

Unveiling Hidden Mortality in Prenatally Diagnosed Trisomy 21: A Cohort Study of 30 Fetuses

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1 INTRODUCTION

- Trisomy 21 is the most common antenatal aneuploidy diagnosis, affecting approximately 0.5–0.7% of pregnancies.
- Postnatal literature reports relatively stable livebirth mortality of 1.4–3.6%, attributed largely to recognised comorbidities (congenital heart disease, gastrointestinal defects).
- Substantial background intrauterine lethality persists in continuing pregnancies and rises with increasing nuchal translucency thickness.
- Livebirth-anchored statistics may therefore under-represent true mortality risk — much of it “hidden” from standard registries.

2 AIM

To quantify **hidden mortality** in a prenatally diagnosed trisomy 21 cohort and to determine whether antenatal ultrasound findings predict adverse outcome.

3 METHODS

- Retrospective cohort of 30 fetuses with trisomy 21 confirmed by invasive testing.
- Five-year study period at a single tertiary fetal medicine unit.
- Review of maternal demographics, detailed ultrasound, fetal echocardiography, serial growth assessment and pregnancy outcome.
- Outcomes classified as livebirth, termination of pregnancy, intrauterine fetal death (IUFD), early neonatal death, or unknown.

OPERATIONAL DEFINITION

Hidden mortality — IUFD or early neonatal death occurring as a complication of the disease itself, rather than explained by a structural anomaly severe enough to be lethal in isolation.

4 RESULTS

Table 1. Cohort characteristics and principal outcomes (n = 30).

Parameter	Value
Fetuses with confirmed trisomy 21	30
Method of diagnosis	Invasive testing
Study period	5 years
Structural anomalies present	15/30 (50.0%)
Hidden mortality	8/30 (26.7%)
Background population prevalence	0.5–0.7%

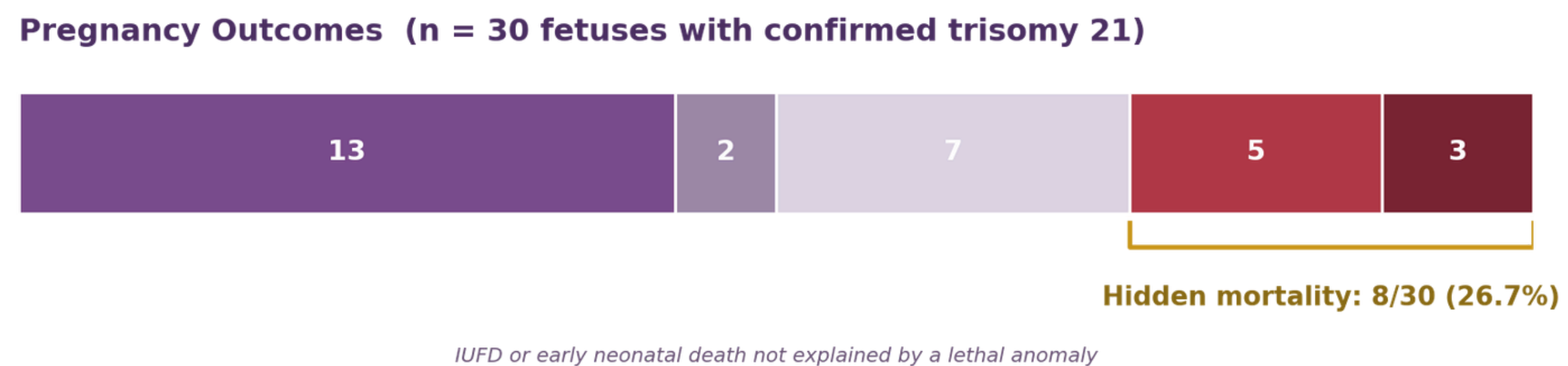


Figure 1. Distribution of pregnancy outcomes (n = 30). Bracket denotes hidden mortality — IUFD (n = 5) and early neonatal death (n = 3) not explained by a lethal anomaly.

26.7% hidden mortality

Eight of 30 fetuses died without a lethal structural explanation.

RESULTS (continued)

Table 2. Pregnancy outcomes, n (%).

Outcome	n (%)
Livebirth	13 (43.3)
Termination of pregnancy	2 (6.7)
Unknown (delivered elsewhere)	7 (23.3)
Intrauterine fetal death	5 (16.7)
Early neonatal death	3 (10.0)
Hidden mortality (combined)	8 (26.7)

Table 3. Subtle antenatal findings, n (%).

Finding	n (%)
Transient hydrops / effusions	11 (37)
Borderline fetal growth restriction	3 (10)
Abnormal fetal heart rate patterns	2 (7)

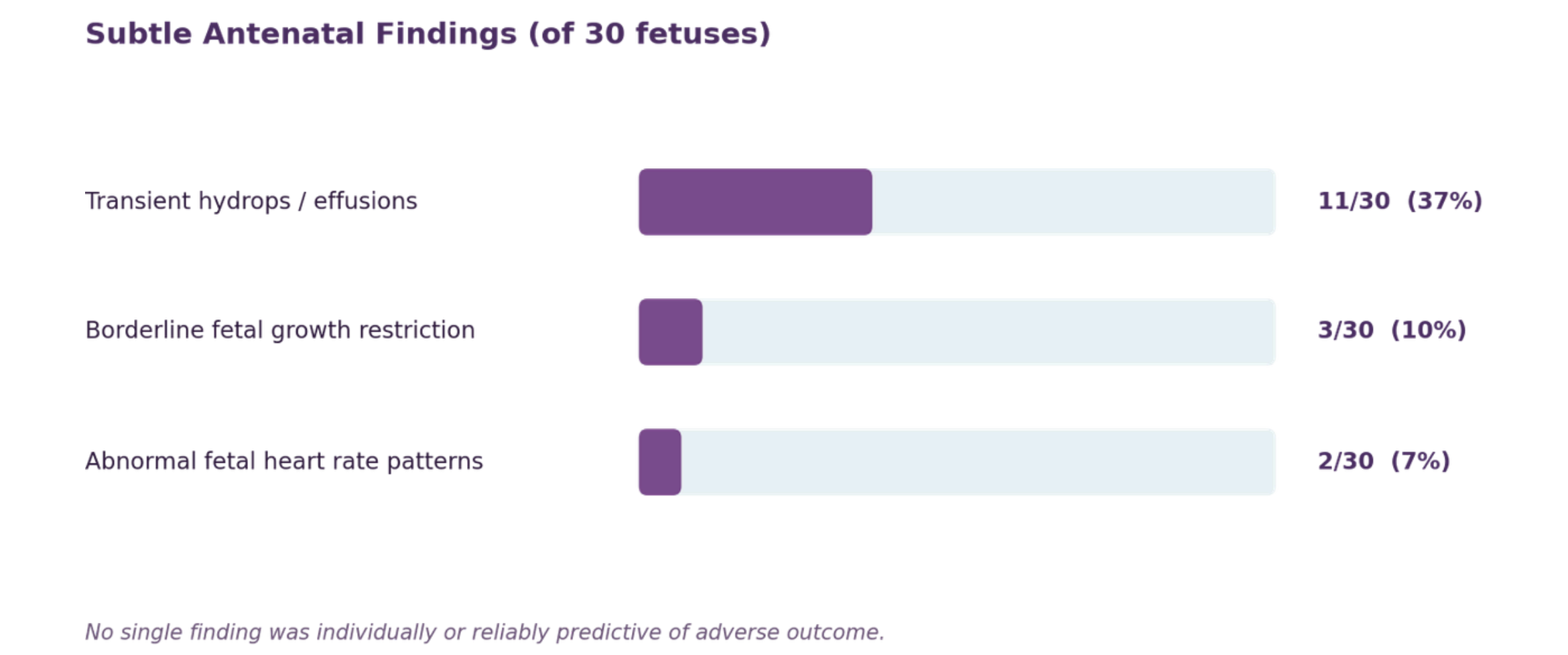


Figure 2. Prevalence of subtle antenatal findings across the cohort. No single finding was individually or reliably predictive of adverse outcome.

5 DISCUSSION

- The observed 26.7% hidden mortality rate aligns with the background intrauterine lethality previously described for trisomy 21 (up to 30–40% between 12 weeks and term).
- A 50% structural anomaly prevalence is consistent with reported postnatal CHD and gastrointestinal defect rates, yet hidden-mortality cases were not reliably explained by major anomalies alone.
- Subtle findings — transient effusions, borderline growth restriction — may reflect early cardiovascular or lymphatic compromise rather than acting as distinct, actionable predictors.
- Livebirth-anchored outcome statistics therefore likely understate the true mortality risk conferred by a prenatal trisomy 21 diagnosis
- Hence, fetal echocardiography is essential in every fetus diagnosed with Trisomy 21

6 CONCLUSION

- A significant proportion of trisomy 21 fetuses experience hidden mortality not explained by lethal anomalies.
- Increased surveillance — longitudinal growth assessment and functional fetal monitoring — may improve risk stratification and counselling.
- Further prospective, multicentre studies are needed to identify reliable predictors of adverse outcome.

REFERENCES

- de Groot-van der Mooren MD, et al. Neonatal mortality and morbidity in Down syndrome in the time of prenatal aneuploidy testing. Eur J Pediatr. 2023;182:319–328.
- Hyett JA, et al. Intrauterine lethality of trisomy 21 fetuses with increased nuchal translucency thickness. Ultrasound Obstet Gynecol. 1996;7:101–103.