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### RESEARCH ARTICLE

#### NLR AND PLR WITH PHOTOTHERAPY IN NEONATAL HYPERBILIRUBINEMIA- MAKING WAY FOR NEW DIAGNOSTIC MARKERS

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#### Abstract

**Objective:** The purpose of this study was to investigate the clinical significance of the platelet to lymphocyte ratio (PLR) and the neutrophil to lymphocyte ratio (NLR) in term neonates and its impact on management of neonatal hyperbilirubinemia on phototherapy

**Materials and Methods:** This observational study was conducted with 20 term neonates diagnosed with neonatal hyperbilirubinemia, and received phototherapy. Exclusion criteria were prematurity, post-maturity, small or large for gestational age according to week of pregnancy, babies born to mothers with GDM or pre-eclampsia and congenital defects.

**Results:** NLR and PLR as predictors of effect of phototherapy, the sensitivity of NLR was 94.44 % while specificity was 86.36%. We noted that the sensitivity of PLR was 84.21%, while specificity of PLR was 80.95%. There was a positive correlation between TC and NLR, weak positive correlation with PLR and a weak negative correlation with lymphocyte levels.

**Conclusions:** NLRs and PLRs were reduced due to phototherapy in term neonates, and these ratios can be used to aid in management in term neonates with hyperbilirubinemia on phototherapy.

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#### Introduction:-

The most prevalent cause of newborn jaundice is indirect hyperbilirubinemia. Bilirubin is one of the end products of heme breakdown. Although bilirubin has antioxidant properties and protects the lungs and intestines, it is also known to have side effects. In order to accomplish this, pathological levels of bilirubin must be reduced. Phototherapy (PT) is the most prevalent treatment for infants with indirect hyperbilirubinemia. By converting bilirubin into its constitutive and structural isomers and colourless oxidation products, PT facilitates the excretion of bilirubin in the urine and bile.

In addition to its clinically significant benefits, PT has been associated with a variety of adverse effects, including loose stools, hyperthermia, dehydration, skin burn, retinitis, low platelet count, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency, and DNA damage. A number of studies have investigated the effects of PT on eosinophils, platelets, T and B lymphocytes. 3,4

There is evidence that phototherapy can directly affect the expression and function of cell surface receptors including adhesion molecules, cytokines, and growth factor receptors. 1-5 The ratios between various white blood

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cells (WBC) are now used to determine the prognosis of various disorders and as markers of possible inflammation. The aim of this study was to determine the neutrophil/lymphocyte ratio (NLR), lymphocyte/monocyte ratio (LMR), and platelet/lymphocyte ratio (PLR) in newborns who received phototherapy for IHB; and to investigate the effect of phototherapy on inflammation and peripheral blood cells.

### Methods And Methodology:-

This is a retrospective observational study that was performed in the Department of paediatrics in a tertiary care centre. All term neonates born after 37 completed weeks of gestation via an uncomplicated and uneventful vaginal delivery were included in the study. The neonates that were diagnosed with indirect hyperbilirubinemia 48 hours of delivery were evaluated prior to initiating phototherapy.

Those neonates born before 37 or after 40 weeks gestation, with congenital anomalies to mothers with co-morbidities were excluded from the study.

Neonates were subjected to routine blood investigations such as CBC, ESR, CRP, peripheral smears and cultures before and after PT

NLR and PLR was calculated for each of the neonates and correlated with the effect of PT.

### Statistical analysis-

data was collected and recorded in an MS excel spreadsheet. Continuous variables were represented as mean and median, while categorical variables were represented as percentages and frequency. Correlation was calculated using student's t test, ANOVA test for independent means and Fisher's exact test. Sensitivity, specificity, positive and negative predictive value was calculated for NLR and PLR. P value less than 0.05 was considered to be statistically significant.

### Results:-

The study included 20 neonates born via full term vaginal delivery. The mean gestational age of the neonates was 38.9 +/- 4.3 weeks. The mean birth weight of the neonates was found to be 2802 +/- 342 gm.

Mean NLR was found to be 2.34 +/- 0.43, while mean PLR was 62.4± 14.9 in the pre-PT group 5.3 ± 1.1 vs 0.72±/0.23 in the post-PT group.

NLR	Group A	Group B
NORMAL	8	19
ELEVATED	12	2

Statistic	Value	95% CI
Sensitivity	94.44%	72.71% to 99.86%
Specificity	86.36%	65.09% to 97.09%
Positive Likelihood Ratio	6.93	2.41 to 19.94
Negative Likelihood Ratio	0.06	0.01 to 0.44
Disease prevalence (*)	45.00%	29.26% to 61.51%
Positive Predictive Value (*)	85.00%	66.31% to 94.23%
Negative Predictive Value (*)	95.00%	73.74% to 99.23%
Accuracy (*)	90.00%	76.34% to 97.21%

The sensitivity of NLR was 94.44 % while specificity was 86.36%. there was a negative correlation between NLR and TC in neonates with hyperbilirubinemiarecieving PT

PLR	PRE-PT	POST-PT
NORMAL	18	5
REDUCED	2	15

Statistic	Value	95% CI
Sensitivity	84.21%	60.42% to 96.62%
Specificity	80.95%	58.09% to 94.55%
Positive Likelihood Ratio	4.42	1.79 to 10.91
Negative Likelihood Ratio	0.2	0.07 to 0.56
Disease prevalence (*)	47.50%	31.51% to 63.87%
Positive Predictive Value (*)	80.00%	61.85% to 90.80%
Negative Predictive Value (*)	85.00%	66.28% to 94.23%
Accuracy (*)	82.50%	67.22% to 92.66%

We noted that the sensitivity of PLR was 84.21%, while specificity of PLR was 80.95%. this is not as sensitive a marker as NLR for effect of PT in neonatal hyperbilirubinemia, but it still has a weak positive correlation with TC.

### Discussion:-

By stimulating the cytokine response, phototherapy may have an effect on peripheral blood cell regulation. Given the physiological changes in the peripheral blood count that occur in the first few days of a newborn's life, it can be challenging to determine the magnitude of this phototherapy effect. Consequently, further research is necessary.

The stimulation of apoptosis and necrosis in mature immune cells resulted in an inhibitory effect of IHB on B lymphocytes in rats, according to a study.

5 When high levels of IHB were administered in vivo (>25 kg/kbw), splenic atrophy, suppression of the bone marrow, leukopenia, lymphocytopenia, and a mitogenic response of T and B cells were observed. In vivo examination of mouse splenocytes revealed that IHB induced oxidative stress and cell death. IHB stimulates apoptosis and necrosis of immune cells by lowering its glutathione content, was the conclusion of the researchers. 5 Diverse studies have evaluated the effects of phototherapy on the antioxidant/oxidant balance and reported that phototherapy may stimulate oxidative stress and have detrimental effects on the antioxidant/oxidant system. 5 It has also been reported that mild bilirubin elevation is associated with a reduction in cardiovascular disease, diabetes, and cancer risk factors. IHB has an inhibiting effect on the classical complement pathway and leukocyte migration at concentrations of 5.6%. 5,6 The effect of phototherapy on the immune system may be in part attributable to bilirubin degradation. 5,6 By affecting both cytokine and bilirubin levels, this may suggest a relationship between high total bilirubin levels and peripheral blood cells. The decrease in bilirubin levels caused by phototherapy may also have an effect on the cellular level by shifting the oxidant-antioxidant balance in favour of oxidative damage. This study demonstrates that after phototherapy, patients' peripheral blood counts were comparable to those of newborns. This may suggest that the effect of phototherapy on peripheral blood counts is mediated by cytokines and/or by lowering the total bilirubin level, thereby affecting the oxidant-antioxidant balance. It is also possible that elevated levels of bilirubin have an effect on the peripheral blood count, necessitating additional research on this topic.

### Conclusion:-

NLR and PLR can be used as diagnostic and prognostic markers in term neonates with hyperbilirubinemia receiving PT.

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