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Fetal magnetic resonance imaging in the evaluation of congenital diaphragmatic anomalies

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Abstract

Background: Congenital abnormalities of the diaphragm cause impairment of lung development and are an important cause of post-natal morbidity and mortality. Congenital diaphragmatic eventration (CDE), a less sinister diaphragmatic anomaly compared to the more common congenital diaphragmatic hernia (CDH), often tends to mimic CDH on prenatal imaging. This study evaluates the role of fetal magnetic resonance imaging (MRI) in differentiating these two entities.

Results: This was a retrospective study which included fetal MRI studies done in patients with ultrasound diagnosis of fetal diaphragmatic anomaly. MRI exam was performed with a 1.5 T superconducting system with eight-element torso array coil. The images were studied by two radiologists experienced in fetal imaging in consensus. Diagnosis of CDE was made if the dome of the diaphragm was visualized as a thin hypointense line separating the lung from abdominal structures on coronal and sagittal MRI sequences. If this thin hypointense line was not visualized, a diagnosis of CDH was made. The findings were then correlated with autopsy/intra-operative findings/post-natal imaging follow-up. A total of 12 patients were included in the study. In these 12 patients, 13 diaphragmatic abnormalities were diagnosed on MRI (1 fetus had bilateral diaphragmatic anomaly). Of the 13 diaphragmatic anomalies detected, 7 (54%) were CDH and 6 (46%) were CDE. The type of diaphragmatic anomaly was correctly identified on MRI in all except one fetus in which CDE was misdiagnosed as CDH. The Fisher exact test statistic value was 0.0047. The result was significant at $p < 0.01$.

Conclusion: Fetal MRI is a useful tool for assessing congenital diaphragmatic anomalies. Visualization of the diaphragm on coronal and sagittal images helps in diagnosis of complete CDE and differentiating it from the more sinister CDH.

Keywords: Congenital diaphragmatic hernia, Congenital diaphragmatic eventration, Prenatal diagnosis, Fetal MRI, Fetal imaging

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Background

The diaphragm is a thin fibromuscular structure which separates the pleural and peritoneal cavities. It develops from four mesodermal elements: the septum transversum, pleuroperitoneal membranes, abdominal wall musculature, and esophageal mesentery [1]. Congenital abnormalities of the diaphragm cause impairment of normal lung development and are an important cause of post-natal morbidity and mortality.

Incidence of congenital diaphragmatic hernia (CDH) is about 1–5 per 10,000 live births [2]. CDH is caused by deficient fusion of the pleuroperitoneal membranes and abdominal wall musculature or due to absence of the pleuroperitoneal membranes [3]. The resultant defect in the diaphragm causes displacement of the intra-abdominal viscera into the thorax. Nearly 90% are intrapleural, and most of these are left sided. They cause cardio-mediastinal shift and lung hypoplasia. They are also associated with other major congenital anomalies—cardiac, gastrointestinal, and neural tube defects [4]. Congenital diaphragmatic eventration (CDE) is less common than CDH with reported incidence of 1 in 10,000 live births. It results from incomplete muscularization of the membranous diaphragm with resultant superior displacement of the diaphragm [5]. Unlike CDH, the diaphragm is intact in eventration. Complete eventration more commonly involves the left hemidiaphragm while partial eventration is more common on the right side. In the newborn period, CDE is usually asymptomatic and may be identified during routine check-up. Occasionally, it can be large enough to cause mediastinal shift and pulmonary hypoplasia. It is important to distinguish CDH from eventration in the antenatal period as the prognosis for CDH tends to be worse compared to CDE [6]. Postnatal mortality rates for CDH are high (around 30–50%) with pulmonary hypoplasia and pulmonary hypertension being causes of high mortality rate [7]. CDE however does not always require surgical repair and has lower postnatal mortality rate. Accurate antenatal diagnosis of CDE and ability to confidently differentiate it from the more common CDH are essential for planning appropriate management and counseling of the parents.

Ultrasonography (USG) is considered the primary imaging modality for antenatal detection of diaphragmatic anomalies. Antenatal USG also plays a role in making volumetric lung measurements which can help predict the outcome of the fetus [8]. However, complete CDE may mimic CDH on antenatal USG [9, 10]. In recent times, fetal magnetic resonance imaging (MRI) is being increasingly performed to diagnose and prognosticate these anomalies [3, 11]. Literature on antenatal diagnosis of CDE is limited to case reports [6, 12–16] with no previous studies directly assessing the ability of fetal MRI to differentiate CDH and CDE. Moreover, the role of fetal MRI in diagnosing CDE is not clearly established in literature. In this retrospective observational study, we assessed the ability of fetal MRI to differentiate these two diaphragmatic anomalies. The objective of the study was to evaluate the role of fetal MRI in differentiating congenital diaphragmatic eventration (CDE) from congenital diaphragmatic hernia (CDH) among fetuses diagnosed to have diaphragmatic anomalies on antenatal USG.

Methods

This was a retrospective study which included the MRI examinations of patients who were referred to the department of radiodiagnosis of our institute for suspected fetal diaphragm abnormalities from November 2010 to July 2019. We included all patients with suspected fetal diaphragmatic abnormalities based on findings on antenatal USG who subsequently underwent fetal MRI in our institute. USG finding of visualization of intra-abdominal contents (like the stomach, small bowel, liver, and spleen) in the thoracic cavity raised suspicion of congenital diaphragmatic anomaly. USG examination however did not differentiate CDH from CDE in these patients. Patients who were lost to follow-up following the MRI examination were excluded from the study. The MR imaging studies were identified using keyword search from the department picture archiving and communication system. The MRI examinations were performed with a 1.5 T superconducting system (Avanto Siemens, Erlangen, Germany) with an eight-element torso array coil. The routine MR sequences obtained in our institution were (1) T2-weighted Half Fourier acquisition single shot turbo spin echo (HASTE) (TR 900 ms, TE 90, FOV 24–28 cm, matrix 256 × 205, number of excitations 1, slice thickness 4.5 mm, intersection gap 0.2 mm) and (2) T1-weighted turbo FLASH (TR 100 ms, TE 4.7 ms, flip angle 70°, FOV 24–28 cm, matrix 256 × 173, number of excitations 1, slice thickness 4.5 mm, intersection gap 0.2 mm). The images were studied by two radiologists experienced in fetal imaging in consensus. Cases were diagnosed as either CDH or CDE based on visualization of the ipsilateral dome of the diaphragm as a thin hypointense line separating the lung from abdominal structures on coronal and sagittal images. The following findings were also recorded: laterality (right/left/bilateral), nature of abdominal contents displaced into the thoracic cavity (stomach, small bowel, large bowel, spleen, and/or liver), and observed/expected lung area to head circumference ratio expressed as percentage (LHR). LHR was calculated by multiplying transverse and anteroposterior dimensions of the contralateral lung at level of the four-chamber view of the heart and dividing the result by the head circumference. This value was

then compared to age-matched controls using a nomogram provided by Peralta et al. [17]. The MRI findings were then correlated with autopsy (in case of medical termination of pregnancy or post-natal demise)/intra-operative findings or post-natal imaging follow-up (in patients treated conservatively).

Results

A total of 12 patients were included in our study. A flow chart of the study outline and results is presented in Fig. 1. Age of the patients included in the study ranged from 22 to 33 years with mean of 24.5 years. Four (33.3%) of the patients were primigravida, and 8 (66.6%) were multigravida. None of the patients had any history of fetal anomalies in previous pregnancies. Gestational age of patients at time of MRI examination ranged from 21 to 31 weeks with mean of 23.2 weeks. Out of the 12 patients assessed, 8 (66.7%) patients presented in the 2nd trimester, and 4 (33.3%) patients presented in the 3rd trimester. No patients presented in the 1st trimester. Fetal echocardiography performed prior to MRI did not reveal any associated intra-cardiac anomalies. Tests for detection of chromosomal anomalies were not available for any of the cases. In these 12 patients, 13 diaphragmatic abnormalities were diagnosed on MRI (1 fetus had bilateral diaphragmatic anomaly). We did not compare the MRI diagnosis with that of USG as detailed USG data were not available. These pregnant women had USG elsewhere and were referred to our center for fetal MRI.

The normal fetal diaphragm is visualized on MRI as a thin curvilinear low signal intensity structure separating the thoracic and abdominal cavities on T2-weighted coronal and sagittal images (Fig. 2). Based on the visualization of this T2 hypointense line, cases were diagnosed as either CDH (no hypointense line present between the thoracic and abdominal contents) or CDE (hypointense line present between the thoracic and abdominal contents). Examples of cases of CDE and CDH are presented in Figs. 3 and 4 respectively.

Of the 13 anomaly studies diagnosed on MRI, 8 were diagnosed as CDH (including one fetus with bilateral CDH), and 5 were diagnosed as CDE. Majority of the diaphragmatic anomalies (11/13, 84.6%) were on the left side. Stomach was the commonest content of herniation (seen in all left-sided diaphragmatic anomalies) followed by small bowel (69%).

Based on post-natal follow-up or autopsy, the final diagnosis made was CDH in 7 out of 13 anomalies (54%) and CDE in 6 out of 13 anomalies (46%). Mean LHR

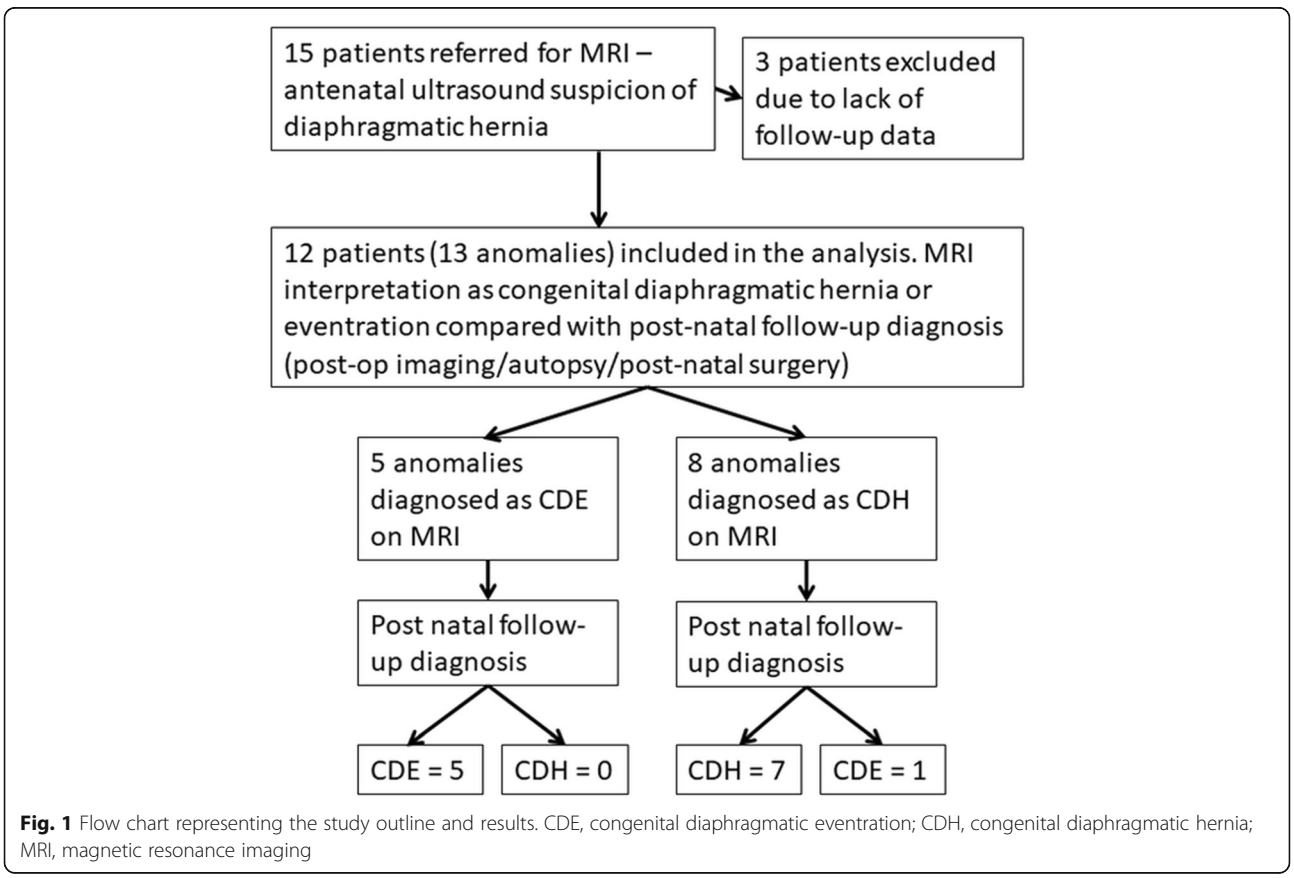

Fig. 1 Flow chart representing the study outline and results. CDE, congenital diaphragmatic eventration; CDH, congenital diaphragmatic hernia; MRI, magnetic resonance imaging

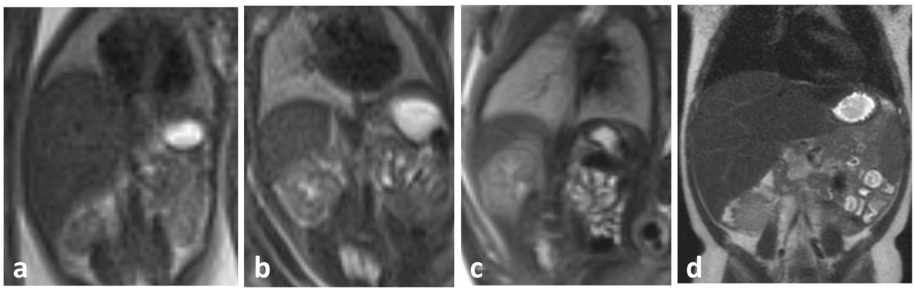

Fig. 2 Selected images of coronal T2-weighted MRI showing the appearance of normal diaphragm (arrows) at 21, 29, and 33 weeks of gestation and in a newborn (**a**, **b**, **c** and **d** respectively)

was 42.1% in CDH group (SD = 21.9) and 33.1% in CDE group (SD = 14.2). Out of the 6 patients identified to have CDH, 4 neonates died immediately after delivery and 2 neonates survived and were operated. These two infants were doing well at 2 months follow-up. Out of the 6 patients identified to have eventration, 2 underwent medical termination of pregnancy, 1 neonate died immediately after delivery, and 3 infants survived after delivery. Of these three, one was operated and is doing well on follow-up while the other two were managed conservatively. The mean LHR of all cases of diaphragmatic anomaly with postnatal demise was 31.3%, and mean LHR in infants alive at 2 months follow-up was 51.2%. There was a statistically significant difference in between these two groups ($p < 0.05$). The demographic details, imaging findings, and postnatal follow-up details of patients included in the study are provided in Table 1.

The type of diaphragmatic anomaly was correctly identified in all except one patient in whom CDE was misdiagnosed as CDH. The Fisher exact test statistic value was 0.0047. The result was significant at $p < 0.01$.

Discussion

The goal of prenatal imaging in congenital anomalies of the diaphragm is to establish the diagnosis and to identify prognostic features which can help in management and counseling. Prenatal USG is the primary imaging modality. The diagnosis of both CDH and CDE is done by observing abdominal viscera within the thoracic cavity. Ancillary findings are mediastinal shift to the opposite side, small abdominal circumference, observing peristalsis within the thoracic cavity, and polyhydramnios.

Accurate prenatal imaging diagnosis of congenital diaphragmatic anomalies is dependent on various factors like gestational age at presentation, size, and side of the diaphragmatic anomaly. The earlier the gestation, the more difficult it is to diagnose these anomalies. Many of these anomalies are detected in the late second trimester or in the third trimester. Establishing a diagnosis of CDH before 24 weeks of gestational age is difficult [18]. Prenatal USG detection of right-sided diaphragmatic anomalies is lower than left because of similar echogenicity of the liver and the lung. The displaced liver in the

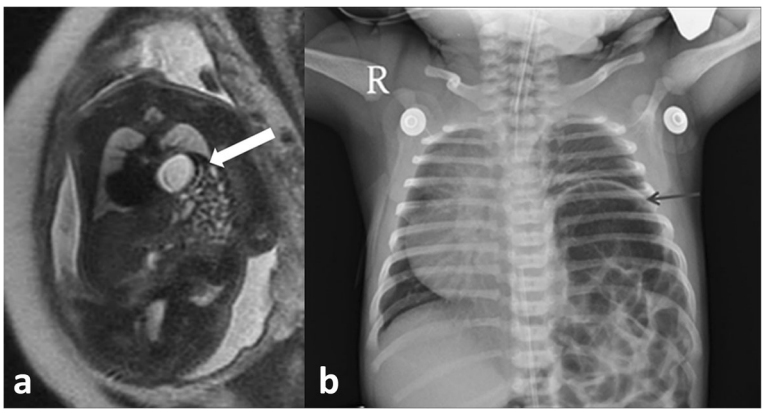

Fig. 3 Thirty-three-year-old G2 P1 L1 at 32 weeks of gestation with features of left-sided eventration. **a** Coronal T2-weighted MRI image of fetal trunk showing the presence of stomach and small and large bowel loops in the thoracic cavity with an intact diaphragm (white arrow). **b** Postnatal chest radiograph showing elevated left hemidiaphragm (black arrow) outlined by the lung superiorly and bowel gasses inferiorly

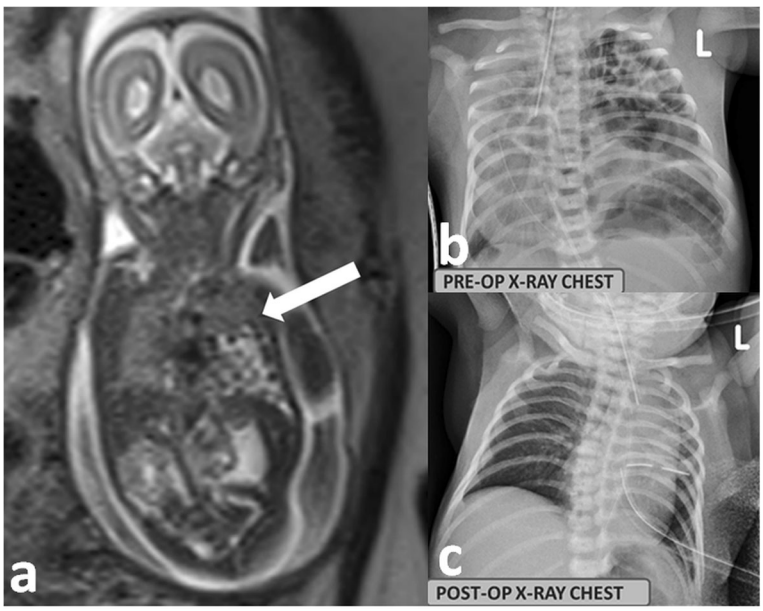

Fig. 4 Twenty-eight-year-old G2 P1 L1 at 21 weeks of gestation with features of left-sided diaphragmatic hernia. **a** Coronal T2-weighted MRI image of the fetal trunk showing the presence of stomach and small and large bowel loops in the thoracic cavity (arrow) with no discernible hypointense line between the left lung and abdominal viscera. **b** Postnatal chest radiograph taken on the 1st day of life showing multiple bowel loops in the left hemithorax with complete mediastinal shift to the right side. Endotracheal tube is noted in situ in the trachea which is deviated to the right side. The baby underwent diaphragm repair surgery. **c** Post-operative chest radiograph showing normal position of both domes of diaphragm with endotracheal tube and left intercostal drainage tube in situ

Table 1 Demography, imaging findings, postnatal outcome, and follow-up details of patients with fetal diaphragmatic anomalies included in the study

S. no.	Gestational age at diagnosis (weeks)	Herniated contents	Laterality of the diaphragmatic anomaly	LHR (%)	MRI diagnosis	Final diagnosis	Outcome
1	31	Stomach, small and large bowel	Left	22.4	CDH	CDH	Died immediately after birth
2	30	Stomach, small and large bowel	Left	18.4	CDH	CDH	Died immediately after birth
3	22	Stomach, part of liver, small and large bowel	Bilateral	Not calculated	CDH	CDH	Died immediately after birth
4	21	Stomach, part of liver, and small bowel	Left	42.5	CDH	CDH	Died immediately after birth
5	24	Stomach, part of liver	Left	42	CDE	CDE	Died 1 month after surgery
6	24	Liver	Right	15.5	CDE	CDE	TOP
7	21	Stomach and part of liver	Left	34.5	CDE	CDE	Operated, doing well
8	32	Stomach, small and large bowel	Left	41.6	CDH	CDE	Conservative management, doing well
9	24	Stomach and small bowel.	Left	13	CDE	CDE	TOP
10	21	Stomach, small and large bowel	Left	79.8	CDH	CDH	Operated, doing well
11	29	Stomach, small and large bowel	Left	48	CDH	CDH	Operated, doing well
12	21	Stomach, part of liver, small and large bowel	Left	52	CDE	CDE	Conservative management, doing well

CDE congenital diaphragmatic eventration, *CDH* congenital diaphragmatic hernia, *LHR* lung head ratio (observed LHR/expected LHR × 100) expressed as percentage, *TOP* termination of pregnancy

thoracic cavity can be misinterpreted as the lung thus resulting in a missed diagnosis. Around 10–25% of cases can be missed on antenatal screening USG [19, 20]. The main advantages of MRI over USG in this scenario are its ability to provide a three-dimensional visualization of the diaphragm irrespective of fetal position and maternal habitus and its better prognostic potential [21].

The fetal lung being primarily composed of water has a uniformly bright signal on T2-weighted MR images. The diaphragm is hypointense on T2-weighted images and can be identified as a thin hypointense line separating the thoracic and abdominal cavities on coronal and sagittal images. In our study, the diaphragm was clearly delineated in all cases of CDE except one. In this case (patient 8 in Table 1), the diaphragm could not be delineated, and hence, this was misdiagnosed as CDH. This was likely related to suboptimal image quality as a result of excessive fetal movements during MRI. The ipsilateral dome of the diaphragm was not visible in any of the cases finally diagnosed as CDH. The mean LHR was significantly lower in cases of post-natal demise compared to infants surviving to 2 months of age (including cases of both CDH and CDE). While MRI-based LHR is well established as a prognostic marker in CDH [22], our study suggests that it can be used as prognostic marker even in cases of CDE.

Literature on prenatal diagnosis of CDE and its differentiation from CDH is limited. Jeanty et al. [23] have documented that presence of pleural or pericardial effusions favor diagnosis of CDE over CDH. In our study, none of the fetuses had pleural or pericardial effusion, and hence, this finding could not be utilized in the diagnosis. Karmazyn et al. [24] have shown that presence of a folding free muscle edge and narrow angle waist favored diagnosis of CDH over CDE in postnatal period although this differentiation was not possible in around one-third of their cases. The findings of their study cannot be directly compared with our study because they had evaluated diaphragmatic defects in infants after birth and not in prenatal period. No previous studies have assessed the role of fetal MRI in differentiating CDE from CDH. In this context, our study has shown it is possible to confidently differentiate these two conditions in antenatal period using fetal MRI.

Limitations of our study are its retrospective nature and small sample size. However, CDE is an uncommon anomaly and multicenter studies can be undertaken for including larger number of patients. We did not include data on genetic/chromosomal studies of the fetuses as it was not available. We did not perform dynamic imaging to assess movement of the fetal diaphragm. We did not compare the accuracy of MRI with that of USG.

Conclusion

We have demonstrated in our study that fetal MRI is a useful tool for imaging the fetal diaphragm. Fetal MRI can consistently demonstrate the elevated hemidiaphragm in cases of CDE. Visualization of the diaphragm on coronal and sagittal images helps in differentiating CDE from the more sinister CDH. Future prospective studies with larger sample size are required to assess the impact of differentiating CDE and CDH during antenatal period on fetal and postnatal management.

Abbreviations

CDE: Congenital diaphragmatic eventration; CDH: Congenital diaphragmatic hernia; FLASH: Fast low angle shot; FOV: Field of view; HASTE: Half Fourier acquisition single shot turbo spin echo; LHR: Lung area head circumference ratio; MRI: Magnetic resonance imaging; USG: Ultrasonography

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Authors' contributions

BB and RR collected the patient data. HM and RR analyzed and interpreted the patient data. HM prepared the manuscript. RR, SS, IS, and CA edited the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this article (Table 1 presents the data collected for purpose of this study).

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Sri Ramachandra University with IEC number NI/20/FEB/74/25.

Consent for publication

No separate individual consent was obtained from patients for this study as it was retrospective in nature, and the examinations were carried out as part of routine clinical care. No patient-identifying information is included in the manuscript material.

Competing interests

None

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