

Thyroid Scintigraphy in the Diagnosis of Congenital Hypothyroidism (CH)

Revisiting The Frequency of Dysmorphogenesis

Chris Worth¹, Indi Banerjee¹, Beverly Hird², Leena Patel¹, Lesley Tetlow²

¹Dept Paediatric Endocrinology, Royal Manchester Children's Hospital, Manchester, UK

²Dept Clinical Biochemistry, Manchester University NHS Foundation Trust, UK

BACKGROUND

- Newborn Bloodspot Screening (NBS) for CH relies on Blood Spot (BS) Thyroid Stimulating Hormone (TSH) measurement on day 5 of life.
- Diagnostic confirmation requires plasma free thyroxine (fT4) and TSH levels.
- Technetium thyroid scintigraphy can be used to define size and location of the thyroid gland.

AIMS

To investigate the utility of scintigraphy to establish the cause of CH and impact on clinical management.

SUBJECTS

Newborns referred to a regional centre 2007 to 2017 on the basis of

- initial screening BS TSH ≥ 20 mU/L OR
- second/subsequent sample ≥ 8 mU/L following a borderline result

METHODS

Scintigraphy and corresponding BS TSH, plasma TSH and plasma fT4 levels were retrospectively reviewed. The cause of CH was categorised as

- Dysmorphogenesis
- Dysplasia
- Ectopia.

RESULTS

- From 534,783 newborns screened by NBS, 418 newborns were referred for possible CH. Of these, 303 were confirmed to have CH and had scintigraphy [Figure 1].
- The cause of CH was dysmorphogenesis, dysplasia and ectopia in 46%, 26% and 28% respectively.
- Median BS TSH was lower in dysmorphogenesis than in ectopia and dysplasia (23 vs 106 vs 172 mU/L, $p < 0.001$) [Figure 2].
- Plasma TSH showed similar differences.
- Median fT4 levels (pmol/L) were higher in dysmorphogenesis than in ectopia and dysplasia (12.1 vs 9.6 vs 4.0 pmol/L, $p < 0.001$).
- Initial median levothyroxine (LT4) replacement doses (micrograms/day) were 25, 37.5 and 37.5 ($p < 0.001$) respectively, consistent with the severity of thyroid dysfunction in each group.
- LT4 dose correlated independently with fT4 levels between dysmorphogenesis and ectopia (ANCOVA $p = 0.01$, $R^2 = 0.41$ for model), but not between dysplasia and ectopia ($p = 0.12$) or between dysmorphogenesis and dysplasia ($p = 0.98$), suggesting diagnosis-specific influence of scintigraphy on initial treatment dose.

Figure 1

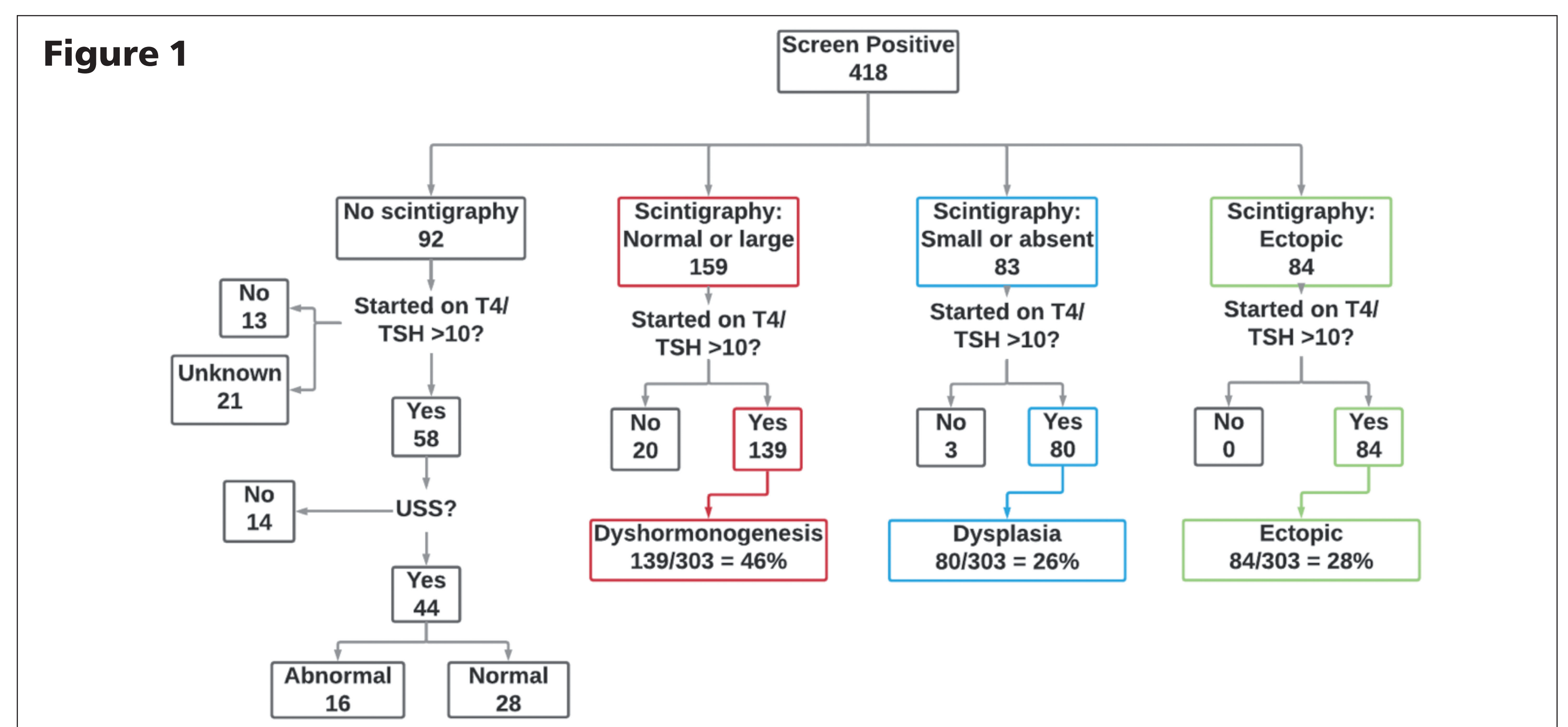
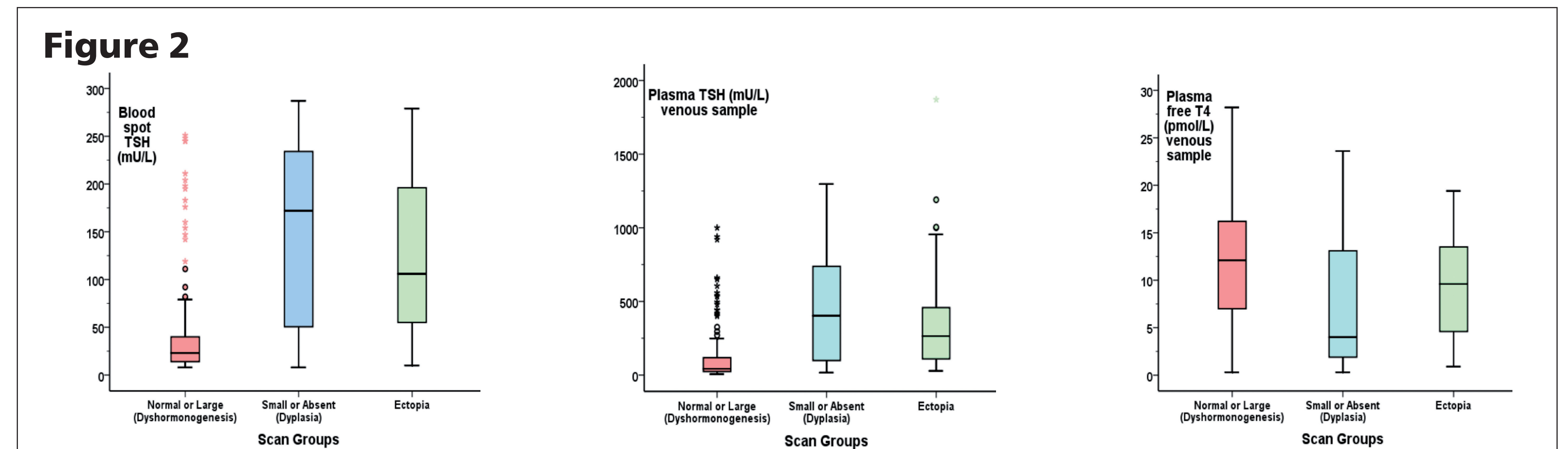


Figure 2



REFERENCES

1. LaFranchi, S. (2011). Approach to the Diagnosis and Treatment of Neonatal Hypothyroidism. The Journal of Clinical Endocrinology & Metabolism, 96(10), pp.2959-2967.
2. Narumi, S., Muroya, K., Asakura, Y., Achi, M. and Hasegawa, T. (2011). Molecular Basis of Thyroid Dysmorphogenesis: Genetic Screening in Population-Based Japanese Patients. The Journal of Clinical Endocrinology & Metabolism, 96(11), pp.E1838-E1842.
3. Nicholas, A. et al (2016). Comprehensive Screening of Eight Known Causative Genes in Congenital Hypothyroidism With Gland-in-Situ. The Journal of Clinical Endocrinology & Metabolism, 101(12), pp.4521-4531.

CONCLUSIONS

- Thyroid scintigraphy and biochemistry demonstrate CH is associated with dysmorphogenesis in 46%, dysplasia in 26% and ectopia in 28% of infants.
- This is contrary to widely held belief that dysmorphogenesis accounts for only 10-15% of all CH.¹
- Scintigraphy identifies ectopia which might be incorrectly classified as dysplasia by ultrasound scan.
- Distinguishing dysmorphogenesis from ectopia and dysplasia is crucial for
 1. initial levothyroxine dosage and long-term clinical management
 2. genetic counselling for families
 3. testing for pathogenic genetic causes.^{2,3}

