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Role of salivary c reactive protein and mean platelet volume in diagnosis of late onset neonatal pneumonia

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Abstract
Background: Late onset neonatal pneumonia (LONP) must be diagnosed accurately and promptly if we are to accurately assess the disease's prevalence, create better strategies for preventing and treating it, and ultimately find a cure. The combined measurement of C- reactive protein (CRP) and mean platelet volume (MPV) could be useful in determining if a patient has bacterial or viral infection and in estimating the likelihood of complications from either. The purpose of this research is to evaluate the usefulness of CRP in saliva (sCRP) and MPV in the identification of LONP.
Methods: This prospective case control research was carried out on 60 full-term neonates. The neonates were classified into 2 equal groups: Group a: included 30 neonates with LONP. Group b: included 30 healthy control neonates. All patients were subjected to thorough medical history taking and physical examination as well as measurement of salivary and serum CRP and complete blood picture for assessment of MPV.
Results: MPV, sCRP, serum CRP and serum CRP / MPV are statistically significant predictors of LONP cases. SCRP at a cutoff value >3.2 is a statistically significant predictor of serum CRP> 6 in patient groups. A stastistically notable positive link between salivary and serum CRP concentrations ($r = 0.476$, $p \leq 0.05$), the research also showed significant link between serum CRP and MPV ($r = 0.547$, $P = 0.002$). There was a statistically evident link between sCRP and MPV concentrations in the pneumonic group ($r = 0.507$, $p \leq 0.05$) in diagnosis of LONP. CRP/MPV ratio as predictor for diagnosis of LONP cases, was a statistically significant predictor at a cutoff value >0.6.
Conclusions: Late-onset neonatal pneumonia may be diagnosed non-invasively with CRP and MPV in the saliva. The ratio of C-reactive protein to mean platelet volume (MPV) is easy to compute and has the potential to serve as a straightforward and reliable biomarker for the identification of late-onset neonatal sepsis.

Keywords: Late onset neonatal pneumonia, c reactive protein, mean platelet volume

Introduction
Despite advances in medicine, neonatal sepsis (NS), which is characterised by systemic symptoms of infection within the first month of life, continues to be an essential clinical syndrome [1].
Still, neonatal sepsis ranks as the third largest cause of infant mortality globally, with a mortality rate of 26%. [2].
Septicemia, asthma, meningitis, osteomyelitis, gout, and urinary tract infections are all examples of neonatal sepsis. A respiratory illness in a new-born is called late onset neonatal pneumonia (LONP). As part of a systemic sepsis condition, it can appear within hours of delivery, or it can appear 7 days later and be localised to the airways [3].
Although there have been significant improvements in new-born care thanks to recent medical advancements, many difficulties persist in the detection and treatment of neonatal infections [4].
Many of the typical lung defences are weakened in the foetus and neonate, increasing their vulnerability to infection; this is why the risk of death from pneumonia in children is highest during the neonatal period [5].
LONP diagnostic accuracy is critical for disease burden estimation, therapy planning, and research into new and improved treatments [6]. Saliva has shown great promise as a diagnostic fluid over the years; its non-invasive sample gathering is what makes it

appealing for use on young children and other vulnerable groups [7].

C-reactive protein (CRP) plays a major role in inborn and acquired immunity; it takes 10-12 h for CRP shows significant rise after infection by 10-12 hrs; and as CRP shows an increase in several conditions, it is used as inflammation biomarkers [8].

Mean platelet volume (MPV) is a hemogram measure that can forecast the onset and severity of sepsis in newborns and is influenced by many inflammation [9].

Therefore, CRP and MPV measurements taken together can be used for both the differential diagnosis of bacterial vs. viral infection and the prognosis of its consequences [10].

The purpose of this research is to evaluate the usefulness of CRP in saliva (sCRP) and MPV in the identification of newborn pneumonia with late start.

Patients and Methods

This study is a prospective case control investigation of gender-neutral full-term infants between the ages of seven and twenty-eight days old. The neonates were divided into two equal groups: Group a: included 30 neonates with late-onset neonatal pneumonia. Group b: included 30 healthy control neonates. Neonates of the same age and gender as those in the LONP group who did not exhibit any signs, symptoms during their follow-up in our OPC were prospectively enlisted in the controls. All of them had negative blood CRP levels.

Parents of the newborns gave their permission after being fully told of the risks and benefits. Before beginning the research, permission was sought and granted by a legal review board.

Exclusion criteria included Neonates with inflammation other than pneumonia, neonates who were exposed to antibiotics before admission and neonates younger than 7 days or infants older than 28 days of life.

All the participants underwent the following: Complete history taking, physical examination, chest examination, measurements of vital signs and anthropometric measures.

Laboratory investigations including salivary and serum CRP measurement and MPV measurement.

Statistical analysis

IBM's statistical programme SPSS version 20.0 was used for the analysis (Armonk, NY: IBM Corp). Quantitative and percentage descriptions were used for qualitative information. Shapiro-Wilk was used to check for normal distribution. The mean and standard deviation were used to characterise the quantitative data, and the findings were deemed statistically significant at the 5% level.

Results

No statistically significant difference was found between both groups regarding age and sex.

Table 1: Comparison between the two studied groups according to demographic data

Demographic data	Group A (n = 30)		Group B (n = 30)		p
	No.	%	No.	%	
Sex					
Male	16	53.3	16	53.3	1.000
Female	14	46.7	14	46.7	
Age (days)					
Mean ± SD.	19.83±5.74		21.50 ± 4.65		0.274

No statistically significant difference between both groups regarding mode of delivery, maternal illness and anthropometric measures was found.

Table 2: Comparison between the two groups regarding mode of delivery, maternal illness and anthropometric measures

Delivery	Group A (n = 30)		Group B (n = 30)		p
	No.	%	No.	%	
NVD	11	36.7	12	40.0	0.791
C.S	19	63.3	18	60.0	
Maternal illness					
Non	26	86.7	26	86.7	
Diabetic	2	6.7	1	3.3	1.000
hypertensive	1	3.3	1	3.3	
UTI	1	3.3	2	6.7	
Anthropometric measures					
Weight (gm)	3534.3 ± 359.67		3626.7 ± 316.2		0.295
Length (cm)	51.02 ± 1.0		50.87 ± 0.57		0.483
Head circumference	35.91 ± 0.58		35.58 ± 0.50		0.483

Table 3: Shows the Clinical characteristics and chest X ray signs for the LONP group (n = 30)

	No.	%
Fever	20	66.7
Cough	21	70.0
Dyspnea		
RD1	5	16.7
RD2	12	40.0
RD3	10	33.3
RD4	3	10.0
Decreases air entry	25	83.3
Fine crepitations	26	86.7
Chest X - Ray finding		
X - Ray G1	3	10.0
X - Ray G2	23	76.7
X - Ray G3	3	10.0
X - Ray G4	1	3.3
Need oxygen support		
Nasal canula	23	76.7
NCPAP	4	13.3
Mechanical ventilation	3	10.0

Group A: 30 neonates with late –onset neonatal pneumonia Resp distress mild (G1); tachypnea >60 +flaring nostrils mod (G2); G1+ intercostals and subcostal retractions Severe (G3); G1+G2+ expiratory grunting advanced (G4); G1+G2+ G3 +central cyanosis Chest x ray finding grade 1 (homog ground glass shadow)

Grade 2 (pneumonic patches and air bronchogram)

Grade 3 (interstitial pneumonia)

Grade 4 (complete white lung)

Notable variations were found between both groups in sCRP, serum CRP and MPV.

Table 4: Comparison between the two studied groups according to MPV, sCRP, serum CRP and Serum CRP/ MPV.

	Group A (n = 30)	Group B (n = 30)	p
Serum CRP	42.53 ± 34.88	5.70 ± 3.15	<0.001**
SCRP	6.17 ± 3.38	3.07 ± 1.24	<0.001**
MPV	9.99 ± 0.94	8.42 ± 0.83	<0.001**
Serum CRP/MPV	4.09 ± 3.29	0.69 ± 0.39	<0.001*

MPV, sCRP, serum CRP and serum CRP / MPV are statistically significant predictors of LONP cases. SCRP is

statistically significant predictor of serum CRP> 6 in patient groups.

Table 5: Validity (AUC, sensitivity, specificity) for MPV, sCRP, serum CRP and Serum CRP/ MPV to discriminate patients from control and Diagnostic Validity (AUC, sensitivity, specificity) for sCRP to predict serum CRP>6 (n=23) from serum CRP ≤6 (n=7) in patient group

	AUC	p	95% C.I		Sensitivity	Specificity	PPV	NPV
MPV	0.871	<0.001**	0.774 – 0.968	>8.8	86.67	80.0	81.2	85.7
Serum CRP	0.807	<0.001**	0.698 – 0.917	>6	76.67	60.0	65.7	72.0
SCRP	0.797	<0.001**	0.675 – 0.918	>3.5#	76.67	83.33	82.1	78.1
Serum CRP/ MPV	0.799	<0.001*	0.688 – 0.911	>0.6098	86.67	56.67	66.7	81.0
SCRP	0.894	<0.002*	0.771-1.018	>3.2#	91.30	71.43	91.3	71.4

A stastistically notable positive link between salivary and serum CRP concentrations (r = 0.476, P ≤ 0.05), and it also showed significant link between serum CRP and MPV (r = 0.547, P = 0.002). There was a statistically evident link between sCRP and MPV concentrations in the pneumonic group (r =0.507, $p \leq 0.05$) in diagnosis of late onset neonatal pneumonia.

Table 6: Relation between serum CRP and sCRP, and MPV, in LONP group / group A (n = 30)

	r_s	p
Serum CRP vs SCRP	0.585	0.001**
Serum CRP vs MPV	0.655	<0.001**
SCRP vs MPV	0.542	0.002**

Discussion

In terms of clinical presentation, dyspnea was the most significant presenting symptom 30 (100%), While fine crepitations were found in 26 (86.7%), Examining the lung revealed diminished airflow in 25 (83.3%), followed by cough 21 (70%) and fever 20 (66.7%).

Most notable were the patient's tachypnea and wheezing on presentation accounting for 30 (85.7%) and 26 (74.3%) of all cases, respectively, with fever coming in at a distant third, accounting for 23 (65.7%), in a prospective case-control research by Omran *et al*. [5] involving 35 full-term neonates diagnosed with late-onset pneumonia and 35 controls. Examination of the thorax revealed fine crepitation in 32 (91.4%), decreased air entrance in 24 (74.3%), and thoracic retractions in 25 (71.4%).

The present research showed that the mean serum CRP was found to be 42.5(±34.8) mg/L in the pneumonic group, with 76.67% sensitivity and 60% specificity at a value > 6 mg/L in detection of LONP. Another research done by Kumar *et al*. [11] a CRP value of 5 mg/dl a sensitivity of 95.2% in proven sepsis and a specificity of 85.3% was shown.

Results from our study revealed that CRP is not a reliable screening test for newborn sepsis (Sensitivity=35.525%, specificity=58.0%, PPV=85%, and NPV=11.83%), contradicting Khan's findings.

However Khan`s [12] research had certain limitations and results might have been more indicative if other screening tests were also considered as screening biomarkers for NS.

Our research looked into the possibility of using CRP in the saliva (sCRP) of infants with late-onset pneumonia as a diagnostic sign. We discovered that there was a statistically significant difference between the sick and controls in terms of sCRP levels ($p \leq 0.001$). In addition, a sCRP cutoff of 3.2 ng/L was found to be highly sensitive (76.6%) and specific (83.3%). Predicting blood CRP ≥ 6 mg/L with sCRP demonstrated 91.30% sensitivity and 71.43% specificity.

Similarly, Iyengar *et al*. [13] found that a sCRP concentration of 4.84 ng/L had 64% sensitivity and 94% specificity for predicting a serum CRP 5 mg/L, and 54% sensitivity and 95% specificity of accurately predicting a serum CRP 10 mg/L.Our results mirror those of Mathur *et al*. [15], who also discovered a modestly significant association between CRP in saliva and CRP in serum (Spearman link coefficient r = 0.582, P = 0.004). SCRP has been found to have a sensitivity of 0.75 and a specificity of 0.93 for predicting a blood measurement of 10 mg/L.

Another cross-sectional research carried out by Barekatain *et al*. [16] showed that SCRP and IL-18 levels were found to be considerably increased in septic infants compared to the healthy group (P = 0.02) which also agreed with our research.

While Tosson *et al*. [17] were investigating the role of sCRP as a diagnostic biomarker in septic infants, they found no significant difference in sCRP values between the septic and controlss (p=0.39). Salivary flow rates differ from patient to patient, so it's possible that these factors contribute to the disparity between our findings and the aforementioned research. The oral environment, such as localized inflammation in the mouth, can also affect CRP concentrations.

Mean MPV was 9.9 0.9 fL in the pneumonic group and 8.4 0.8 fL in the controls, demonstrating a statistically significant difference. At a limit of 8.8 fL, MPV exhibited excellent diagnostic precision, with a sensitivity of 86% and a specificity of 80% for identifying pneumonic neonates. Both blood and sublingual CRP were significantly correlated with MPV.

Omran *et al*. [5] discovered a substantial difference in MPV levels between infants with pneumonia and those without, and a significant association between MPV and CRP in serum and saliva, findings that we corroborated. With 80% sensitivity and specificity 9.0 fl, MPV exhibited excellent diagnostic accuracy in identifying pneumonic infants.

Pamudji *et al*. [18] also stated that Mean platelet volume with 7.44 fL had 80% sensitivity, 84.2% specificity in diagnosis of neonatal sepsis.

Our research found that CRP/MPV ratio was significantly higher in the pneumonic group compared to the controls.

Omran *et al*. [19] found statistical notable variation between infants with late-onset sepsis and controls at a threshold value of 0.90, which corroborated our findings. He also proposed that the ratio of C-reactive protein to membrane-bound pyruvate (CRP/MPV) is a straightforward and reliable measure for the identification of late-onset neonatal sepsis.

The group size is limited, for one thing, and SCRP detection may be affected by several variables, including salivary flow rate, circadian rhythm, salivary gland type, salivary stimulus, nutrition, age, gender, and sampling technique. The sensitivity and accuracy may change depending on the aforementioned variables. Our research shows that PVI are

helpful in many research designs, but their clinical use is constrained by a number of technical problems. Three aspects of the measurement process-the haematology instrument used, the anticoagulant, and the period between sampling and analysis*are of primary concern.

SCRP and MPV are suitable as diagnostic biomarkers in LONP.

Further studies are required to assess the link between sCRP and MPV and the severity of late onset neonatal pneumonia, response to treatment and disease progression for optimization of treatment. Studies on larger scales are necessary to clarify the cutoff value of sCRP and MPV for diagnosis of LONP. Other inflammatory biomarkers; salivary and serum Interleukin-10 for example should also be investigated for beneficial use as diagnostic biomarkers of LONP.

Conclusions

There were statistically significant variations between infants with late-onset pneumonia and controls in terms of both CRP and MPV levels in their saliva. Late-onset new-born pneumonia may be diagnosed non-invasively using CRP in the baby's saliva. The ratio of C-reactive protein to membrane permeability antigen (MPV) is easy to compute and has the potential to serve as a straightforward and reliable biomarker for the identification of late-onset neonatal sepsis.

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Nil

Conflict of Interest

Nil

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