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Color Doppler Evaluation of Cerebral & Umbilical Pulsatility Ratio and its Usefulness in the Diagnosis of Fetal Growth Restriction

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Abstract: ***Introduction:*** *Fetal growth restriction (FGR) refers to the failure of a foetus to attain its genetically determined growth potential and affects 5–10% of pregnancies. Doppler ultrasound techniques are extensively used today to assess placental - umbilical and foetal cerebral blood flow abnormalities. The study aimed to examine the colour Doppler evaluation of cerebral & umbilical pulsatility ratio and its utility in the diagnosis of foetal growth restriction.* ***Methodology:*** *This prospective observational study included 69 clinically diagnosed cases of FGR of 31 - 41 weeks gestation. Two groups were formed based onabnormal perinatal outcomes (APO). The UMB PI, the MCA PI, and the C/U ratio were calculated.* ***Results:*** *The mean MCA PI ratio was 1.46±0.39 in the group without APO and 1.21±0.37 in the group with APO [p=0.0145]. At the same time, the UMB PI was comparable among both groups. The mean PI ratio in the group without APO was 1.44±0.53, and in the group with APO was 1.32±0.65. Most of them had a PI ratio >1 in both groups. A negative correlation was noted in MCA PI, UMB PI and PI ratio, where only MCA PI was significant. At a cut - off of 1.09, the MCA PI ratio showed a sensitivity of 75.00% and a specificity of 79.17%. Further, at a cut - off of 0.79, the UMB PI ratio showed a sensitivity of 78.38% and a specificity of 86.96%.* ***Conclusion:*** *Among different markers examined in the study, UM PI had high efficacy in both the early and the latter part of the third trimester.*

Keywords: Intrauterine growth retardation, middle cerebral artery pulsatility index, middle cerebral artery to umbilical artery pulsatility index ratio, pulsatility index, umbilical artery pulsatility index.

1. Introduction

Fetal growth restriction (FGR) is the failure of a foetus to reach its genetically determined growth potential and affects 5–10% of pregnancies. An increase in perinatal mortality and morbidity is connected with foetal growth limitation. This is due to the prevalence of intrauterine foetal death, intrapartum foetal morbidity, and surgical births. Iatrogenic prematurity is relevant in cases of preterm FGR, which occur before 34 weeks of gestation. Neonatal patients with FGR experience respiratory complications, polycythemia, hypoglycemia, intraventricular haemorrhage, and hypothermia. [1–3] Cerebral palsy can lead to developmental delay and behavioural disorders over time. A growing body of research indicates a relationship between FGR and adult metabolic syndrome. [4, 5] Barker et al. discovered in a longitudinal study of 13, 517 men and women born between 1924 and 1944 in Helsinki University Hospital that a combination of small size at birth and accelerated weight gain during childhood appeared to be responsible for an increased risk of coronary heart disease, type 2 diabetes, and hypertension. It has been hypothesised that FGR may guide a prenatal compensatory mechanism that modifies adult vulnerability to disease. [4, 5]Intrauterine growth restriction, also referred to as foetal growth restriction, is defined as foetuses with estimated foetal weight (EFW) that is less than the 10th percentile for gestational age on sonography diagnosis; however, various definitions exist globally and include EFW cutoff values below the 3rd, 5th, and 15th percentiles. When the foetal biometry and foetal weight are below the average for the gestational age, the foetus is referred to as "small for gestational age. "There is a diverse collection of foetuses that are small for their gestational age. [6, 7]Recent research by Marconi et al. analysed the prognosis of FGR newborns with an aberrant pulsatility index of the umbilical artery based on birth weight/gestational age criteria and intrauterine growth charts. [8] Commonly investigated parameters include the Umbilical artery, the middle cerebral arteries, and the uterine arteries. Peak systolic velocity, end - diastolic velocity, the resistive index, the pulsatility index, and the ratios of the resistive and pulsatility indices of the middle cerebral artery and umbilical artery are examined. In FGR, the umbilical blood flow is dramatically reduced, primarily due to alterations in placental vascular resistance. Numerous studies showed the importance of Doppler indices in predicting the negative fate of FGR foetuses and in distinguishing FGR from SGA foetuses. [9] In conjunction with biometry, Doppler sonography of the UA and MCA is an essential tool for identifying FGR foetuses at risk for a bad outcome. This study aimed to examine the colour Doppler ratio of cerebral and umbilical pulsatility and its diagnostic utility for foetal growth restriction.

2. Material and Methods

This prospective observational study was conducted in the Department of Radiodiagnosis, Al - Ameen Medical College, Vijayapura. After obtaining ethical clearance and informed consent, 69 clinically diagnosed case of IUGR (based on a decrease or no increase in abdominal girth / fundal height and Insufficient weight gain), LMP (Last menstrual period) of the patient is well known, Gestational age of the patient is between 31 and 41 weeks, Singleton pregnancy, live fetus with no sign of chromosomal abnormality and clinical diagnosis of placental insufficiency

were included and the study was performed from November 2020 to October 2022. Cases in which a congenital anomaly is detected in the newborn, fetal anaemia and cases in whichfetal Doppler examination was not possible up to 7 days before birth were excluded from the study. All the cases were divided into two groups; With APO (n=32) and Without APO (n=27). A pre - structured proformawas used for the collection of clinical data. A high - resolution Duplex Doppler sonography was done using GE LOGIQ P9 and SIEMENS ACUSON X300 ultrasound machines with a 5 - 13MHz linear transducer. All the data were recorded and compared.

Statistical Analysis:
Data were entered in Microsoft Excel and analyzed using statistical software SPSS version 26 (SPSS Inc., Chicago, IL, USA). The continuous variables were evaluated by mean (standard deviation) or range value when required. The dichotomous variables were presented in number/frequency and were analyzed using the Chi - square test. A p - value of <0.05 or 0.001 was regarded as significant.

3. Results

Most of the patients were aged between 25 - 30 years with twogravidas. [Table - 1]The mean MCA ratio in groups without APO and with APO was 4.16±1.39 and 3.44±1.35, respectively. The mean UMB ratio in the group without APO was 2.78±0.79, and with APO was 2.70±0.95. The mean MCA RI varied significantly among both groups [p=0.0220]. The mean UMB RI in the group without APO was 0.63±0.12; in the group with APO,, it was 0.62±0.16. The mean RI ratio was noted higher in the group with APO. The mean MCA PI ratio was 1.46±0.39 in the group without APO and 1.21±0.37 in the group with APO [p=0.0145]. At the same time, the UMB PI was comparable among both groups. The mean PI ratio in the group without APO was 1.44±0.53, and in the group with APO was 1.32±0.65. In the group with and without APO, most of them had a PI ratio >1. [Table - 2] All the parameters negatively correlated with the abnormal perinatal outcome (APO). The age (- 0.1476), umbilical ratio (- 0.1161), UMB RI (- 0.124), RI ratio (- 0.1051), UMB PI (- 0.1439) and PI ratio (- 0.151) showed very weak correlation with APO. It was non - significant among the study population. However, the MCA ratio (- 0.2589), MCA RI (- 0.2999) and MCA PI (- 0.2977) had a weak correlation with APO and were statistically significant. [Table - 3; Figure - 1] The diagnostic accuracy of the UMB ratio was more than the MCA ratio (72.88%vs 67.80%). [Table - 4; Figure - 2] We found that thediagnostic accuracy of the PI ratio was higher than the RI ratio. However, the specificity of the RI ratio was more than the PI ratio. [Tbale - 5; Figure - 3] At a cut - off of 1.09, the MCA PI ratio showed a sensitivity of 75.00% and specificity of 79.17%. Further, at a cut - off of 0.79, the UMB PI ratio showed a sensitivity of 78.38% and a specificity of 86.96%. [Table - 6; Figure - 4]

4. Discussion

In the present study, 59 women were divided into two groups: those with APO (n=27) and those without (n=32). The majority of women in the group without APO were aged 25 - 30 (51.8%), followed by 19 - 24 (40.74%) and 31 - 36 (7.41%). Similarly, the majority of group APO cases were aged 19 - 24 (53.13%), followed by those aged 25 - 30 (37.50%) and 31 - 36 (9.38%). The majority of cases in both, with (40.63%) and without (44.44%) APO groups, were 2nd gravida, followed by 3rd gravida and primigravida. Also, only one patient in each group had G4 gravida status. According to **Khanduri S et al. [**10], the enrolled women ranged in age from 18 to 37 years, with a mean age of 26.13±4.21 years. In contrast, **Al Hamayel et al. [**11] found that most women enrolled in their study were nulliparous. In addition, **Gudmundsson et al. [**12] reported that the median age of the recruited women was 27 (range: 18 to 35) and that 45 were nulliparous. Although, there was no discernible difference between age and obstetric characteristics. Consistent with previously reported studies, both extremes of maternal age groups (<20 years and 42–44 years) had a greater risk ratio for preterm birth, perinatal mortality, low Apgar score, congenital defects etc. [13, 14]In the present study, cases without APO had higher mean PI, RI, and S/D values for UMB and MCA than APO cases. In contrast, **Khanduri S et al.** [10] found that at all visits, umbilical artery, mean PI, RI, and S/D values were considerably higher in IUGR than in non - IUGR patients. Still, MCA PI, RI, and S/D values were significantly lower in IUGR than in non - IUGR cases. The mean RI ratio was [1.21±0.33] in cases without APO and [1.14±0.33] in cases with APO. The mean PI ratio without APO was [1.44±0.53], and with APO, it was [1.320±.65]. The majority of cases without (77.78%) and with (68.75%) APO had PI ratios greater than 1. In contrast, ten instances in the group with APO and sixwithout APO had a PI ratio of less than 1.

In pregnant women with an abnormal perinatal outcome, all of the parameters exhibited an insignificant negative correlation, such as age (r= - 0.1476), umbilical ratio (r= - 0.1161), UMB RI (r= - 0.124), RI ratio (r= - 0.1051), UMB PI (r= - 0.1439), and PI ratio (r= - 0.151) had a very weak correlation with APO. In the research population, it was insignificant. Nevertheless, the MCA S/D ratio (r= - 0.2589), MCA RI (r= - 0.2999), and MCA PI (r= - 0.2977) showed a weak correlation with APO and were statistically significant. Furthermore, **Al Hamayel et al.** [11] noted a substantial positive correlation between each pairwise combination of S/D and PI (r = 0.94), S/D and RI (r = 0.97), and PI and RI (r = 0.92), indicating collinearity between these parameters.

The AUC for the MCA S/D ratio was 0.580, but the UMB S/D ratio was 0.656, indicating that the umbilical ratio is more accurate than the MCA S/D ratio. The UMB S/D ratio showed a statistically significant difference (p=0.041). The sensitivity, specificity, PPV, and diagnostic accuracy of the UMB ratio [72.22 %; 73.91 %; 81.25 %; and 72.88 %, respectively] are all higher than those of the MCA S/D ratio [67.57%; 68.18%; 62.71% and 67.80%, respectively] in terms of sensitivity, specificity, PPV, and accuracy. Similarly, **Khanduri S et al.** [10] reported that the sensitivity of the UMB S/D ratio was 61.5%, specificity was 87.0%, PPV was 88.9%, and diagnostic accuracy was 88.9%. While they acknowledged that the MCA ratio was more specific than sensitive, the MCA S/D ratio was determined to be 46.2% sensitive and 78.3% specific, with a PPV and diagnostic accuracy of 78.3% and 78.3%,

respectively. **Khanduri S et al.** [10] and others reported a low IUGR prediction discriminant value for the umbilical artery S/D ratio. [15]. Nonetheless, in a different study by **Wang et al.** [16], the sensitivity, specificity, and PPV of the umbilical artery S/D ratio were observed to be 80.0%, 83.7%, and 50.0%, respectively, which is much greater than that observed in the present study, with the exception of the PPV. According to studies, preterm is a significant predictor of NICU admission in SGA infants with IUGR, as opposed to an abnormal S/D plus PI or an abnormal S/D alone. This study, however, did not examine SGA infants with normal intrauterine growth [17]. In this investigation, the AUC for the PI ratio was 0.737, and the AUC for the RI ratio was 0.675%, indicating that the PI ratio is more accurate than the RI ratio. The difference in AUC between the two is statistically significant. The sensitivity of the PI ratio is greater than that of the RI ratio. Similarly, PI ratio diagnostic accuracy is better than RI ratio diagnostic accuracy. Nevertheless, the specificity of the RI ratio (71.43%) was greater than that of the PI ratio (68.75%). In the present study, the MCA PI ratio has an AUC of 0.65 and a p - value of 0.039*.75.00% was the sensitivity of the MCA PI ratio. Specificity, positive predictive value and diagnostic accuracy of the MCA PI ratio were 79.17%, 84.37%, and 76.67%, respectively. **Khanduri S et al.** [10] reported that MCA PI was more specific than sensitive. **Bano et al.** [18] showed that the sensitivity, specificity, and positive predictive value (PPV) of MCA PI were 8.9%, 100%, and 100%, respectively, with a diagnostic accuracy of 54.4%. Despite these values being significantly lower in the present study, we noticed that the diagnostic accuracy of MCA PI was 76.67 %. In the present study, the UMB PI ratio has an AUC of 0.757% and a p - value of 0.001*. The sensitivity, specificity, positive predictive value, and diagnostic accuracy of the UMB PI ratio were determined to be 78.38%; 86.96%; 90.62%; and 81.67 %, respectively, which was shown to be better than the MCA PI ratio [75.00%; 79.17%; 84.37%; and 76.67%, respectively]. This indicates that the UMB PI ratio is considerably more precise than the MCA PI ratio. In addition, **Khanduri S et al.** [10] noted the UMB PI ratio's lesser sensitivity and higher specificity, 82.1% and 87.0%, respectively. In their study, however, the PPV and diagnostic accuracy of the UMB PI ratio were higher [91.4% and 83.9%, respectively] than in the present study. Similarly, the specificity and PPV of MCA PI were discovered to be more in their research. [10]Umbilical blood flow is significantly reduced in IUGR, primarily due to alterations in placental vascular resistance. **Giles et al.** [19] observed that a decrease in the number of resistance vessels in the tertiary stem villi of the placenta leads to an increase in resistance, which decreases flow through the UA and increases the UA PI. The term for this condition is umbilical placental insufficiency. [18] In asymmetrical growth retardation, the UA PI is high, while the MCA PI is low. Therefore, the C/U ratio is lower than usual in fetuses with growth retardation. [18] Several other investigations showed contrastingly high [20] and low [21] UMB PI, although **Gudmundsson et al.** [12] found identical results. The PI of the umbilical artery is a substantially more specific criterion than a sensitive one. Literature indicates that the pulsatility index initially declines and then climbs; therefore, by the third visit (late third trimester), the pulsatility index reaches its peak, and the criteria become more sensitive. In instances of placental insufficiency, diastolic flow diminishes, resulting in an increased PI value [12]. **Bano et al.** [18] revealed that the Cerebral - umbilical ratio is a more accurate predictor of SGA foetal fate than MCA PI alone. According to several research, the MCA PI was statistically significant compared to the UA PI. [22]The results of this study indicate that colour Doppler is an effective tool for predicting APO in high - risk pregnancies. Among the several markers evaluated in the study, umbilical artery PI was the most effective.

5. Conclusion

The findings in the present study thus suggest that Doppler flowmetry is a useful method for predicting IUGR in high - risk pregnancies. Among different markers examined in the study, umbilical artery PI had high efficacy in both early as well as the latter part of the third trimester. Yet, to confirm the diagnostic utility of the UMB PI, additional large, prospective studies are required.

Conflict of Interest - All authors declare no conflict of interest.

Source of Funding - None

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Tables and Figures

Table 1: Demographic profile ofenrolled patients among groups (n=69)

		Without APO (n=27)		With APO (n=32)		P - VALUE
		N	%	N	%	
AGE	19 - 24	11	40.74%	17	53.13%	X=1.225 p=0.5421
	25 - 30	14	51.85%	12	37.50%	
	31 - 36	2	7.41%	3	9.38%	
GRAVIDA	G1	7	25.93%	8	25.00%	X=0.2139 p=0.9753
	G2	12	44.44%	13	40.63%	
	G3	7	25.93%	10	31.25%	
	G4	1	3.70%	1	3.13%	

Table 2: Doppler ultrasound findings of enrolled patients among groups (n=69)

		Without APO		With APO		P - VALUE
		MEAN/N	SD/%	MEAN/N	SD/%	
MCA SD RATIO		4.16	1.39	3.44	1.35	t=2.014 **p=0.0488***
UMBILICAL SD RATIO		2.78	0.79	2.70	0.95	t=0.3476 p=0.7294
MCA RI		0.74	0.08	0.68	0.11	t=2.356 **p=0.0220***
UMB RI		0.63	0.12	0.62	0.16	t=0.2673 p=0.7902
RI RATIO		1.21	0.33	1.14	0.33	t=0.8117 p=0.4203
MCA PI		1.46	0.39	1.21	0.37	t=2.523 **p=0.0145***
UMB PI		1.06	0.29	1.03	0.41	t=0.3187 p=0.7511
PI RATIO		1.44	0.53	1.32	0.65	t=0.7676 p=0.4459
PI RATIO	<1	6	22.22%	10	31.25%	X=0.6039 p=0.4371
	>1	21	77.78%	22	68.75%	

Table 3: Correlation analysis of cases with APO vs other parameters

CORRELATION ANALYSIS				
APO vs.	**Spearman r**	**95% confidence interval**	**Correlation**	**P value**
AGE	- 0.1476	- 0.3955 to 0.1204	Very Weak	0.2647
MCA SD RATIO	- 0.2589	- 0.4888 to 0.004766	**Weak**	**0.0477***
UMBILICAL SD RATIO	- 0.1161	- 0.3681 to 0.1519	Very Weak	0.3813
MCA RI	- 0.2999	- 0.5220 to - 0.03972	**Weak**	**0.0210***
UMB RI	- 0.124	- 0.3750 to 0.1440	Very Weak	0.3495
RI RATIO	- 0.1051	- 0.3585 to 0.1627	Very Weak	0.4281
MCA PI	- 0.2977	- 0.5203 to - 0.03738	**Weak**	**0.0220***
UMB PI	- 0.1439	- 0.3923 to 0.1241	Very Weak	0.277
PI RATIO	- 0.151	- 0.3984 to 0.1170	Very Weak	0.2537

Table 4: Comparison of MCA ratio and UMB ratio

		MCA SD RATIO				UMBILICAL SD RATIO			
With APO		**TP**	25	**FP**	7	**TP**	26	**FP**	6
Without APO		**FN**	12	**TN**	15	**FN**	10	**TN**	17
AUC		0.580				0.656			
Standard error		0.075				0.071			
p - value		0.294				**0.041***			
Asymptotic 95% Confidence Interval	Lower Bound	0.432				0.516			
	Upper Bound	0.728				0.796			
Cut - off		2.95				2.15			
Sensitivity		67.57%				72.22%			
Specificity		68.18%				73.91%			
PPV		62.71%				81.25%			
NPV		78.12%				62.96%			
Diagnostic Accuracy		67.80%				72.88%			

Table 5: Comparison of PI ratio and RI ratio

		PI Ratio				RI Ratio			
With APO		**TP**	22	**FP**	10	**TP**	24	**FP**	8
Without APO		**FN**	5	**TN**	22	**FN**	8	**TN**	20
AUC		0.737				0.675			
Standard error		0.068				0.070			
p - value		**0.002***				**0.021***			
Asymptotic 95% Confidence Interval	Lower Bound	0.604				0.538			
	Upper Bound	0.871				0.813			
Cut - off		1.10				1.55			
Sensitivity		81.48%				75.00%			
Specificity		68.75%				71.43%			
PPV		68.75%				75.00%			
NPV		81.48%				71.43%			
Diagnostic Accuracy		74.58%				73.33%			

Table 6: Comparison of MCA PI ratio and UMB PI ratio

		MCA PI Ratio				UMB PI Ratio			
With APO		**TP**	27	**FP**	5	**TP**	29	**FP**	3
Without APO		**FN**	9	**TN**	19	**FN**	8	**TN**	20
AUC		0.657				0.757			
Standard error		0.073				0.065			
p - value		**0.039***				**0.001***			
Asymptotic 95% Confidence Interval	Lower Bound	0.514				0.629			
	Upper Bound	0.800				0.885			
Cut - off		1.09				0.79			
Sensitivity		75.00%				78.38%			
Specificity		79.17%				86.96%			
PPV		84.37%				90.62%			
NPV		67.86%				71.43%			
Diagnostic Accuracy		76.67%				81.67%			

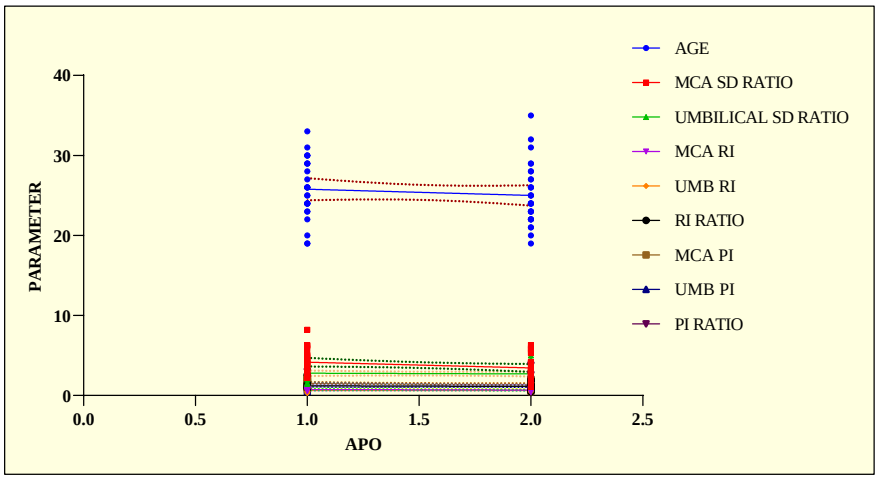

Figure 1: Correlation analysis of pregnant women with APO vs other parameters

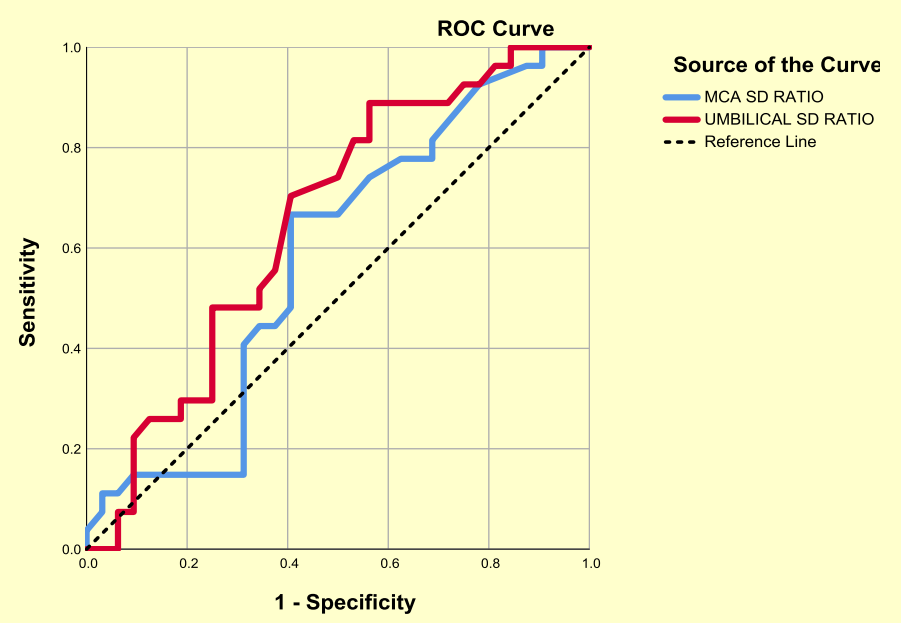

Figure 2: Comparison of MCA ratio and UMB ratio

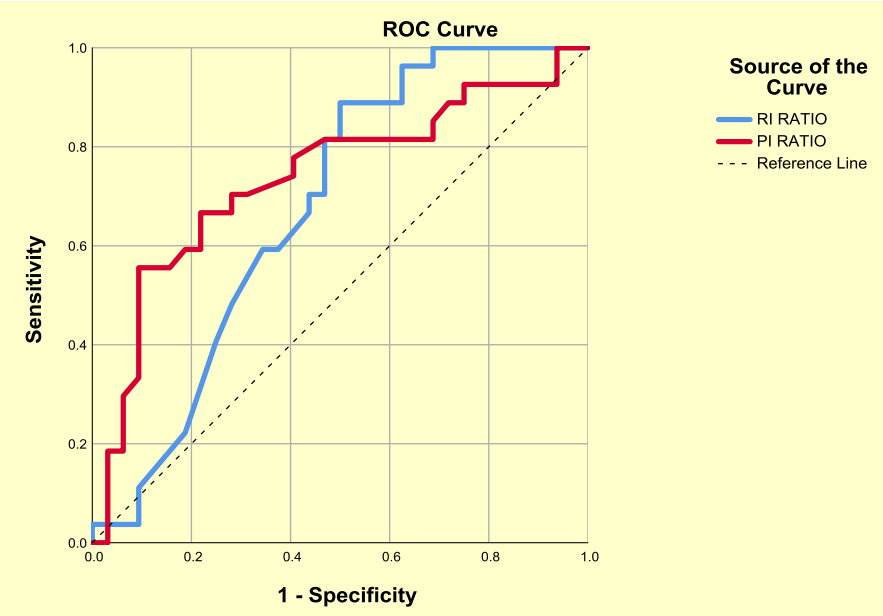

Figure 3: Comparison of PI ratio and RI ratio

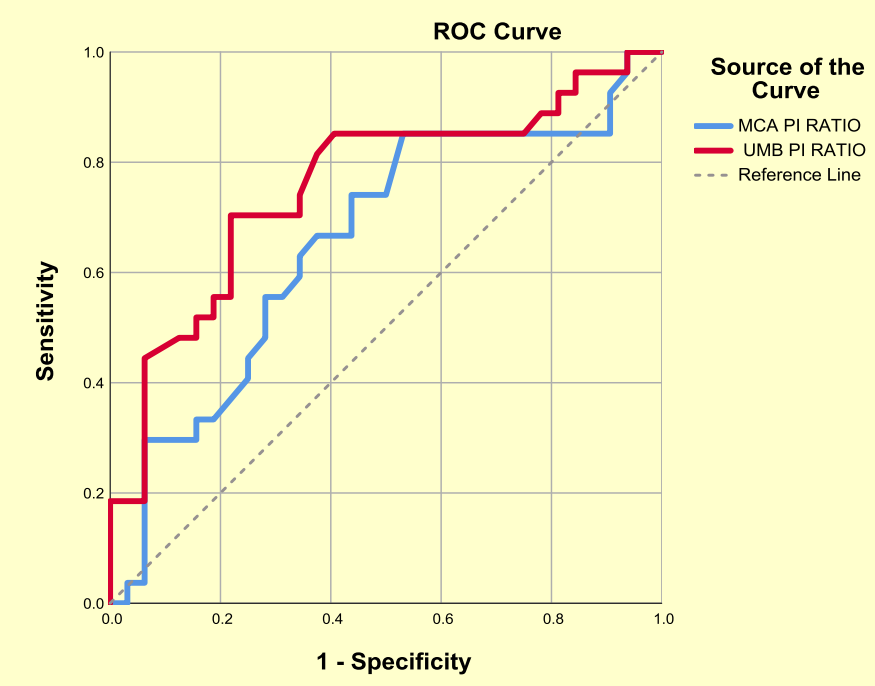

Figure 4: Comparison of MCA PI ratio and UMB PI ratio