RESEARCH ARTICLE

Hematological Markers: Testing a New Diagnostic Modality for Intrahepatic Cholestasis of Pregnancy

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ABSTRACT

Background: Intrahepatic Cholestasis of pregnancy (ICP) is the most common pregnancy specific liver disorder presenting usually in the 3rd trimester with unexplained pruritis, elevated serum bile acids and/or raised liver enzymes. ICP is associated with adverse perinatal outcomes. Serum total bile acids (TBA) are considered as a gold standard for diagnosis of ICP but are time consuming, expensive and not readily available everywhere. Neutrophil to Lymphocyte ratio (NLR), Mean Platelet Volume (MPV) and Red cell Distribution Width (RDW) are haematological inflammatory biomarkers and are routinely available on a simple complete blood count test when asked for.

Aims: To study the role of haematological inflammatory markers in Intrahepatic Cholestasis of Pregnancy (ICP) and their association with the severity of the disease.

Methods: This prospective case-control study was done in a tertiary care setting in New Delhi, from January 2021- August 2022(20 months) wherein 82 women with ICP were recruited after a written and informed consent. NLR, MPV, RDW and TBA levels were done. 82 healthy women with uncomplicated pregnancies served as the control group.

Results: Both cases & controls were comparable in terms of sociodemographic characteristics. Mean TBA levels were 22.85+/-7.82 in mild cases (60 subjects) & 66.20+/-26.97 (22 severe cases). Cases delivered earlier between 37–38 weeks. Majority of women delivered vaginally & was statistically significant. Cases developed more fetal distress (42.7% vs 9.8%). NLR and MPV were significantly raised ($p<0.05$) while RDW was lower in cases. The cut off for NLR & MPV were statistically significant.

Conclusion: Mean Platelet Volume can serve as a good screening tool with a high sensitivity (95.1%) while NLR can serve as a confirmatory test as it has high specificity (96.3%) to make diagnosis of ICP, although further exploration with larger multicentric studies is required.

Keywords: Hematological inflammatory biomarkers, Intrahepatic Cholestasis of Pregnancy, NLR (Neutrophil to lymphocyte ratio), MPV (Mean platelet volume), RDW (Red cell distribution width) and TBA (serum total bile acids)

Introduction:

Intrahepatic Cholestasis of pregnancy (ICP) is the most common pregnancy specific liver disorder presenting usually in the 3rd trimester with unexplained pruritis, elevated serum bile acids and/or raised liver enzymes. ICP is associated with adverse perinatal outcomes like preterm birth, meconium-stained liquor, fetal distress and stillbirth. Traditionally, ICP has been diagnosed on the basis of itching along with raised liver function tests. Recent evidence[1,2,3,4] suggests that liver function tests cannot predict risk of fetal demise and that only maternal total bile acid concentrations results are associated with the risk of stillbirth. Serum total bile acids (TBA) are considered a gold standard for diagnosis but are time consuming, expensive and not readily available everywhere.[1] Neutrophil to Lymphocyte ratio (NLR), Mean Platelet Volume (MPV) and Red cell Distribution Width (RDW) are haematological inflammatory markers and are routinely available on a simple complete blood count test when asked for. It is thought that ICP is a state of low-grade inflammation. Recent studies[5,6,7] indicate an association between haematological parameters and diseases with low grade chronic inflammation like pre-eclampsia, cardiovascular diseases and some malignancies but the role of haematological parameters in women having ICP still requires further exploration. With this intent, we planned to study the role of these markers in ICP, their association with the severity of disease in an effort to find an inexpensive and easy way to diagnose and prognosticate women with ICP.

Material and Methods:

This prospective case-control study was done in a tertiary care setting in New Delhi, India over a period of twenty months (January 2021- August 2022) wherein 82 women with ICP were recruited after a written and informed consent. A prior approval was obtained from Institutional Ethics Committee for Human Research [IECHR/2020/47/48].

Cases were defined as women with singleton pregnancy in their third trimester with unexplained pruritis, without skin rash and raised TBA levels ≥10µmol/L. The control group consisted of 82 healthy, age matched women with uncomplicated singleton pregnancies in the third trimester. (Fig 1)

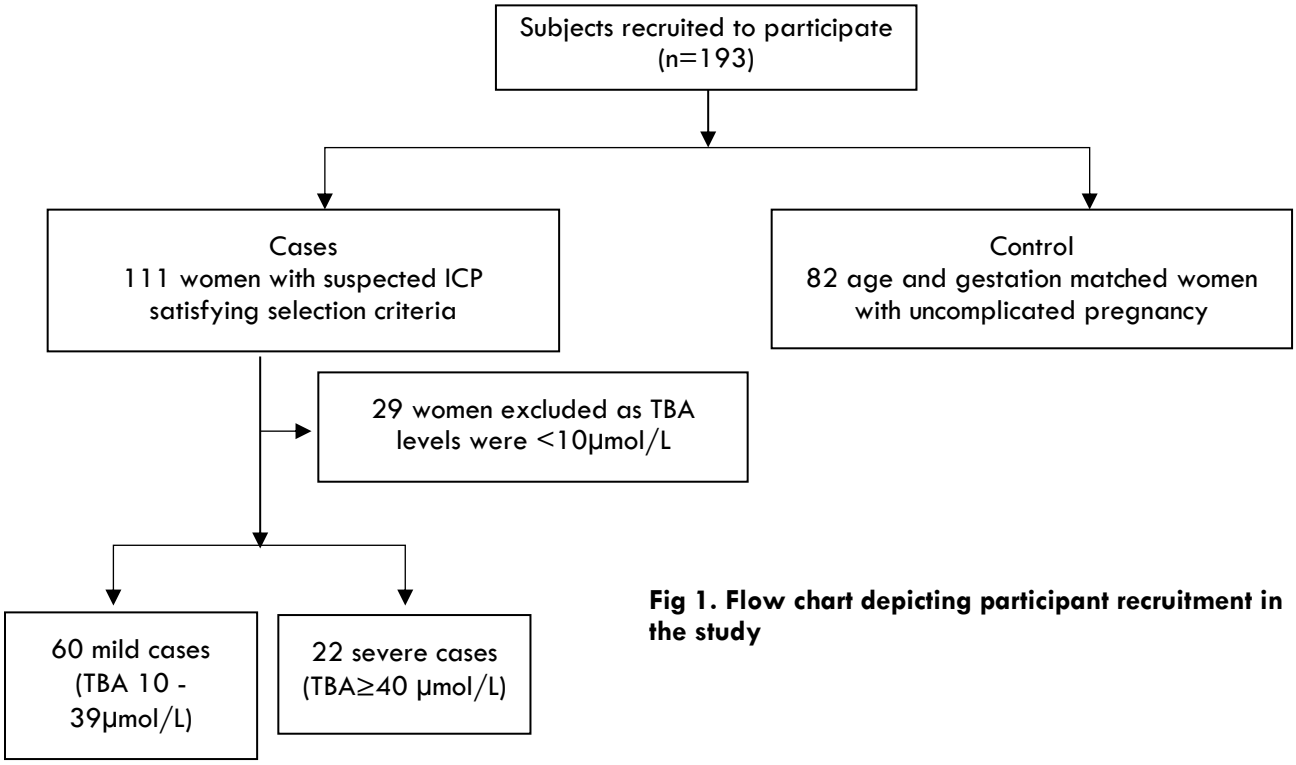


Fig 1. Flow chart depicting participant recruitment in the study

Women with any condition that could alter the values of NLR, MPV or RDW such as obstetric complications like pre-eclampsia, gestational diabetes mellitus, anaemia or any chronic illness like diabetes, hypertension, thyroid dysfunction, renal or hepatobiliary disease were excluded from the study.

After a detailed clinical history and examination and before starting any medical management, 2 ml venous blood was collected in a plain vial early in the morning, following ten hours of fasting. TBA

levels were determined by spectrophotometry as per manufacture's protocol. 2 ml of blood was collected in an EDTA vial and sent to haematology laboratory for evaluation of NLR, MPV and RDW values. On the basis of fasting TBA levels, ICP cases were defined as pruritis without rashe and TBA≥10µmol/L; mild ICP as TBA between 10-39µmol/L and Severe as TBA ≥40 µmol/L. Both cases and controls were followed till delivery as per the hospital protocol. Maternal and neonatal outcomes were recorded in the case record form.

The **statistical analysis** was done using version 20.0 SPSS. Continuous variables were reported as the mean with standard deviation (SD) or median (inter-quartile) range depending upon the normality of distribution. Kolmogorov-Smimov test of Normality was used to determine whether the sample data for NLR, MPV and RDW was drawn from a normally distributed population. Unpaired t-test or Mann Whitney U test were done to compare the continuous variables between the two groups. The Chi-square test was used for categorical variables. To assess the correlation of the bio-markers within the group, Pearson correlation was used. Receiver Operating Characteristic (ROC) Curve was applied to find the optimal cut-off of biomarkers to discriminate between cases and controls. To assess the independent risk factors associated with the cases, binary multivariable logistic regression was applied. The p-value of <0.05 was considered significant.

Results

A total of 82 cases and 82 controls were finally analyzed. Both the groups were comparable in terms of age, religion, education, employment and parity although primigravida women were predominant in both the study groups. 22.44% multiparous women with ICP had a history of ICP in their previous pregnancies. Of these 8 were in the mild group and 3 in the severe group which was statistically significant. Women with ICP delivered at an earlier mean gestational age of 37 week and 4 days compared to controls who delivered at a mean age of 38 weeks and 3 days and this was statistically significant(p=0.002). (Table 1)

Table 1. Socio-demographic and obstetrical profile amongst controls and cases

Parameters	**Control(n=82) n (%)**	**Cases(n=82) n(%)**	**P value**
1.Age (Mean±SD)	24.81±2.87	25.7±3.48	0.063*
2.Religion			
Hindu	59(72.0)	46(56.1)	0.074[a]
Muslim	23(28.0)	36(43.9)	
3.Education			
Uneducated	4(4.9)	11(13.4)	0.061[a]
Primary and secondary	28(34.1)	40(48.8)	
Senior secondary	29(35.4)	22(26.8)	
Graduate and above	21(25.6)	9(11)	
4.Employment status			
Unemployed	78(95.1)	80(97.6)	0.405[a]
Employed	4(4.9)	2(2.4)	
5.Gravida			
1	40(48.8%)	33(40.2%)	0.679[a]
2 or more	42(51.2%)	49(59.7%)	
GA at delivery (Mean±SD)	38.3±1.4	37.4±2.3	0.002*

*** Unpaired Student t-test; [a] Chi-square test**

Only 3(3.6%) out of 82 cases gave a positive history of ICP in the first-degree relatives.

Mean TBA levels in the mild and severe ICP group were 22.85 and 66.20 µmol/L respectively. TBA levels were significantly raised in the severe category and the difference between mild and severe category was statistically significant (p-value < 0.001).

Table 2. Labour correlates amongst controls and cases

	Control(n=82) n(%)	Cases(n=82) n(%)	p value (Chi-square test)
1. Mode of labour onset			
Spontaneous	59(72)	43(52.4)	0.010
Induction	23(28)	39(47.6)	
2. Mode of delivery			
Vaginal	75(91.5)	58(70.7)	0.001
Caesarean	7(8.5)	24(29.3)	

More cases than controls underwent induction of labour (IOL) and this difference was statistically significant (p=0.01). Amongst mild vs severe cases, 25 vs 14 underwent IOL respectively (p=0.078).
Majority of women had a vaginal delivery in the study population (91.5% in controls & 70.7% in cases). A greater number of Caesarean sections were performed in emergency in women with ICP (n=25). (Table 2)
The number of vaginal deliveries were more compared to caesarean sections (13 vs 11) in the mild group and was statistically significant when compared against the severe group (47 vs 11, p=0.012).

Table 3. Foetal outcomes in cases and controls

	Control n(%)	Cases n(%)	p value
1.Fetal distress	8(9.8)	35(42.7)	<0.001 [a]
2.MSL	9(11)	18(22)	0.058 [a]
3.Birth wt. in kg (Mean ± SD)	2.79±0.34	2.72±0.61	0.346*
4.NICU admission	0	5(6.09)	<0.001[a]
5.IUD	0	2(2.4)	0.155[a]
6. Stillbirth	0	2(2.4)	0.155 [a]

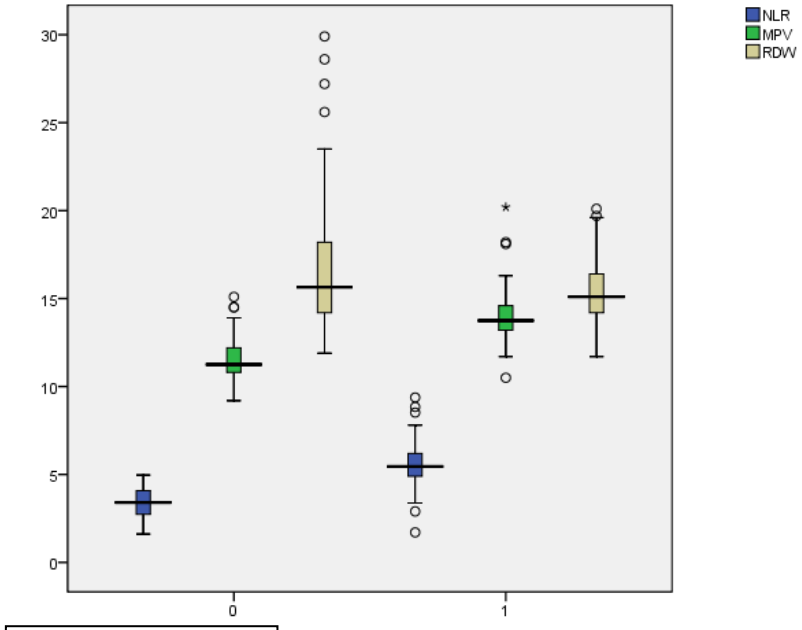
*** Unpaired Student t-test; [a] Chi-square test**

The mean birth weights amongst cases and controls were comparable (2.79±0.0.34 kg and 2.72±0.61 kg respectively).
Foetal distress was observed more amongst ICP group (42.7 %) than controls (9.8 %) and was statistically significant with a p-value of less than 0.001.The cause of fetal distress could not be found out in a majority of cases, though meconium stained liquor (n=18), one or more loops of cord around neck (n=4) and one each as asymmetric IUGR with AEDF, chorioamnionitis, obstructed labour, bleeding placenta previa and cord prolapse were noted.
6% neonates amongst cases needed NICU admission due to various reasons while no admissions were required in the control group, the difference being statistically significant (p-value <0.001).
Two of the foetuses died in-utero and two stillbirths were observed amongst cases while no such incidents were reported in the control group (p=0.155 each). (Table 3)
In the mild vs severe sub-category similar adverse fetal outcomes were noted.
Kolmogorov-Smimov test of Normality (Table 4) was used to determine whether the sample data for NLR, MPV and RDW was drawn from a normally distributed population and was found to be skewed in all the groups (Fig. 2). Therefore, median values with interquartile ranges (IQR) were calculated and NLR and MPV difference was statistically significant. (Table 5)

Table 4. Kolmogorov -Smimov test of Normality

	Kolmogorov -Smimov test of Normality			
Marker	**Group**	**Statistic**	**df.**	**Sig.**
NLR	Control	0.075	82	0.200
	Case	0.113	82	0.011
MPV	Control	0.131	82	0.001
	Case	0.105	82	0.027
RDW	Control	0.176	82	<0.01
	Case	0.138	82	0.001

Fig 2: Skewed pattern of data distribution in population for all biomarkers:



Group 0- controls
Group 1 - cases

Table 5: Median values of biomarkers with interquartile ranges (IQR):

	Control Median(IQR)	Cases Median(IQR)	p-value Chi-square test
NLR	3.40(1.3)	5.45(1.3)	<0.01[a]
MPV	11.46(1.4)	13.91(1.5)	<0.01[a]
RDW	15.65(4.0)	15.1(2.2)	0.064[a]

ROC Curves (Receiver Operating Charateristic curves) were applied to biomarkers in both groups to find out the optimal cut off of biomarkers to discriminate between cases and controls. (Fig. 3a, 3b and 3c)

Fig 3a: ROC curve for NLR

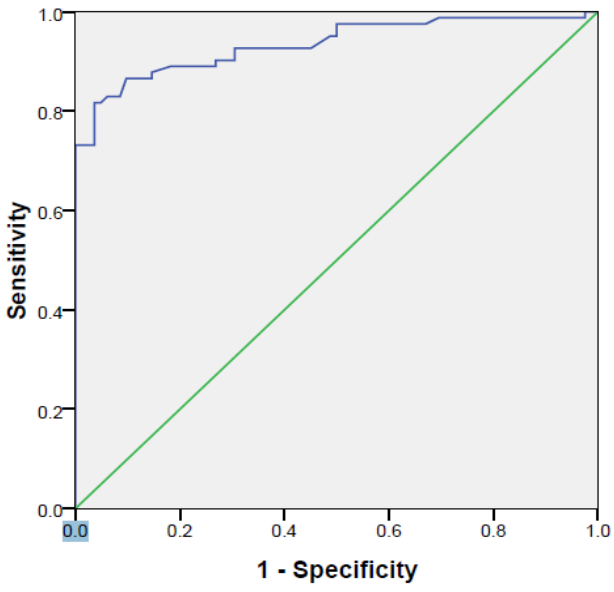


Fig 3b: ROC curve for MPV

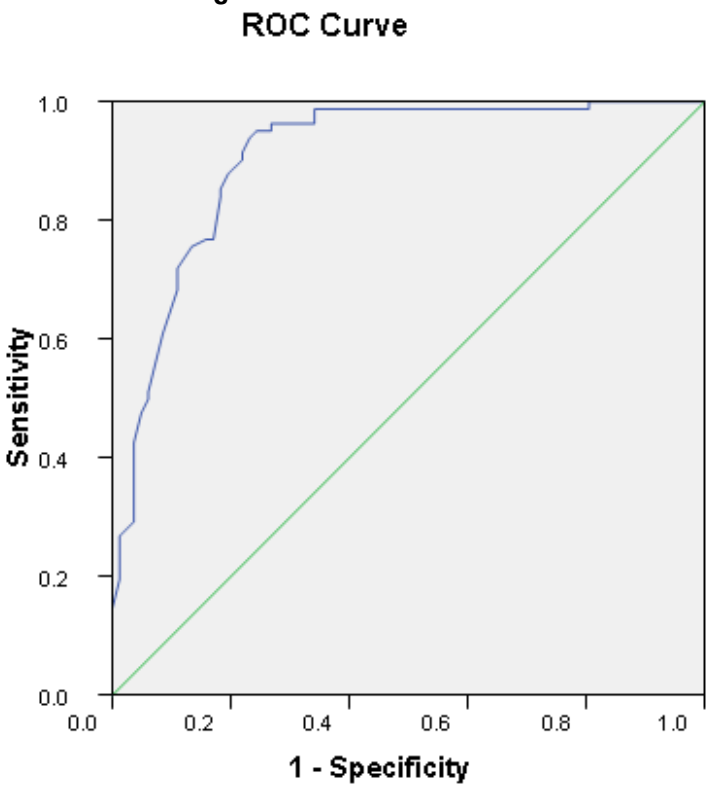


Fig 3c: ROC curve for RDW

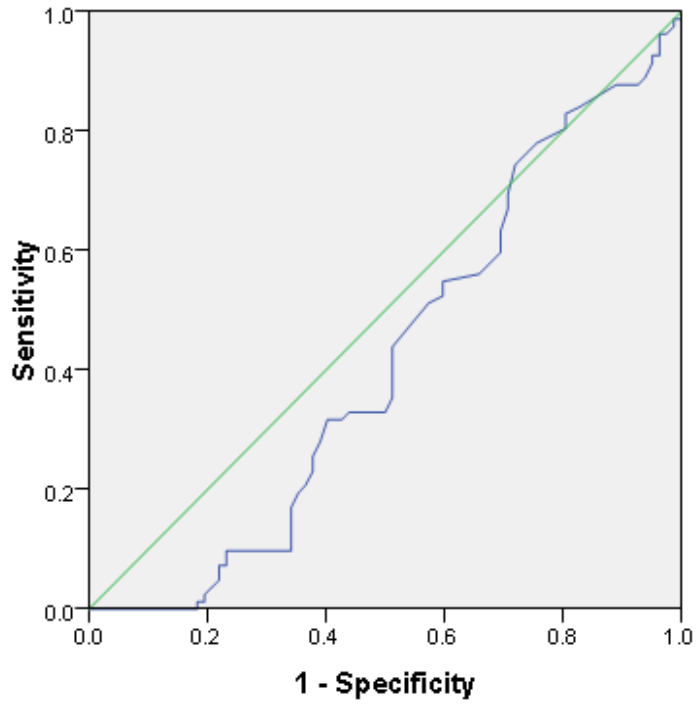


Table 6: Agreement (sensitivity, specificity and accuracy) for markers to diagnose ICP:

	Youden index	Cut-off	AUC	p-value	Sensitivity	Specificity	PPV	NPV
NLR	0.780	4.82	0.934[0.895-0.974]	<0.001	81.7	96.3	95.7	84.0
MPV	0.707	12.25	0.907[0.861-0.954]	<0.001	95.1	75.7	79.6	93.9
RDW*			0.416[0.328-0.504]	0.065				

*** the cut-off value is not valid because RDW is not statistically significant.**

Table 6 shows that the cut off obtained for NLR was 4.82 with high specificity and positive predictive value and for MPV, the cut off was 12.25 with a high sensitivity and negative predictive value and both were statistically significant. (Table 6)

No cut off value for RDW could be obtained as p-value was not statistically significant.

Table 7. Correlation between NLR, MPV, RDW and TBA levels among cases

	Rho value	p-value (Pearson coefficient)
TBA vs NLR	0.164	0.141
TBA vs MPV	0.202	0.069
TBA vs RDW	-0.060	0.594
NLR vs MPV	0.018	0.875
NLR vs RDW	-0.108	0.335
MPV vs RDW	-0.177	0.112

To assess the correlation between NLR, MPV, RDW and TBA levels amongst ICP cases, Pearson's correlation was used which found no correlation for the same. (Table 7)

Similarly, no optimal cut-offs could be obtained for any of the biomarkers to differentiate between the mild and severe subcategory.

DISCUSSION

ICP is the most common pregnancy specific liver disorder, affecting 1.2 to 1.5% of Indian -Asian pregnancies.[1] Most commonly a diagnosis of exclusion, it occurs in 3rd trimester of pregnancy and is associated with adverse foetal outcomes. Serum bile acid levels are the most specific and sensitive marker for the diagnosis of ICP but are expensive, take 36 hours to 10 days for reporting and are not universally available.[1,2,3,4]

In the current study, mean maternal age was comparable amongst cases and controls (25.7±3.48 vs 24.8±2.8, p-0.063). Studies[5-10,] in literature reveal that both groups had a slightly higher maternal age of ≥ 26 years but less than 35 years.

Gravidity was comparable amongst cases and controls and also in the mild vs severe subcategories in congruence with those reported by Oztas,[6] Kirbas,[7]Yilmaz,[8] and Yayla[9] though Kebapcilar et al[5] reported majority of the subjects as primigravida.

As per standard guidelines[1,11,12], the termination of pregnancy in ICP should be done after 37 completed weeks to minimize the risk of intrauterine deaths and stillbirths. In our study, women with ICP delivered at an earlier mean gestational age than controls (37 weeks+4 days vs 38weeks+3 days, p-0.002). Similar observations between both the groups were reported in the studies done by Kirbas et al,[7] Yilmaz et al[8] and Yayla et al.[9]

Amongst the mild vs severe cases, gestational age at delivery was comparable (37weeks+6 days vs 38 weeks +0 days respectively) in the present study, however Kirbas et al[7] noted that mean GA at delivery was lower in severe vs mild cases (35week+6days vs 37week+2days, p-<0.001), similar to Yayla et al[9] (35week+3day vs 36week+6days, p<0.05)

Literature[1,13] suggests a high recurrence rate (45 to 90%) of the disease and 11 to 16 times increased risk of the disease in the family. In the present study, 11 out of 49 (22.44%) multiparous women with ICP had a history of cholestasis in the earlier pregnancy , out of which 8 were in the mild while 3 belonged to the severe group. Positive family history of ICP was noted in only 3 cases. Brouwers et al[14] observed that 14.9% patients had a positive history of ICP during previous deliveries. Likewise, Pata et al[15] found 2 out of 12 multiparous women had previous history of ICP and seven out of total 32 cases had a positive family history. Kebapcilar et al[5] observed that 69% gave a positive past history of ICP. Yayla et al[9] reported 4 (7.5%) women with prior ICP history in the mild group vs 2 (6.4%) in the severe group.

Normally maternal serum bile acid levels remain below 10µmol/L throughout the pregnancy in a healthy subject whereas to diagnose ICP, the levels should be more than 10µmol/L. Furthermore, ICP cases were divided as mild (TBA levels 10 -39 µmol/L) and severe group (TBA ≥40 µmol/L). In the present study, Mean TBA levels in the mild and severe ICP groups were 22.85±7.82 and 66.20±26.97 µmol/L respectively. Similar observations were reported in a number of studies[7,9,16] with TBA in mild vs severe cases (18±5.9 vs 57.3±28.6, 21.3±8.7 vs 69.5±57.07 and 21.5±12.7 vs 68.9±62) respectively.

Induction of labour in the control group was mostly done for post-dated pregnancy and premature rupture of membrane, whereas in the ICP group at 37-38 weeks to avoid unfortunate consequences of the disease like stillbirth and intrauterine fetal death as planned induction is advisable in ICP women. 47.6% of cases and 28% of controls were subjected to induction of labour for the reasons mentioned above (p-value 0.010). Similarly, Glantz et al[17] noted that planned deliveries were done in 21% controls, 24% mild and 32% severe category patients of ICP. Brouwers et al[14] also observed planned delivery being conducted in 74.07% mild, 88.37% moderate and 80.95% severe group of ICP women. Similarly, strong association was established between ICP and induction of labour (aOR 11.76, 95% CI 11.04–12.52) in the evaluation done by Shemer et al.[18] Out of the 82 subjects in each group, 43 cases and 57 controls went into spontaneous labour.

In the current study, majority of women had a vaginal delivery both amongst cases and controls. The indications for emergency caesarean deliveries in cases were fetal distress, thick meconium stained liquor with fetal distress and failed induction whereas in controls, it was fetal distress and non-progression of labour. The number of vaginal deliveries were more in the mild group in comparison to the severe ICP group. A study by Yayla et al[9] reported more caesareans (83.6%) in severe than the mild category (54.7%) though different from Brouwers et al[14] where more emergency caesarean sections were done in mild (13%) and moderate (16.3%) subgroups as compared to the severe (4.8%). Shemer et al[18] also noted that women with ICP had a higher risk of undergoing an emergency caesarean section (aOR 1.26, 95% CI 1.13-1.33).

In the present study, foetal distress was observed more amongst ICP cases and severe subcategory. Although no cause was found in a majority, still meconium stained liquor (MSL), loop of cord around the foetal neck, Absent End Diastolic Flow (AEDF), chorioamnionitis, obstructed labour, active bleeding in placenta previa, cord prolapse were some of the causes.

Meconium staining of liquor (MSL) is hypothesised to be caused by bile acid induced stimulation of colonic peristalsis in the foetus[13]. Bile acids are thought to be cardiotoxic in the foetus[13]. Chen et al[19] observed the frequency of foetal distress to be more in severe ICP cases (24.2%) compared to the mild group (3.6%) (p= 0.003) similar to our observation. Yayla et al[9] observed higher incidence of fetal distress (12.9% vs 3.7 %) and MSL (9.6% vs 3.8%) in severe cases when compared to mild. Shemer et al[18] noted the risk of MSL (aOR 1.41, 95% CI 0.72–2.72) was not increased significantly in ICP patients. Yilmaz et al[8] reported similar rates of MSL in controls vs cases (11.1% vs 13.3%).

Mean birth weight in the present study in cases was comparable to controls and also in the mild and severe sub groups. Similar observations were reported by Ling Du et al[16] (3350±139 vs 3180±128 grams) and Brouwers et al[14] disease (3290 vs 3180 grams respectively). Oztas et al[6] reported no significant difference in mean birth weight of controls (3210 grams) and cases (3050 grams) while Yilmaz et al[8] found a significant difference in birth weight (3.165 kgs in controls vs 2.845 kgs in cases, p-0.0005). The birth weight trajectory followed a downward trend with increasing bile acids in the studies reported in literature in congruence with the present study.

6% neonates amongst cases needed NICU admission due to reasons like low birth weight, neonatal jaundice, meconium aspiration syndrome, respiratory distress syndrome and neonatal sepsis while no admissions were required in the control group (p<0.001). 13.6% of neonates in severe group vs 3.4% in mild group needed NICU care. Similar to our observation Brouwers et al[14] noted that the admission to neonatal care unit was more in severe cholestatic group followed by moderate and mild group (9.5%, 2.3% and 0.9% respectively, p-value 0.062). Oztas et al[6] reported 18.8% NICU admissions in cases vs 3% in controls (p<0.001) in accordance to the present study. Observations in the studies by Yilmaz et al[8] and Yayla et al[9]
are also corroborated by this study.

Two in utero foetal deaths and two stillbirths were recorded in cases though none in the control group, with one each in the mild and severe group. MSL with two loops of cord around neck was found in one of the IUFD while sudden massive abruption was the cause in the second. Amongst stillbirths, MSL was seen in one while no apparent cause was found in the other. Shemer et al[18] did not find an increased risk of perinatal death in ICP cases

(aOR 0.45, 95% CI 0.15–1.40). Similar to current study, Brouwers et al[14] observed two foetal deaths of a total of 215 ICP cases. Yayla et al[9] reported mortality in one of the severe ICP cases although the cause of death was not mentioned.

The inflammatory markers NLR and MPV were significantly raised in women with ICP as compared to their healthy counterparts, although no relationship could be elicited between these markers and severity of ICP in our observation.

The literature review suggests[10,12] that larger platelets can play an active role in hemostasis as they contain more granules and adhesion receptors. High levels of MPV gives greater prothrombotic potential, thus platelets aggregate swiftly with collagen, having raised levels of intracellular thromboxane A2 and procoagulant surface protein like P-selectin and GpIIb/IIIa. Cytokines then activate MPV and endothelial cells, promoting platelet aggregation and thrombus formation and thus increase inflammation.

In the present study, the cut off value obtained for NLR was 4.82 (sensitivity- 81.7%, specificity- 96.3%, PPV- 95.7% and NPV- 84%) and for MPV was 12.25 (sensitivity- 95.1%, specificity- 75.7%, PPV- 79.6% and NPV- 93.9%) and was statistically significant. As RDW was statistically insignificant, its cut off value was invalid and therefore not calculated.

There was no correlation amongst TBA, NLR, MPV and RDW values in our study.

A study by Kebapcilar[5] in 2010 observed a significant difference in the MPV values between women with ICP vs healthy controls (mean MPV- 10.9 vs 8 f/l, p-<0.001) and a positive correlation between MPV and TBA values(r=0.418, p<0.001). MPV is an indicator of platelet activation.

Oztas et al[6] studied 117 ICP subjects and 100 healthy pregnant women to evaluate the role of routine laboratory parameters in prediction of adverse pregnancy outcomes in ICP. The median value of NLR and the mean value of MPV in the case group was significantly higher as compared to the control group (NLR-4.2 vs 3.4, p=0.004, MPV- 11 vs 10.2, p<0.001). The RDW values were found to be decreased in cases than controls and the difference was insignificant (14% vs 14.1%, p=0.054). The cut off of MPV to predict adverse fetal outcomes was 11.2 fl with a sensitivity of 58% and specificity of 76% (p=0.018). These findings were in congruence with the present study.

Kirbas et al[7] enrolled 70 healthy controls, 33 mild and 32 severe ICP cases. The mean NLR values amongst these three groups were 2.32, 3.97, 5.59 respectively which significantly increased with increasing severity of ICP (p< 0.001). The cut off of NLR to diagnose ICP was 2.93 (sensitivity- 91%, specificity- 84%, PPV-83%, NPV-91%) and to predict the severity of the same was 4.05 (sensitivity- 78%, specificity- 67%, PPV-69%, NPV-76%). They also evaluated the relationship between NLR and fasting TBA values and in conflict with the present study found a significant positive correlation amongst them with a regression coefficient of 0.034 and a p-value of <0.001.

Yilmaz et al[8] found that RDW was significantly higher in control vs ICP (14.2 vs 15.2, p<0.0003) and in mild vs severe group (14.9 vs 15.2, p= 0.006) in contrast to our study.

Yayla et al[9] observed that NLR had no role in diagnosis of ICP with a mean NLR of 4 and 4.1 in controls and cases respectively (p=0.77). RDW significantly decreased in ICP group vs controls (mean RDW of 15.1 vs 17.1 respectively, p<0.001) while MPV significantly increased (mean MPV- 9.2 vs 8.2 respectively, p=0.004) and that RDW and MPV could predict the severity of ICP as RDW significantly decreased while MPV significantly increased with increasing severity of the disease (Mean RDW – 17.1, 15.5, 14.3 and Mean MPV- 8.2, 8.7 10.1 in controls, mild and severe group respectively with p< 0.001 for both), similar to our study.

Silva et al[10] observed that NLR was significantly lower in ICP cases than controls (mean NLR 3.2 vs 4.2 respectively, p<0.01) while MPV was significantly higher (mean MPV – 9.8 vs 9.1 respectively, p<0.01). RDW values were comparable between the two groups. Neither of the above three could be used to predict the severity of the disease as their values were comparable between the mild and severe groups.

Strengths:

To the best of our knowledge, this is the first Indian study to evaluate the role of haematological inflammatory markers in ICP. It is a matched prospective case-control study with a good sample size. Diagnostic accuracy of haematological markers in ICP was evaluated and was found comparable to those reviewed in literature. Both nulliparous and multiparous women were included making the results more generalised. Result of this study might be of great help in low resource settings for diagnosis of ICP.

Limitations:

The results of this study were limited to one hospital which may not be generalised for all settings. The results cannot be applied to larger populations at present but multicentric studies with

a larger subset of population may help extrapolate the results to resource limited areas.

Conclusion

Our results conclude that MPV can serve as a good screening tool due to its high sensitivity while NLR can be used as a confirmatory test because of its high specificity to make a diagnosis of ICP. We recommend that instead of cumbersome and expensive methods, simple and cost- effective components of hemogram may be used as a diagnostic modality and may predict possible adverse pregnancy outcomes, though future studies with a large sample size should be done to corroborate the same. These readily available markers may have a great potential for early diagnosis and in turn facilitate better management of ICP, especially in low resource settings.

Conflicts of Interest Statement

The authors declare no conflict of interest related to this manuscript.

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None

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