	1.79-25.27	71.4 %	72.9%

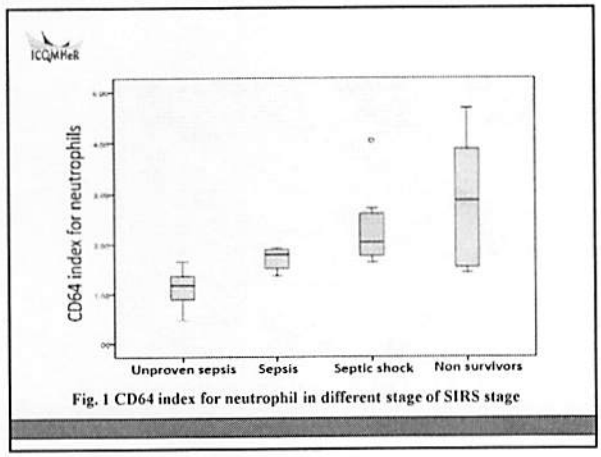


Fig. 1 CD64 index for neutrophil in different stage of SIRS stage

Discussion

- ✓ In our study, mortality caused by SIRS were 22.6%, in line with epidemiology study from 26 countries that reported the hospital mortality rate was 25% and did not differ by age or between developed and resource-limited countries [Weiss et al., 2015].
- ✓ CD64 index were increased as the degree of sepsis deteriorated.
- ✓ Index of CD64 neutrophil were highest in nonsurvival patient and lowest in unproven sepsis. In concordance with study by Livadity et al. (2006) revealed that CD64 were significantly and positively associated with stages of sepsis.

- ✓ CD64 indexes for neutrophils can discriminated SIRS with sepsis and without sepsis [Grosell-Grenc et al., 2008].
- ✓ Kobold et al. (2002) that presenting a trend towards higher values of neutrophil-CD64 in non-survivors compared with survivors.
- ✓ However, the index of CD64 between sepsis and septic shock and nonsurvivors; and between septic shock and nonsurvivors were not significantly different. This could be explained by an outlier value (4.03) of CD64 index found in one septic shock patient which may be affected the mean value on this group (Fig.1).
- ✓ Similar with study by Velasques el al (2013): although there was significant correlation between 28 days mortality and CD64 neutrophil in univariat analysis, but in multivariate analysis there were no significant different.
- ✓ Godnic et al. (2005) also showed very small difference between values of sepsis and septic shock, so there was no statistical significance but they could distinguish between SIRS and septic shock (p = 0.038).
- ✓ Contrary to the study by Gosh et al (2018) and Kobold et al. (2002), they demonstrated no significance difference of CD64 between survivor and nonsurvivors. Both of this studies afflicted by the limitation of a small sample size.

- ✓ The role of CD64 neutrophil as predictor of sepsis outcome reported with variably result.
- ✓ Djorjevic (2015) shown that index of CD64 neutrophil on the first day was a good outcome predictor.
- ✓ De Jong (2016) demonstrated that CD64 neutrophil could discriminate between critically ill patient with positive blood culture and negative blood culture and also were correlated with the degree of sepsis.
- ✓ Muzlovic et al (2016) demonstrated that index CD64 netrophill could diagnose sepsis and predict 30-day survival in subjects after ventilator associated pneumonia (VAP).
- ✓ Meanwhile, Danikas et al (2008) shown increased expression of CD64 netrophil in survival sepsis patients compared with nonsurvivors but not correlated with disease outcome. Study by Cid, et al (2011) also showed higher nCD64 expression in survivors compared to nonsurvivor.

- ✓ Despite the relatively small number of the patients included in this study, we performed ROC curves which showed high sensitivity and specificity, positive and negative predictive value of the CD64 neutrophil index for predicting the prognosis.
- ✓ In line with previous study by Livaditi (2016), showed AUC 0.75, sensitivity 66.7%, specificity 73.9%, PPV 72.7% and NPV 68%.
- ✓ Study by Chen et al. (2014) demonstrated AUC of 0.752 (p = <0.001), with cut-off value 1.835, sensitivity 60%, and specificity 80.23%.
- ✓ Two other study also reported similar AUC, 0.707 [Hsu et al., 2011] and 0.71 [Cid et al., 2011].
- ✓ Relatively different cut-off values were reported in a different study, probably due to different flow cytometry measurement methods [Hassuna et al., 2016].

Conclusion

- ✓ There were difference of mean CD64 index in children with SIRS on first day admission in hospital depend on clinical disease state and outcome.
- ✓ The mean of CD64 index were higher in the severe outcome, thus index CD64 neutrophil could be prognostic biomarker for sepsis.

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Thank you