BJOG: An International Journal of Obstetrics & Gynaecology

WILEY

BJOG An International Journal of Obstetrics and Gynaecology

RESEARCH ARTICLE OPEN ACCESS

The Postnatal outcomES of Fetal Cortical mAlformations (PESCA) Study: A Multicentre Historical Cohort Study

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Received: 26 April 2025 | **Revised:** 2 December 2025 | **Accepted:** 3 December 2025

Keywords: fetal cortical malformations | malformations of cortical development | MRI | neurodevelopment | neurosonography | prenatal diagnosis

ABSTRACT

Objectives: To provide further evidence on the outcomes associated with fetal malformations of cortical development (MCD), currently informed by data from symptomatic paediatric cohorts, this study provides a new classification system.

Design: Multicentre retrospective cohort study.

Setting: Fetal medicine units of three tertiary centres in the United Kingdom and Italy.

Population: 118 foetuses diagnosed with MCD by ultrasound and/or magnetic resonance imaging included.

Methods: The cases were classified according to their presumed aetiology (genetic, haemorrhage, dysgenesis, infection) and imaging findings (focal, diffuse, mantle, sulcation). Neurodevelopmental delay was classified as mild, moderate or severe. Cases with missing information on postnatal outcome were excluded.

Main Outcome Measures: Postnatal neurodevelopmental outcome ascertained from the infant's neurological assessments according to international performance scales, depending on the age.

Results: There were 52/118 (44%) livebirths, 64/118 (54.2%) terminations of pregnancy (TOP) and 2/118 (1.6%) intrauterine demises. Twenty-five of 46 cases (54.3%, 95% CI 39–69.1) that survived the neonatal period had a normal or mildly delayed neurological development. The commonest aetiology was genetic, and the most frequent radiological finding was reduced sulcation. The best neurological outcome was found in children with focal lesions; those with diffuse hemispheric lesions had the worst one.

Conclusion: This is the largest cohort of foetuses diagnosed with MCDs systematically classified by aetiology and radiological findings. In this retrospective cohort of liveborn survivors, over half had normal or mildly abnormal neurodevelopmental outcomes. Prognosis varied according to lesion pattern and suspected aetiology. Fetal MCDs in this study had better neurodevelopmental outcomes than previously reported, though findings should be interpreted with caution given selection and follow-up limitations.

Natalia Abadia-Cuchi and Francesca Felici are joint first authors.

Basky Thilaganathan and Alessandra Familiari are joint last authors.

1 | Introduction

Central nervous system (CNS) malformations are one of the most frequent congenital anomalies that can be detected prenatally during the routine anomaly scan or the third-trimester scan [1], and among the most difficult fetal conditions to manage in terms of clinical impact and prognosis. Malformations of cortical development (MCD) comprise a large, heterogeneous group of disorders with disrupted cerebral cortex formation ranging from abnormal cortical gyri, delayed appearance of landmark sulcation, and/or abnormal cortical thickness to overt cortical loss [2].

MCDs represent a challenge in prenatal diagnosis, particularly due to the difficulty in parental counselling. Typically, a very guarded clinical prognosis is given following the diagnosis of fetal MCD, including neurological impairment, epilepsy, autism, cerebral palsy, and intellectual disability [3, 4]. However, these prognoses have been extrapolated from clinical outcomes in postnatal cohorts consisting typically of symptomatic individuals undergoing neurological evaluation. The latter ignores the possibility that there may be asymptomatic individuals with MCD that have not presented to clinical services, thereby introducing significant bias to the existing postnatal data used for prenatal counseling [5, 6].

A recent systematic review on fetal MCDs found 371 reported cases with 74 livebirths, of which only 30 cases had any kind of postnatal neurological follow-up [7]. The published literature is inconsistent, non-standardised, and confusing in its use of terminology for classification of fetal MCDs. The resulting paucity of data on the relationship between presumed aetiology and radiological findings with postnatal neurodevelopmental outcome makes counselling of antenatal MCDs very challenging. The *P*ostnatal outcom*ES* of fetal *C*ortical m*A*lformations (PESCA) study is a multicentre historical cohort study designed to evaluate the natural history and postnatal outcomes based on a new pragmatic and systematic classification system for fetal MCDs.

2 | Methods

2.1 | Study Design

The PESCA study is a multicentre historical observational cohort study of foetuses with a diagnosis of MCD. Pregnancies with a diagnosis of fetal MCD were identified by searching the IntelliSpace PACS database (IntelliSpace PACS—Enterprise 4.4, Philips, Amsterdam, The Netherlands), Viewpoint database (ViewPoint 5.6.26.148, GE Healthcare, Illinois, United States), and local hospital databases in St George's Hospital, London, United Kingdom; Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; and Azienda Ospedaliero—Universitaria di Parma, Parma, Italy, for scans performed between January 2013 and July 2024. An extensive search of fetal intracranial abnormalities was conducted in order not to miss any cases of fetal MCDs, since this diagnosis is quite rare and usually coexists with other major abnormalities. Two authors (NA-C and FF) reviewed case by case to identify those foetuses with a diagnosed MCD and excluded those cases with an intracranial abnormality without an MCD. Cases of confirmed MCD with genetic or chromosomal abnormalities, multiple pregnancies, and cases with maternal comorbidities were not excluded. Postnatal outcomes were retrieved by electronic clinical charts reporting tests and clinical evaluations about survival, neurodevelopment, epilepsy, scales and genetic details. There was no patient or public involvement in the design, conduct, or reporting of this study. To date, no established core outcome set (COS) exists for fetal malformations of cortical development (MCDs), and therefore no COS was applied.

2.2 | Participants

This study included all pregnancies with a fetal diagnosis of a MCD, with or without coexisting CNS or extra-CNS abnormalities, regardless of gestational age at diagnosis. Included patients had been referred for a suspected fetal CNS anomaly and managed at the Fetal Medicine Units (FMU) of the three involved hospitals. To confirm fetal MCDs, all patients underwent a targeted transvaginal sonographic examination of the fetal CNS (neurosonography) when foetuses were in cephalic presentation, including midsagittal anterior, coronal, and sagittal planes according to international guidelines [8, 9] and fetal magnetic resonance imaging (MRI). A standard fetal MRI protocol has been adopted for all the radiological exams (Table S1). Postnatally diagnosed MCDs, brain abnormalities that did not include the cortical malformations, and livebirths with no postnatal follow-up were excluded from the study. Inclusion and exclusion criteria are detailed in Figure 1 (flowchart of the study). Clinical and demographic data for cases without a prenatal diagnosis of malformations of cortical development (MCD) were not collected, as these cases were not intended to be part of the analytical cohort. Therefore, no comparative analysis between included and excluded cases could be performed.

2.3 | Classification of Fetal MCDs

Ultrasound and MRI images and reports were reviewed by four different authors (FF and NAC for ultrasounds, SA and MM for MRI). All MCD cases were classified according to aetiology and by image findings according to PESCA criteria (Figure 2).

When one case had more than one prenatal scan/MRI, the images were reviewed and classified according to the most recent scan/MRI and to the most prominent features.

At the beginning of the data collection process, several online meetings were arranged between the centres to discuss, resolve uncertainty, and align the method and process of classification using the PESCA criteria.

Aetiology was assigned according to the working prenatal diagnosis into these categories: genetic, infection, vascular, haemorrhage, and dysgenesis/unknown. The cases classified as *genetic* included both pregnancies with an ascertained genetic problem

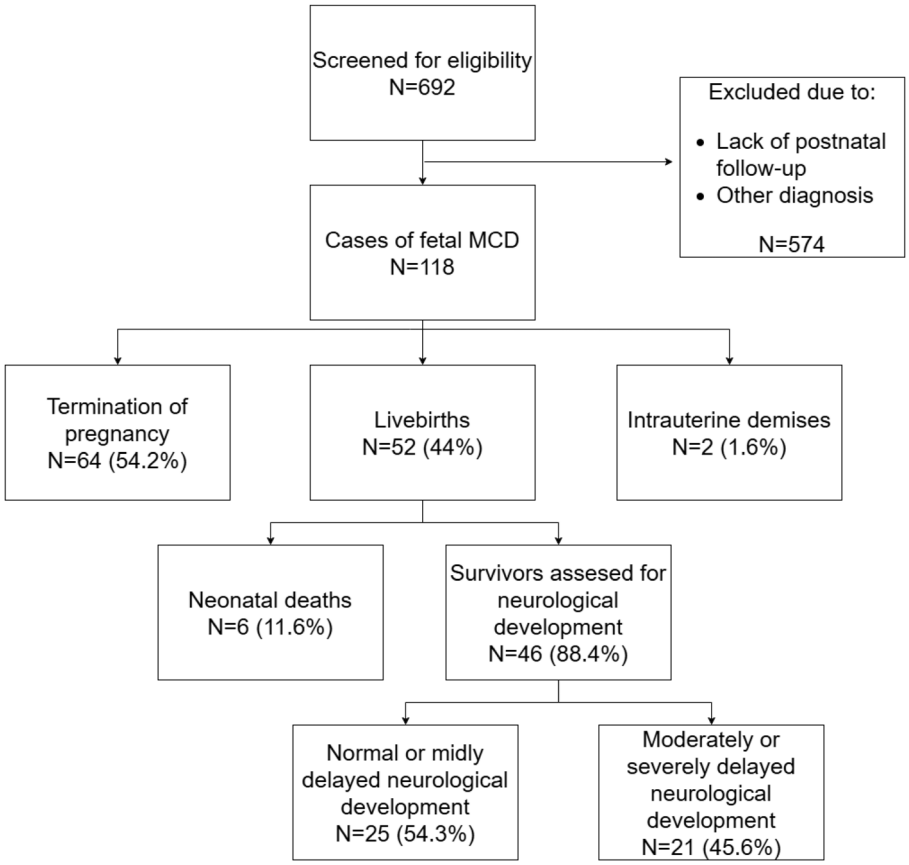

FIGURE 1 | Flowchart of the study.

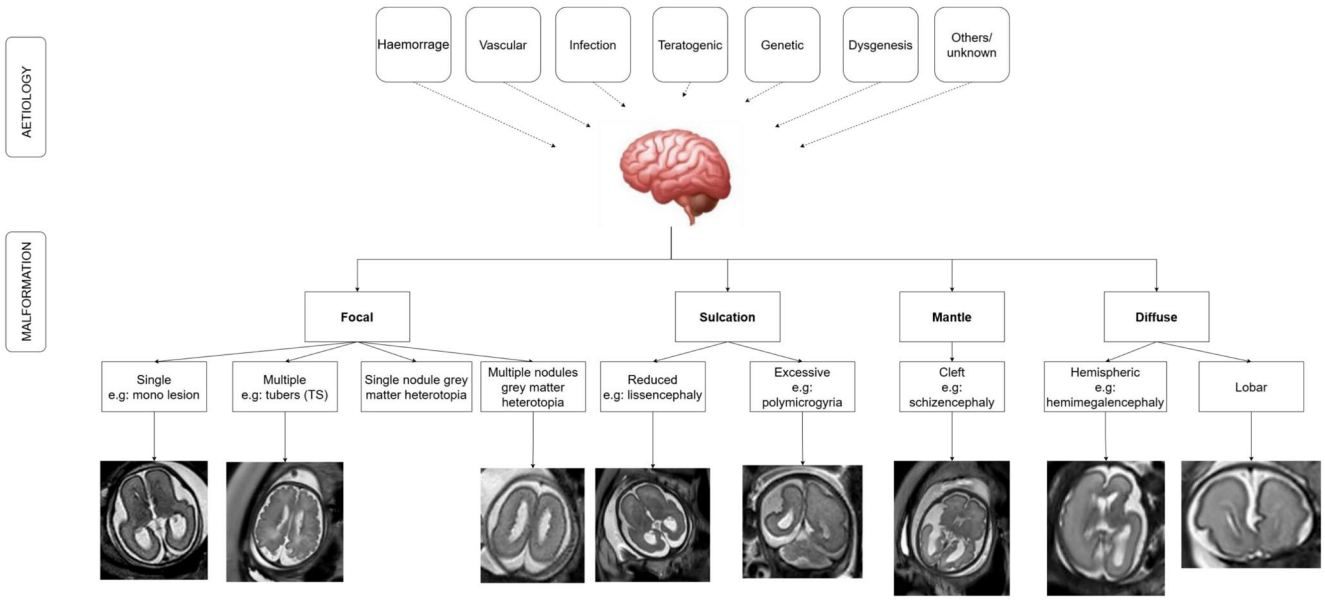

FIGURE 2 | Classification of fetal malformations of cortical development by aetiology and by radiological (morphological) findings. The latter were classed as four groups which involved: focal lesions/nodules, abnormalities of sulcation, defects of the cerebral mantle and diffuse lobar/hemispheric cerebral changes. TS, tuberose sclerosis.

(prenatal confirmation via invasive procedure) or a presumed genetic cause because the MCD was diagnosed in the context of a polymalformative setting including additional ultrasound features. Other aetiology categories were:

- *Infections*: MCD can result from congenital infections (CMV, Zika, toxoplasmosis) which disrupt neuronal proliferation and migration, leading to abnormal cortical development.

- *Vascular*: Ischemic or hypoxic insults during fetal brain development can impair normal cortical formation, often producing focal or diffuse abnormalities.
- *Haemorrhage*: Intrauterine bleeding can destroy or distort developing brain tissue, causing porencephalic cysts, cortical thinning, or abnormal sulcation.
- *Dysgenesis/unknown*: Intrinsic developmental errors interfere with neuronal proliferation, migration, or organization, resulting in structural malformations. Sometimes, the exact cause cannot be identified, or it may be multifactorial, including metabolic disorders, toxic exposures, or undetermined mechanisms.

The image findings were classified radiologically into four main categories according to the type and extent of lesions: focal lesions, abnormal sulcation, mantle defects and diffuse cortical abnormalities (Figure 1).

- *Focal lesions* are localized cortical abnormalities, such as focal cortical dysplasia or heterotopia, where normal tissue organization is disrupted in a restricted area.
- *Reduced or excessive sulcation* refers to abnormal gyral patterns, ranging from simplified gyral formation (lissencephaly, pachygyria) to excessive folding (polymicrogyria).
- *Mantle defects* involve disruptions in cortical continuity or thickness, often seen in conditions like schizencephaly or cortical clefts.
- *Diffuse cortical abnormalities* affect the cortex globally, leading to widespread disorganisation, as in diffuse lissencephaly or microlissencephaly, where the entire cerebral mantle shows structural alteration.

When more than one type of MCD was identified on imaging, the case was assigned to more than one classification, with one marked as the predominant type.

2.4 | Variables

Demographic data and pregnancy outcome were documented in all cases. Postnatal neurological follow-up was collected from the hospital databases if available. Postnatal imaging was documented when available, as was postnatal data on epilepsy and definite aetiology of the MCD. Postnatal neurodevelopmental outcome was ascertained from the infant's neurological assessments documented in hospital records through paediatric and neuropsychiatric evaluations at their reference hospital, according to the Leiter International Performance Scale-Revised scale [10] the Griffiths Developmental scales [11] the Vineland Adaptive Behaviour Scale Second Edition [12]; and the Child Behaviour Checklist for Ages 1½–5 (CBCL 1½–5) [13]. In a few cases ($n = 7$), neurodevelopment was ascertained from an informal telephone interview with the parents when such documentation was not available (Table S2). Six newborns died within 2 months after birth, and neurodevelopmental assessment was not possible due to the extremely young age.

3 | Results

A total of 692 cases were screened for eligibility. Out of these cases, 118 were diagnosed with a fetal MCD and 574 were excluded. The main reason for exclusion was the lack of pregnancy and postnatal follow-up data. There were 52/118 (44%) livebirths, 64/118 (54.2%) terminations of pregnancy (TOP), and 2/118 (1.6%) intrauterine demises. Among the livebirths, 46/52 (88.4%) cases survived the neonatal period (Figure 1).

Pregnancy characteristics are listed in Table 1: Among the 52 included livebirths, the median gestational age at birth was 38.1 weeks, and the median birthweight was 2842 g. There were six neonatal deaths. Five of these children had severe genetic syndromes, and one had a malignant tumour. Neonatal deaths were excluded from the postnatal data since these children had a condition that was incompatible with life, and neurological assessment was precluded. Details on the cortical lesions and diagnosis of these children are listed in Table S2.

3.1 | Etiological and Radiological Findings

The PESCA classification of fetal MCDs either by presumed aetiology or image finding is shown in Table 2. Only two cases were diagnosed solely by ultrasound scan, while the 116 remaining cases were assessed with ultrasound and MRI. Mean gestational age was 24 weeks at the time of the ultrasound scan and 26 weeks at the time of the MRI. The commonest etiological classification was genetic ($n = 63/118$, 53.4%) and dysgenesis/unknown causes ($n = 33/118$, 27.9%). Out of the 52 livebirths and neonatal deaths, 31/52 (49.6%) were classified as genetic. Of these cases, 20/31 (64.5%) were presumed to be genetic and only 11/31 (35.5%) had a confirmed genetic diagnosis prenatally, although five additional cases were confirmed to be genetic postnatally. Cytomegalovirus (CMV) was the cause of all the infective aetiology. The commonest image classifications were reduced sulcation ($n = 35/118$, 29.6%) and diffuse hemispheric MCD ($n = 32/118$, 27.1%) (Table 2). The highest livebirth rates were in cases radiologically classified as excessive sulcation ($n = 7/10$, 70%) and focal multiple lesions ($n = 7/10$, 70%). Similarly, cases etiologically classified as hemorrhagic had the highest livebirth rate ($n = 4/5$, 80%). On

TABLE 1 | Demographic and patient characteristics of the included patients. Data provided as number (%) or median (IQR).

Included pregnancies with livebirths ($n = 52$)	
Multiple pregnancy	3/52 (5.7%)
Maternal age	31.5 (7)
Nulliparous	28/52 (53.8%)
Multiparous	24/52 (46.2%)
Smokers	5/52 (9.6%)
Gestational age at birth (weeks)	38.1 (3)
Birthweight (g)	2842 g (1248)
Preterm deliveries (< 37 weeks)	13/52 (25%)
Neonatal deaths	6/52 (11.5%)

TABLE 2 | Classification of fetal MCDs by aetiology and radiological findings. The numbers and (%) of medical abortions, stillbirths, and livebirths are also shown. The image classification groups are not mutually exclusive (IUD, intrauterine demise; TOP, termination of pregnancy).

	TOP ($n=64$)	IUD ($n=2$)	Livebirths ($n=52$)
Aetiology			
Genetic ($n=63$)	30/63 (47.6%)	2/63 (3.2%)	31/63 (49.2%)
Dysgenesis/Other ($n=33$)	20/33 (60.6%)	0	13/33 (39.4%)
Infection ($n=10$)	7/10 (70%)	0	3/10 (30%)
Vascular ($n=7$)	6/7 (85.7%)	0	1/7 (14.3%)
Haemorrhage ($n=5$)	1/5 (20%)	0	4/5 (80%)
Image findings			
Focal single ($n=19$)	9/19 (47.4%)	0	10/19 (52.6%)
Focal multiple ($n=10$)	3/10 (30%)	0	7/10 (70%)
Heterotopia ($n=8$)	5/8 (62.5%)	0	3/8 (37.5%)
Reduced sulcation ($n=35$)	21/35 (60%)	1/35 (2.8%)	13/35 (37.2%)
Excessive sulcation ($n=10$)	2/10 (20%)	1/1 (10%)	7/10 (70%)
Cleft ($n=5$)	3/5 (60%)	0	2/5 (40%)
Diffuse lobar ($n=9$)	6/9 (66.7%)	0	3/9 (33.3%)
Diffuse hemispheric ($n=32$)	18/32 (56.25%)	2/32 (6.25%)	12/32 (37.5%)

the other hand, the highest rates of termination of pregnancy were in cases classified as vascular in origin ($n=6/7$, 85.7%) or radiologically classified as diffuse lobar ($n=6/9$, 66.7%).

3.2 | Neurological Outcomes

Neurological outcomes are summarised in Table 3, Figure 3 and Figure 4 and fully described in Table S2. Children ranged from 2 months to 8 years at the time of the most recent evaluation. Out of the 46 surviving infants, 25 (54.3%, 95% CI 39–69.1) had a normal or mildly delayed neurological development, and 21 (45.6%, 95% CI 30.9–61.0) had a moderately or severely delayed neurological development (Figure 3). The highest rate of normal or mildly abnormal postnatal neurodevelopment was in cases etiologically classified as dysgenesis/unknown ($n=9/12$, 75%; 95% CI 42.8–94.5). Congenital CMV infection had the worst neurological outcomes among the etiologies ($n=2/3$, 66.7%; 95% CI 9.4–99.2). Focal lesions had the best neurological outcomes among radiological findings ($n=5/6$, 83.3%; 95% CI 35.9–99.6; and $n=7/9$, 77.8%; 95% CI 40–97.2, multiple and single focal lesions, respectively). Interestingly, although diffuse lobar lesions had a relatively good outcome among radiological findings ($n=2/3$, 66.7%; 95% CI 9.4–99.2), diffuse hemispheric lesions had the worst postnatal outcomes ($n=1/8$, 12.5%; 95% CI 0.3–52.7) (Table 3).

4 | Discussion

4.1 | Main Findings

This study demonstrates that approximately 55% of the liveborn infants with an antenatally diagnosed cortical MCD have a normal or only mildly abnormal neurological outcome. The commonest presumed aetiology for these anomalies was either genetic or unknown, making up more than 80% of the included cases. The most frequent radiological (morphological) findings were reduced sulcation and diffuse hemispheric lesions, contributing about 60% of the cases, even though this classification was not mutually exclusive since two or more lesions could coexist.

4.2 | Strengths and Limitations

This study includes the largest cohort of antenatally diagnosed foetuses with MCD managed at referral FMU. One of the strengths of the present study is that, unlike previous publications, 84% of the cases had formal neurological follow-up. Moreover, the systematic PESCA framework was created for fetal MCDs, which categorises cases according to radiological findings and aetiology. Furthermore, periodic meetings were held between the three centres to discuss and align the classification of uncertain findings. Although much lower than in previous studies [3, 14, 15], the termination rate was still greater than 50%, reflecting the guarded prognosis provided to parents by clinicians citing the available postnatal literature. The termination rate is in fact the major limitation of this study as it is possible that the most severe or uncertain cases were terminated, making selection bias of outcomes a possibility that limits the generalizability of these findings. Moreover, although most of the cases had formal paediatric follow-up, there was a lack of standardised follow-up for these children postnatally, and there is a variable follow-up duration among the included children. Furthermore, the neurological outcome of the most recent cases is uncertain due to insufficient time to assess developmental milestones. In this same line, it was not possible to undertake a sensitivity

TABLE 3 | Cases classified by postnatal neurodevelopmental outcome according to aetiology and image findings. The total numbers and (percentages) are also shown. Percentages in brackets refer to the rate of cases in the single category.

	Normal/mild ($n=25$)	95% CI	Moderate/severe ($n=21$)	95% CI
Aetiology				
Genetic	12/26 (46.2%)	29.6–66.6	14/26 (53.8%)	33.4–73.4
Dysgenesis/Other	9/12 (75%)	42.8–94.5	3/12 (25%)	5.5–57.2
Infection	1/3 (33.3%)	0.8–90.6	2/3 (66.7%)	9.4–99.2
Vascular	1 (100%)	2.5–100	0	0–97.5
Haemorrhage	2/4 (50%)	6.8–93.2	2/4 (50%)	6.8–93.2
Image findings[a]				
Focal single	7/9 (77.8%)	40–97.2	2/9 (22.2%)	2.8–60
Focal multiple	5/6 (83.3%)	35.9–99.6	1/6 (16.7%)	0.4–64.1
Heterotopia	2/3 (66.7%)	9.4–99.2	1/3 (33.3%)	0.8–90.6
Reduced sulcation	4/9 (44.4%)	13.7–78.8	5/9 (55.6%)	21.2–86.3
Excessive sulcation	3/6 (50%)	11.8–88.2	3/6 (50%)	11.8–88.2
Cleft	1/2 (50%)	1.3–98.7	1/2 (50%)	1.3–98.7
Diffuse lobar	2/3 (66.7%)	9.4–99.2	1/3 (33.3%)	0.8–90.6
Diffuse hemispheric	1/8 (12.5%)	0.3–52.7	7/8 (87.5%)	47.4–99.7

[a]Cases that had more than one image finding were classified by the predominant lesion.

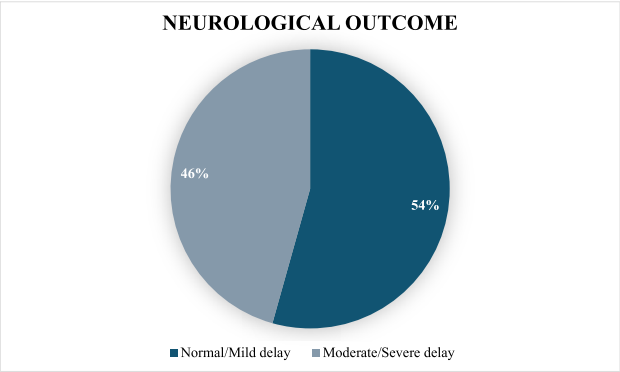

FIGURE 3 | Overview of the neurological outcome of the included foetuses.

analysis to exclude the impact of preterm birth on neurodevelopmental outcomes. However, as there were only three children who survived the neonatal period born before 34 weeks' gestation, it seems unlikely that prematurity was a significant confounder in this study. Lastly, the ideal study design would possibly be a prospective cohort study, but the rarity of the condition makes a retrospective cohort study the best option to report on neurological outcomes of fetal MCDs. It is possible that some MCDs were not suspected antenatally and therefore not imaged postnatally. In this light, it is fair to say that the prevalence of developmental delay is at most 50% but could be lower. The retrospective design, the high termination rate, and the variation in follow-up data limit the possibility of drawing robust, general prognostic conclusions applicable across all types of cortical malformations.

4.3 | Interpretation

A postnatal classification for MCDs has already been proposed based on presumed pathophysiological mechanism [15]. However, its utility is limited in the prenatal setting where cortical development is continuously evolving and the necessary focus on prognosis may be based on very limited data and frequently, solely on image findings. The prevalent terminology in the published literature was mainly variable from presumed aetiology (i.e., genetic), pathophysiological process (i.e., dysgenesis) or findings (i.e., lesions) from prenatal ultrasound/MRI imaging [7]. What happens in practice is that these descriptions are used interchangeably and confusingly to describe the very same MCD lesions [7]. Because of these limitations, a practical framework based on radiological (morphological) findings alone was developed to provide a simpler approach to postnatal diagnosis of MCDs, but such a system is not available for prenatal MCDs [16]. The PESCA framework proposed in this study makes a distinction between aetiology versus radiological findings, and would enable both comparison of data between similar cases and systematic evaluation of pregnancy outcomes (Figure 1). However, it is important to note that the heterogeneity of outcomes reported in this cohort, together with the acknowledged limitations, strengthens the importance of individualised, case-by-case counselling and the need for more robust data from prospective cohorts as the prognosis is strongly dependent on lesion type, associated findings, presumed aetiology, and genetic confirmation. The use of a more objective method of classification for these very heterogeneous and complex malformations can be extremely helpful in providing individualised counselling based on

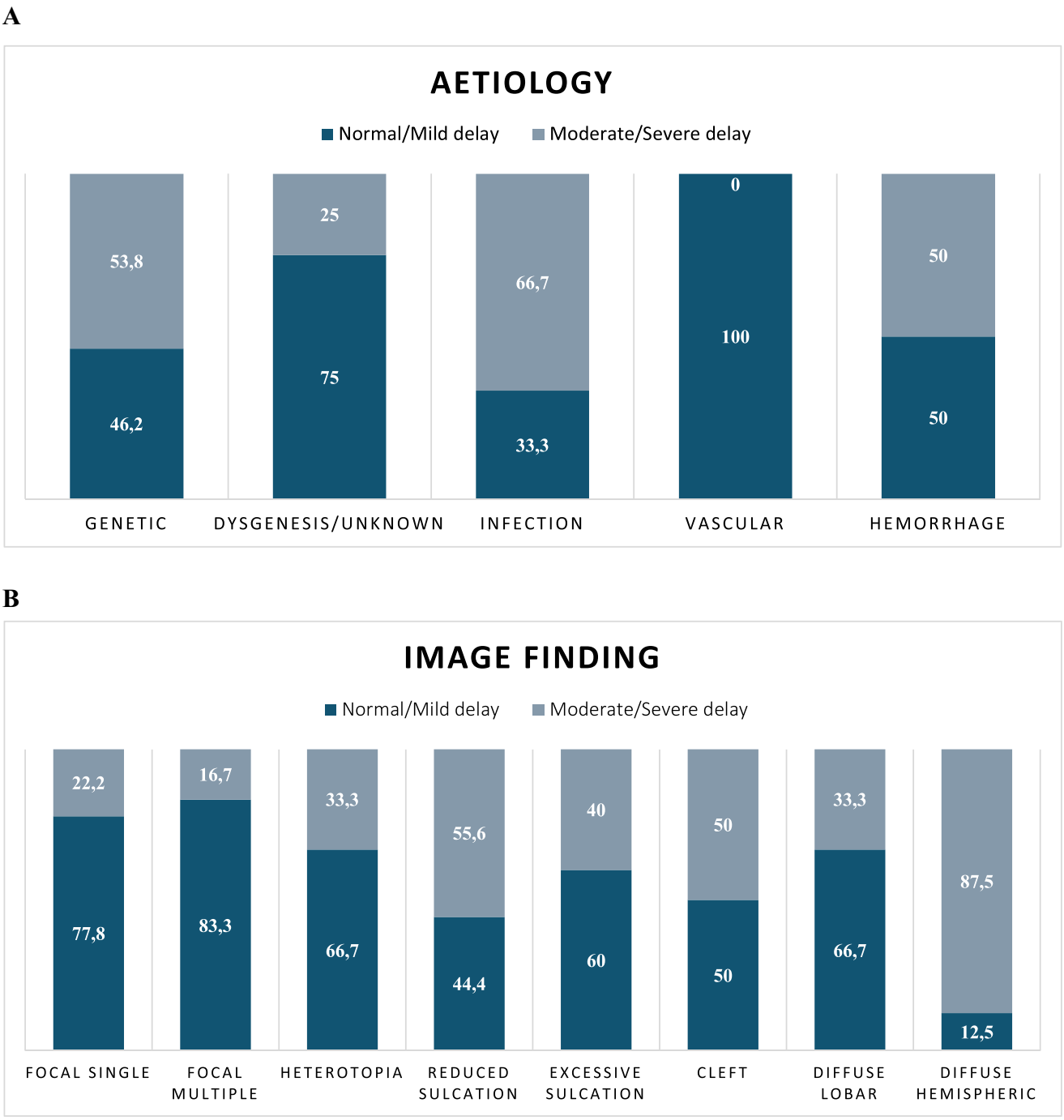

FIGURE 4 | Neurological outcome of included foetuses according to suspected aetiology (A) and image finding (B).

detailed imaging, suspected aetiology, and multidisciplinary interpretation. Future studies are needed in order to further develop the PESCA classification of MCDs and to provide further evidence which will improve the accuracy of prenatal counselling.

4.4 | Natural History

The overall livebirth rate in our study was over 40%, which is higher than in previously published works [3, 7, 17]. It is possible that the most severe cases were terminated during pregnancy, making selection bias of outcomes a possibility that would limit the generalisation of the findings of this study. The livebirth rate in this study varied significantly depending on the presumed aetiology of the lesion, from as low as 15% when the presumed aetiology was vascular to as high as 80% when the aetiology was haemorrhagic. The livebirth rate also varied substantially according to the ultrasound scan or MRI findings. Up to 70% of the pregnancies with a fetus diagnosed with an MCD with a pattern of excessive sulcation or focal multiple lesions were liveborn. Conversely, when the MCD was diffuse lobar, reduced sulcation, diffuse hemispheric, or grey matter heterotopia, less than 40% of the parents decided to continue with the pregnancy. These differences in livebirth rate according to the presumed aetiology or the imaging findings, which do not correlate with

the postnatal neurodevelopment, reflect the burden that prenatal diagnosis and counselling have on parental choices.

4.5 | Postnatal Outcome

There is significant variation in neurological outcome with the rate of normal or mildly abnormal neurological increasing from 12% for diffuse lobar changes up to more than 80% in the case of focal lesions (Table 3). Focal lesions (single or multiple) seemed to have the best postnatal outcomes with approximately 80% of the children having normal or mildly abnormal neurodevelopment. The latter group was made up mainly of cases of tuberous sclerosis and arachnoid cysts resulting in focal cortical remodeling [18–20]. Poor neurodevelopmental outcome in this group could be due to other genetic syndromes or associated lesions, which have a more guarded prognosis [21]. Diffuse hemispheric lesions have the worst neurological outcome, with only 12.5% of the children having either a normal or mildly abnormal neurological development. Conversely, 66.7% of the children with diffuse lobar lesions had normal neurodevelopment, which suggests that the more limited the lesion, the better the outcome. However, the numbers are small in the latter group ($n = 3$).

Fetal MCDs of infective aetiology had the worst postnatal outcomes, which is in line with published data [22–24]. Congenital CMV infection is the leading cause of sensorineural hearing loss and an important cause of neurodevelopmental delay in children and was also the main cause of congenital infection in our study [22–24]. Around half of the children with a genetic diagnosis had normal neurodevelopment and notably, when aetiology was uncertain, neurodevelopment was normal in 75% of the cases. This is likely to reflect relatively minor findings that have no or little impact on postnatal neurodevelopment, such as the cortical remodelling subsequent to an arachnoid cyst, or possibly an over-diagnosis. In addition to the 46 children who survived the neonatal period, there were six neonatal deaths, of which five had a confirmed genetic syndrome with a poor prognosis and one had a suspected malignant tumour. These six cases reflect the most severe facet of cortical malformations, which is concordant with the available literature [16, 25, 26].

Another important factor to consider for poor neurological development is prematurity, which in our cohort was 25% of the cases. However, among the children born < 37 weeks in our population who had a poor postnatal outcome and/or died, they all had an underlying condition justifying the outcome rather than the prematurity (Table S2).

5 | Conclusion

In the largest multicentre cohort study of fetal MCDs, we utilised a practical and workable framework that enables both comparison of data between centres and prospective counselling on the expected postnatal outcome. In our cohort, fetal MCDs have a better than previously expected postnatal and neurodevelopmental outcome that is related to both the etiological classification and radiological findings. Our results can help in structuring parental counselling and highlight the need for solid prospective data, which will ensure the provision of absolute risks for antenatally diagnosed fetal MCDs.

Author Contributions

S.A., F.K., P.F., A.D., E.d.P., E.B., M.M., and S.G. collected the data from the three centres and reviewed all the images. N.A.-C. and F.F. analysed the final dataset and wrote the first draft of the manuscript; A.B. and T.G. critically reviewed the manuscript; B.T. and A.F. planned the study, interpreted the results, and reviewed the first draft of the manuscript.

Acknowledgements

The authors have nothing to report.

Funding

The authors have nothing to report.

Ethics Statement

Data are reported according to the STROBE statement for reporting retrospective studies. The PESCA study was ratified by the Ethics Committee of Fondazione Policlinico Universitario Agostino Gemelli IRCCS (ID: 6713, 09/05/2024) and by the Ethics Committee of Azienda Ospedaliero Universitaria di Parma. As a retrospective study of routinely collected clinical data, the HRA online assessment tool confirmed exemption from requiring research ethics committee review in England.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Fetal Brain MRI protocol. **Table S2:** Included patients with extensive description of prenatal and postnatal radiological findings, suspected aetiology, pregnancy outcome and details about the neurological and postnatal outcome. Genetic testing details are also provided.