2017 ATA guidelines recommend using trimester and method specific TSH reference intervals defined from a local population. These reference intervals however, are scarce. We aimed to establish intervals indirectly by mining data from our pathology database.

Methods

TSH, fT4 and FT3 measured by the Abbott Architect method from pregnant women over 2014-2016 were extracted from the Douglass Hanly Moor Pathology database together with gestational age and clinical notes, which have been routinely typed in to the laboratory information system by the data entry staff for each episode. Gestational age is recorded as given by the doctor or auto-calculated from EDD or LMP. Episodes with history of thyroid disease, positive thyroid auto-antibodies, pregnancy-related complications or TSH being markedly abnormal were excluded. The manufacturer’s quoted reference interval for non-pregnant women was 0.35-4.94 mU/L for TSH, 9.0-19.0 pmol/L for FT4 and 3.6-5.7 pmol/L for FT3.

Microsoft Access 2013 was used for Keyword search, SPSS version 24 for statistical analysis and MedCalc for Box-and-Whisker plots. The reference intervals are reported as 2.5th and 97.5th for TSH (non-Gaussian) and mean ± 2SD for FT4 and FT3 (Gaussian).

Gestational age partitioning: Early trimester (T) 1: 4-6 weeks; late T1: 7-13 weeks; T2: 14-27 weeks; T3: ≥28 weeks.

Results

Of 91,960 episodes from 64,221 women, 30,240 were used in the final analysis. 61,720 episodes (67.1%) were removed:

- Exclusion Category: Criteria and Keywords used
- Thyroid disease or treatment: Hypothyroid, hyperthyroid, Graves, Hashimoto’s, pit disease, goitre, thyroidectomy, on thyroxine, T4, T3, PTU, CBZ, etc.
- Gestational age unclear: Gestational week, LMP or EDD not provided
- Multiple TTF’s: More than one test during the same pregnancy
- Diabetes/GDM: GDM, T1D, T2D, diabetes, insulin, metformin, etc.
- IVF or Pregnancy complications: IVF, miscarriage, PV bleeding, etc.
- Thyroid Antibodies: Raised antibodies
- Twin Pregnancy: Twin
- Possibly post-partum: Gestational age ≥39/40
- Biochemically hyperthyroid: Suppressed TSH with markedly raised fT4 ± FT3
- Intercurrent illness: Unwell, diarrhoea, abdo pain, etc.
- Hypothyroid: TSH>10 mU/L

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Discussion

The Abbott Architect TSH upper limit in late T1 (2.69 mU/L) is much lower than both the 2017 ATA cut-off of 4.0 mU/L recommended when the trimester and method specific intervals are unavailable and the manufacturer’s non-pregnant upper limit of 4.94 mU/L. Of those data included in late T1 (n=11,556), the flag rate for elevated results using each of the above TSH cut-offs would be 2.5% (n=287), 0.4% (n=45) and 0.1% (n=16), respectively.

Figure 1 shows the distribution of data used for establishing reference intervals for TSH, FT4 and FT3 in (a) early T1 (4-6 weeks), late T1 (7-13 weeks), T2 (14-27 weeks) and T3 (≥28 weeks) of gestation. TSH distributions were non-Gaussian in all the partitions and a left shift was observed in 7-13 weeks of gestation. The distributions of FT4 and FT3 are relatively Gaussian. A left shift in FT4 was observed in T2 and T3.

Figure 2 shows box-and-whisker plots of the data used for TSH, FT4 and FT3 reference intervals in 4-6, 7-13, 14-27 and ≥28 weeks of gestation. The central box represents the values for the lower to upper quartile (25th to 75th percentile). The middle line represents the median. Values below and above the horizontal lines are outliers according to Tukey’s outlier test. Red dots: far outliers.

Table. Gestational age-specific and population-specific TSH, FT4 and FT3 reference intervals for the Abbott Architect method by local data mining. (The 2.5th – 97.5th intervals for FT4 and FT3: mean±2SD to mean±2SD)