

BACKGROUND

Maternal hypertension has been associated with congenital heart disease¹. However, there remain questions about the broader range of birth defects associated with hypertension and differences in risk among offspring of women with pre-gestational vs. gestational diagnosis. We evaluated associations using data from one of the world's largest population-based active birth defects surveillance systems and a novel statistical approach.

PURPOSE

To determine prevalence of birth defects associated with pre-gestational and gestational hypertension.

METHODS

We performed a phenome-wide association study (PheWAS) to evaluate risk of a broad range of birth defects among offspring of women with hypertension, overall and stratified by timing of diagnosis, among all livebirths (N>6,500,000) and birth defects cases regardless of pregnancy outcome (N>290,000) in Texas during 2005-2015. We randomly divided data into discovery (60%) and replication (40%) partitions and used Poisson regression to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) for any birth defect and 130 specific defects with >10 cases diagnosed among exposed offspring. Multivariable models were adjusted for maternal age, race/ethnicity, education, previous livebirths, and BMI. Birth defects associated with maternal hypertension at a Bonferroni-adjusted threshold ($p < 3.8E-4$) in discovery were re-tested in replication; those associated with maternal hypertension at $p < 0.05$ and with the same direction of effect were considered statistically significant. To maximize precision, we estimated PRs and 95% CIs for replicated defects in the pooled dataset.

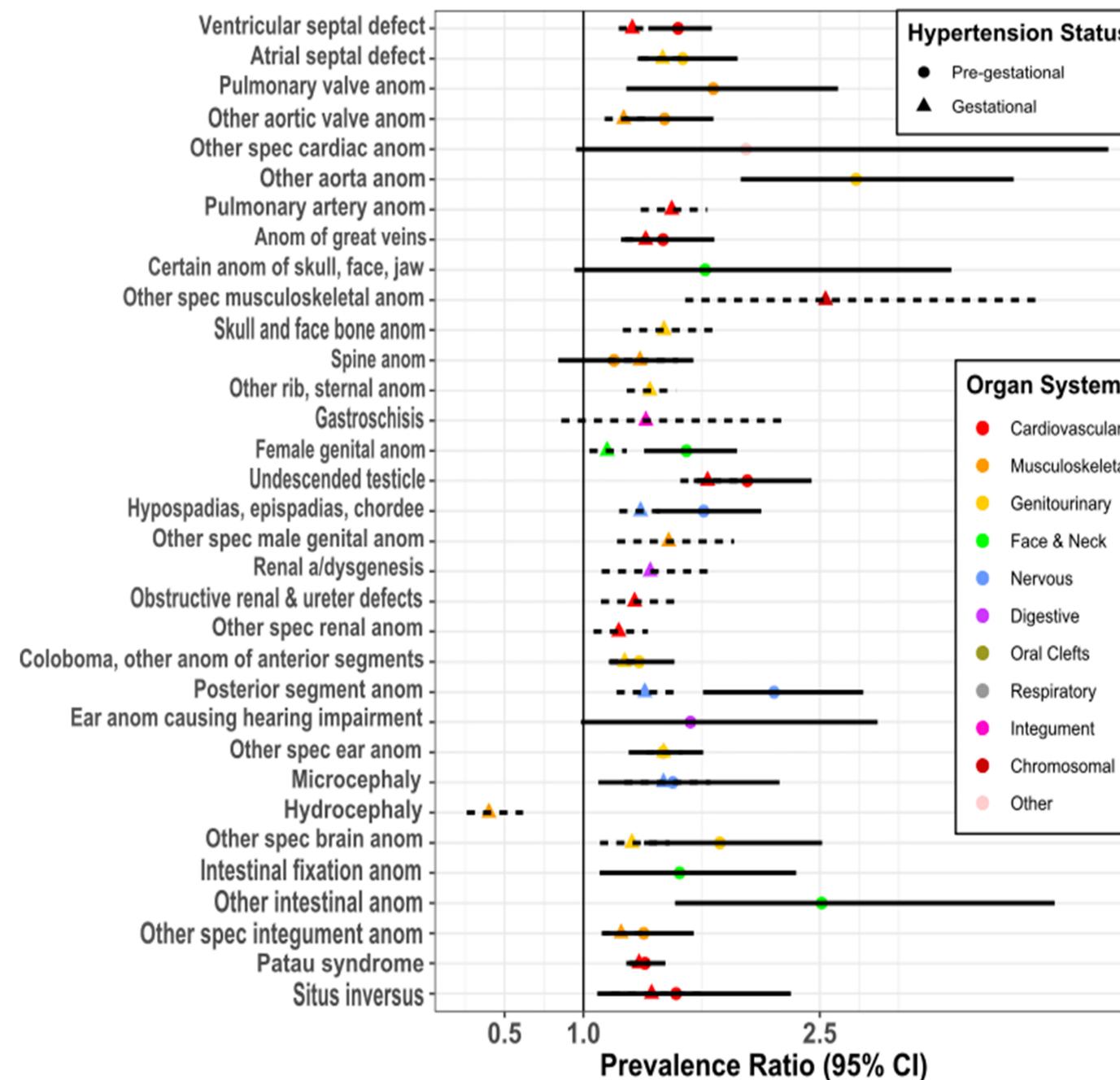


Fig 1: Prevalence ratios for associations between pre-gestational and gestational hypertension and birth defects, which are identified and color-coded by organ system. Only birth defect associations that replicated are included in this figure.

RESULTS

Maternal hypertension was associated with:

- increased prevalence of any birth defect (PR 1.32, 95% CI 1.30-1.34)
- non-isolated birth defects (PR 1.38, 95% CI 1.35-1.40)
- 27 specific birth defects, including novel (e.g., microcephaly) and previously reported phenotypes (e.g., hypospadias, ventricular septal defects).

Pre-gestational compared to gestational hypertension was a stronger risk factor for:

- any birth defect (PR 1.38, 95% CI 1.34-1.43 vs. 1.28, 95% CI 1.26-1.30)
- non-isolated birth defects (PR 1.47, 95% CI 1.41-1.54 vs. 1.35, 95% CI 1.32-1.38)
- several specific birth defects (Figure 1)

CONCLUSION

Our findings suggest that maternal hypertension is associated with a broad range of structural birth defects across organ systems. Nearly 30 structural birth defects were differentially associated with pre-gestational and gestational hypertension. Increased risk of birth defects may be a result of reduced uteroplacental perfusion². Further studies are needed to elucidate the genetic and environmental factors underlying these associations.

REFERENCES

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