

BACKGROUND & OBJECTIVE

Stillbirth rates in England and Wales have plateaued at around 4.0 per 1,000 births, against a national ambition to halve them. RCOG, ACOG, RANZCOG and SOGC all identify examination of the placenta, cord and membranes as the single most useful element of perinatal death evaluation, yet reported diagnostic yield ranges from 11% to 65%. Lesions with a high recurrence risk include chronic histiocytic intervillitis (75-100%), chronic villitis (10-50%), vascular malperfusion (10-25%) and chorioamnionitis associated preterm birth(10-25%).

Objective To examine placental histopathology in pregnancies with adverse outcomes and its role in determining the cause of fetal or neonatal death

METHODS

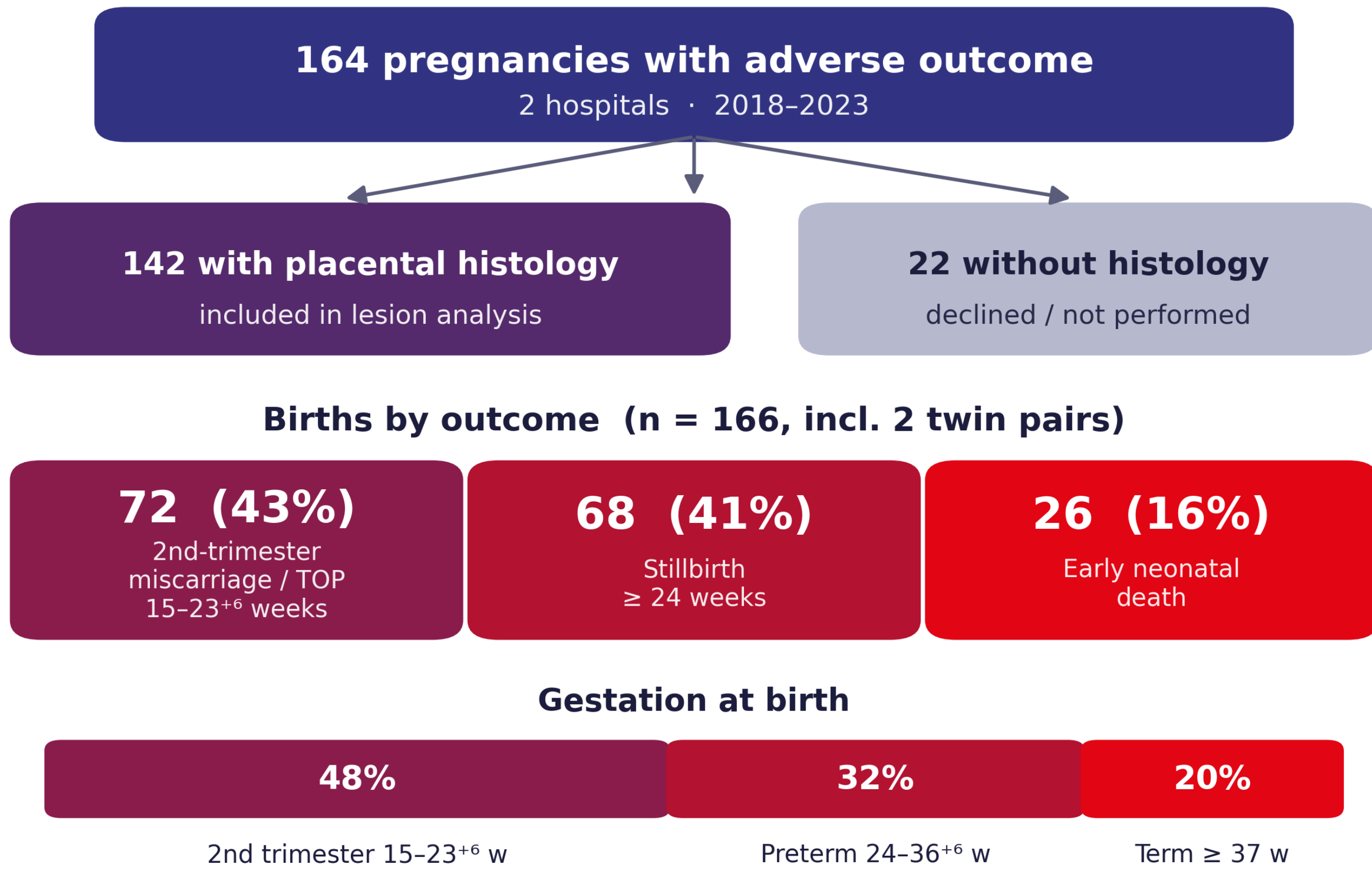
- Retrospective observational study across two sites — Epsom Hospital and St Helier Hospital — serving a multi-ethnic South-West London and Surrey population, 2018–2023
- All second-trimester losses ≥ 15 weeks, stillbirths and early neonatal deaths; congenital and genetic anomalies excluded to avoid confounding (n = 164)
- Placental histology, postmortem reports and maternal records reviewed by a single observer to minimise bias
- Data analysed qualitatively and quantitatively; placental findings categorised using established histopathological criteria

STUDY POPULATION

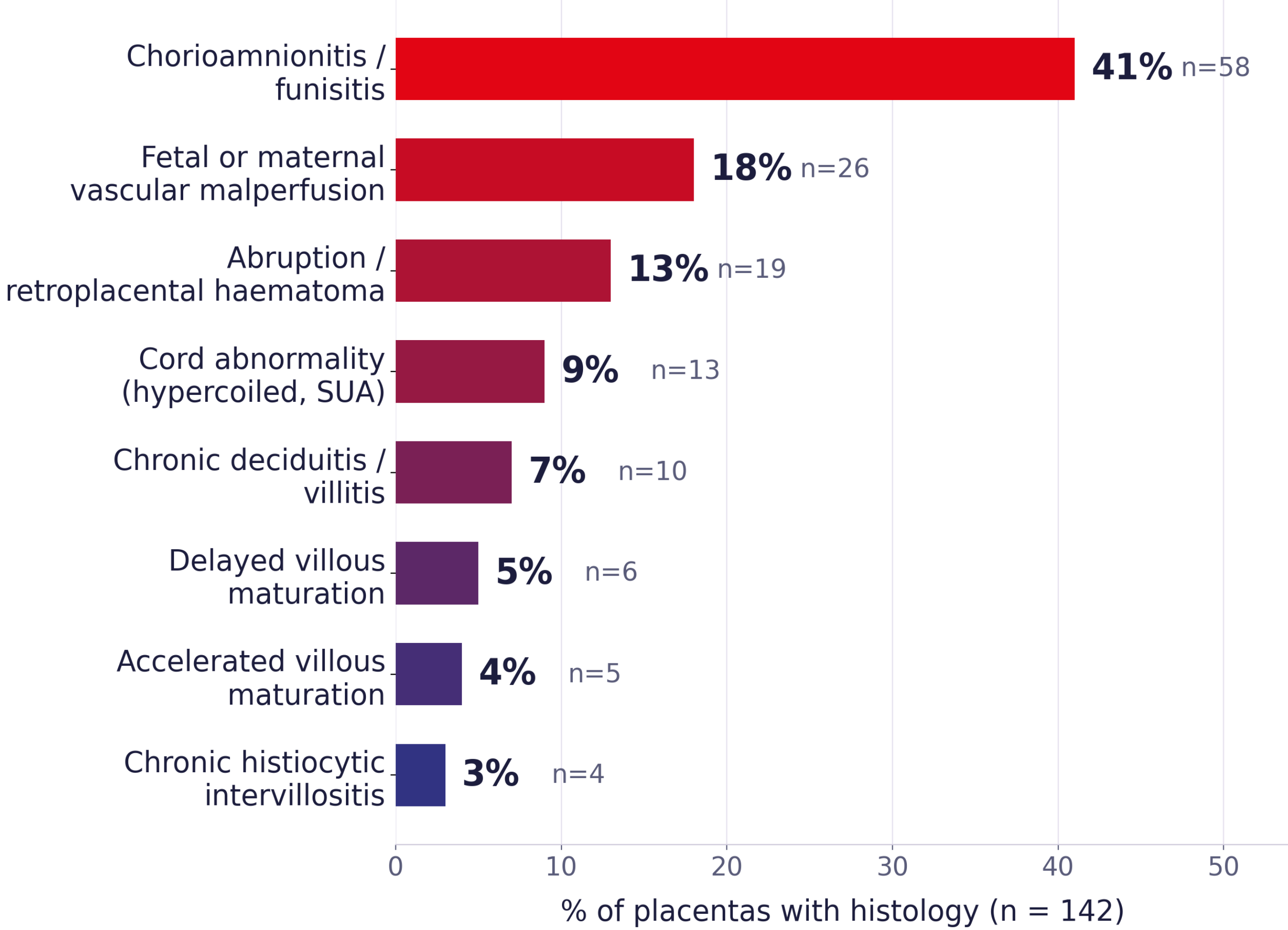
Characteristic	n	%
Age	< 35 years	109
	≥ 35 years	55
BMI	< 19	1
	19 – 25	65
	26 – 35	83
	> 35	15
Ethnicity	White	94
	South / SE Asian	32
	Black	22
	Mixed	16
Smoking	Current, former or vaping	19
Maternal	Gestational HTN / pre-eclampsia	5
	Gestational diabetes	8
	Pre-existing medical condition *	24
Previous loss	> 2 first-trimester miscarriages	9
	Any second-trimester loss	12

* Pre-existing medical conditions include chronic hypertension, hepatic fibrosis with congenital heart disease on rivaroxaban, fibroids > 5 cm, Factor V Leiden with / without protein S deficiency and history of DVT, NK+, hypothyroidism, glomerular sclerosis on tacrolimus, type 1 diabetes mellitus on insulin, psoriatic arthritis, systemic lupus erythematosus, immune thrombocytopenia.

STUDY COHORT

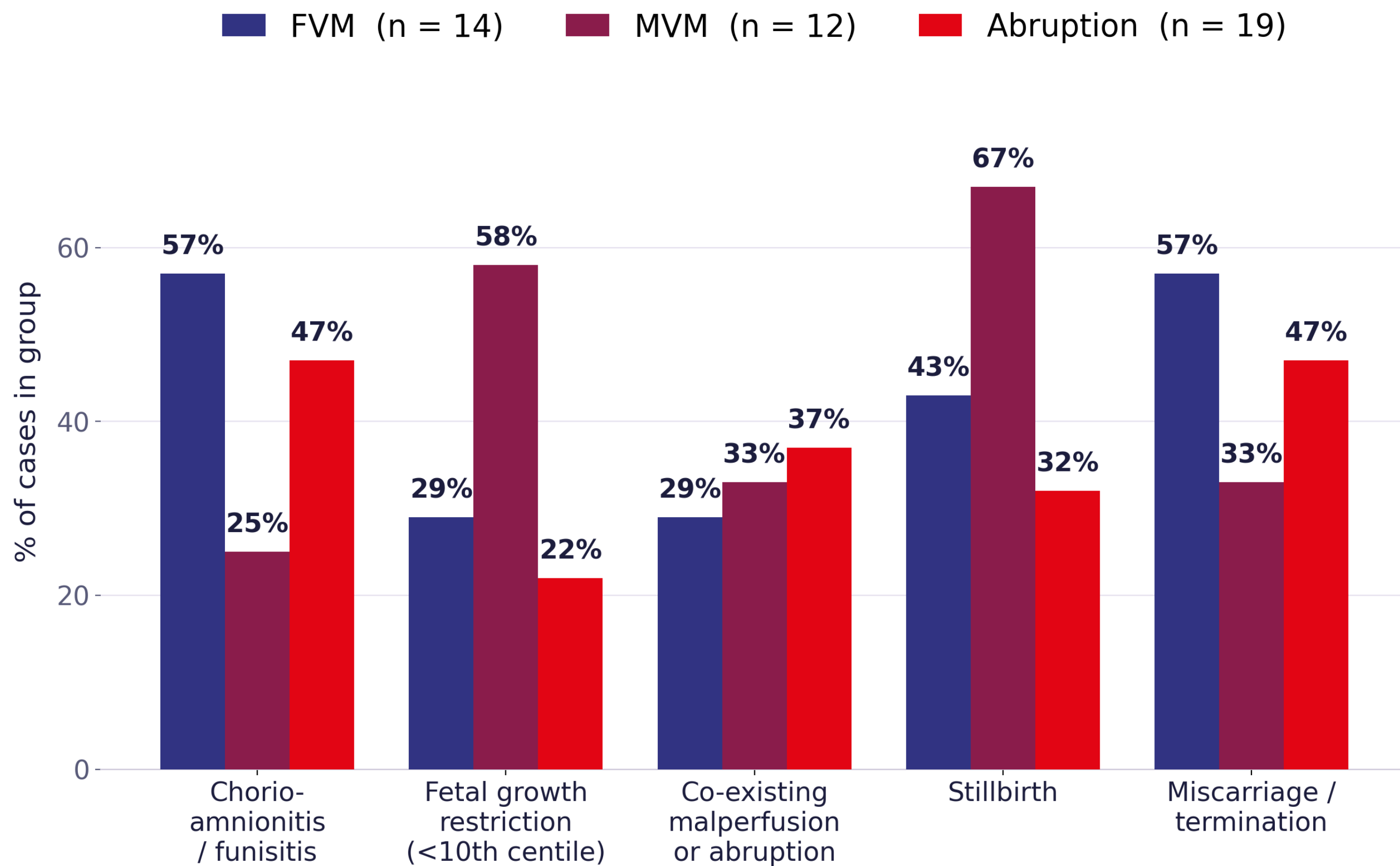


PLACENTAL LESIONS IDENTIFIED



Multiple lesions may co-exist within one placenta, so percentages do not sum to 100%. Histology was unavailable in 22 of the 164 cases.

PATTERNS OF ASSOCIATION



Fetal vascular malperfusion n = 14

An inflammatory phenotype. Acute chorioamnionitis with a fetal inflammatory response in 8/14 (57%) and hypercoiled cords in 3/14 (21%) against 4.9% cohort-wide. Isolated cases showed fetal thrombotic vasculopathy, velamentous cord insertion and gestational diabetes.

Maternal vascular malperfusion n = 12

An ischaemic, growth-restricted phenotype. Small placentas in 5/12 (42%) versus 4.3% without MVM, and fetal growth restriction in 7/12 (58%) with all fetuses with stillbirth after 31 weeks being growth restricted . Associated with chronic hypertension (n = 3), SLE (n = 1) and early-onset pre-eclampsia at 19 weeks (n = 1).

Abruption / retroplacental haematoma n = 19

A mixed phenotype. Infection in 9/19 (47%), co-existing fetal or maternal malperfusion in 7/19 (37%) and growth restriction in 4/19 (22%). The cohort's only thrombophilia — Factor V Leiden with protein S deficiency — presented with abruption.

Chronic histiocytic intervillitis

4 cases · all losses between 16 and 21 weeks

Three of the four women were South Asian. Two had markedly low PAPP-A (0.19 and 0.06 MoM) and screened positive for trisomy 21 with normal invasive or cell-free testing. Two fetuses were growth-restricted. One woman was a known recurrent case with two previous intrauterine deaths at 18–21 weeks.

Notable rare findings

Breus' mole — 26-year-old South Asian woman had an antepartum hemorrhage and spontaneous delivery at 21 weeks, after a previous loss at 22 weeks associated with abruption. Placental examination revealed a massive subchorionic thrombohaematoma.

Umbilical cord aneurysm — with thrombosis and rupture alongside a single umbilical artery, causing intrauterine death at 34 weeks, in a woman with gestational diabetes.

CONCLUSIONS

- Placental examination remains one of the most important investigations after perinatal death — it is the only way to identify conditions such as chronic histiocytic intervillitis, present in **3%** of the placentas examined.
- Chorioamnionitis was the commonest finding (**41%**), but as it may follow rather than cause fetal death, the vascular malperfusion seen in **18%** and abruption in **13%** carried the greater diagnostic weight in our cohort.
- Lesions with a high recurrence risk — chronic histiocytic intervillitis (3%), chronic villitis (7%) and vascular malperfusion (18%) — were found in **around a quarter** of the placentas examined; identifying these could guide targeted surveillance and preventative strategies in subsequent pregnancies.
- A significant proportion of cases remain without a specific diagnosis — the priority for future research, alongside uniform terminology and standardised classification.

*REFERENCES

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- Redline, R. W., Ravishankar, S., Bagby, C. M., Saab, S. T., & Zarei, S. (2021). Four major patterns of placental injury: a stepwise guide for understanding and implementing the 2016 Amsterdam consensus. In *Modern Pathology* (Vol. 34, Issue 6, pp. 1074–1092). Springer Nature. <https://doi.org/10.1038/s41379-021-00747-4>