

Trimester-Specific Reference Intervals for Thyroid Hormone Assays on the Abbott ARCHITECT® Analyzer

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Abstract (revised)

Proper maternal thyroid function is important for the health of both the mother and developing child, particularly during the first trimester. Elevated maternal thyroid stimulating hormone (TSH) and thyroid peroxidase antibodies (TPO-Ab) have been associated with a variety of adverse pregnancy outcomes, including increased risk for pre-term birth, post-partum thyroid disease, and impaired neuropsychological development in the child. Pregnancy produces profound physiologic changes in the mother, which in turn complicates the interpretation of maternal thyroid function tests. For this reason, the U.S. National Academy of Clinical Biochemistry (NACB) recommends, "trimester-specific reference intervals should be used when reporting thyroid test values in pregnant women". The objective of our study was to establish trimester-specific reference intervals for thyroid hormone assays on the Abbott ARCHITECT system. Serum samples were obtained from pregnant women as part of routine antenatal testing. These samples were then tested for TSH, free thyroxine (FT4), total thyroxine (TT4), free triiodothyronine (FT3), total triiodothyronine (TT3), TPO-Ab and thyroglobulin antibodies (Tg-Ab) using the Abbott ARCHITECT analyzer. Samples with a positive TPO-Ab and/or Tg-Ab test were excluded. TSH data were log-transformed for analysis. Trimester specific mean, and 2.5th – 97.5th percentile ranges for each analyte are reported below:

	Trimester, Median (2.5th – 97.5th)		
	First	Second	Third
TSH (mIU/L)	1.04 (0.086 – 2.841)	1.02 (0.18 – 2.81)	1.14 (0.30 – 2.92)
	N = 788	N = 529	N = 502
Free T4 (pmol/L)	13.79 (10.48 – 18.31)	12.17 (9.49 – 15.87)	11.10 (8.57 – 13.65)
	N = 796	N = 530	N = 504
Total T4 (nmol/L)	110.6 (71.3 – 171.3)	134.8 (94.3 – 183.3)	136.7 (93.9 – 194.0)
	N = 793	N = 530	N = 503
Free T3 (pmol/L)	4.67 (3.51 – 6.25)	4.48 (3.39 – 5.87)	4.27 (3.31 – 5.62)
	N = 797	N = 530	N = 504
Total T3 (nmol/L)	1.78 (1.24 – 2.75)	2.15 (1.42 – 3.21)	2.19 (1.35 – 3.19)
	N = 797	N = 530	N = 504

Elevated maternal TSH (i.e., >97.5th trimester-specific percentile) was found in 5.2%, 4.2% and 2.5% of women in the first, second and third trimesters, respectively. The prevalence of a positive TPO-Ab and/or Tg-Ab result was 21.4%, 19.8% and 15.7% for each trimester. Based on our study, we have established trimester-specific reference intervals for the ARCHITECT thyroid panel that will aid in the interpretation of maternal thyroid function tests during pregnancy. In addition, our data show a significant prevalence of elevated TSH and TPO-Ab in this population and suggest screening of pregnant women for thyroid dysfunction may be warranted.

Background

Proper maternal thyroid function during pregnancy is important for the health of the mother and developing child.

- Maternal thyroid dysfunction has been associated with adverse outcomes such as increased risk for pre-term birth, post-partum thyroid disease, miscarriage and abnormal neuropsychological development of the child.
- To ensure optimal maternal/fetal health, it is important to understand maternal thyroid status during pregnancy.

Pregnancy results in significant physiologic changes that profoundly affect maternal thyroid function.

- For these reasons, the U.S. National Academy of Clinical Biochemistry (NACB) recommend trimester-specific reference intervals be used to interpret thyroid function tests in pregnant women.

The objective of our study was to establish trimester specific reference intervals for thyroid assays on the Abbott ARCHITECT *i2000*_{SR}.

Materials and Methods

Serum samples were obtained from pregnant women as part of routine antenatal testing.

Samples were then tested for TSH, free thyroxine (FT4), total thyroxine (TT4), free triiodothyronine (FT3), total triiodothyronine (TT3), antibodies to thyroid peroxidase (TPO-Ab), and antibodies to thyroglobulin (Tg-Ab). All testing was performed using the Abbott ARCHITECT *i2000*_{SR}.

Reference intervals (2.5th to 97.5th percentiles) were calculated using antibody negative specimens. TSH data were log-transformed for analysis.

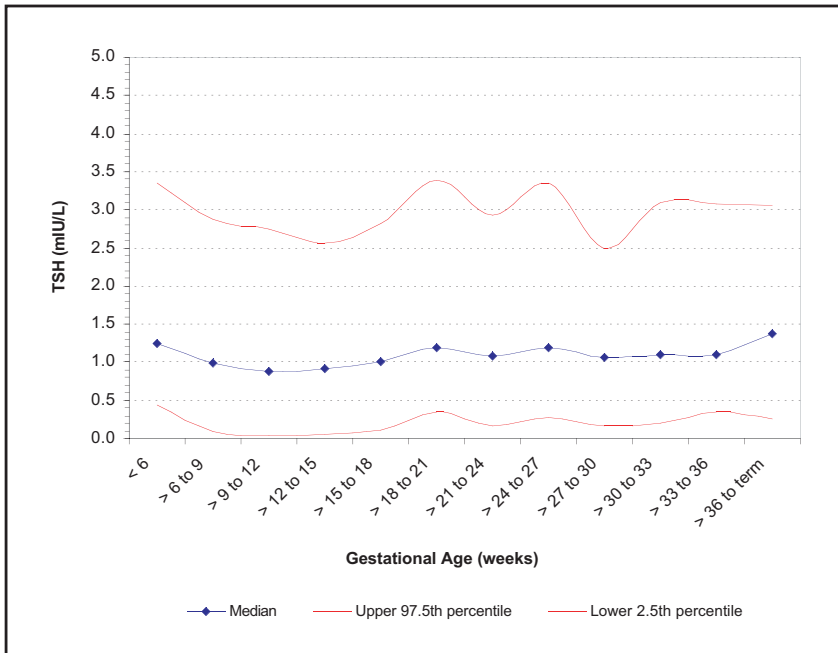
Prevalence of abnormal tests (i.e., outside gestational age-specific reference intervals) was then determined.

Study Population

Trimester	N	Median Gestational Age (weeks)	TPO-Ab and/or Tg-Ab Positive N
First (0 to 12 weeks)	1014	7.6	217 (21.4%)
Second (>12 to 24 weeks)	661	16	131 (19.8%)
Third (>24 weeks to term)	598	32	94 (15.7%)
Overall	2273	13	442 (19.4%)

Results

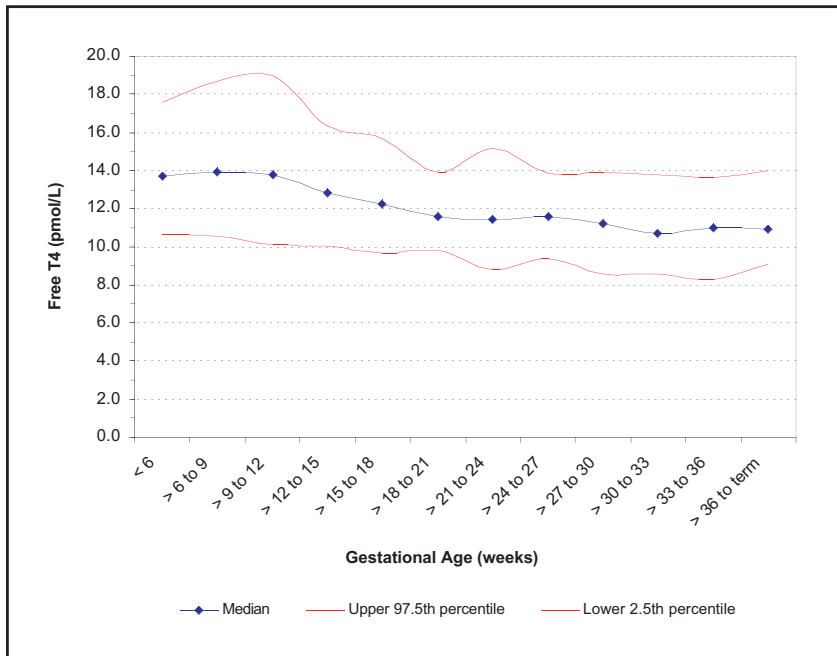
TSH



TSH (mIU/L)					
Gestational Age	N	Mean	Median	2.5th	97.5th
1st trimester	788	0.8638	1.0387	0.0861	2.8410
≤6 weeks	210	1.1900	1.2400	0.4306	3.3507
>6 to 9 weeks	294	0.8077	0.9869	0.0840	2.8782
>9 to 12 weeks	284	0.7300	0.8734	0.0300	2.7490
2nd trimester	529	0.9352	1.0201	0.1755	2.8147
>12 to 15 weeks	240	0.8188	0.9142	0.0605	2.5654
>15 to 18 weeks	96	0.9527	0.9996	0.1096	2.8187
>18 to 21 weeks	86	1.1561	1.1902	0.3502	3.3815
>21 to 24 weeks	107	1.0448	1.0808	0.1566	2.9281
3rd trimester	502	1.1130	1.1375	0.2967	2.9189
>24 to 27 weeks	97	1.1796	1.1869	0.2728	3.3455
>27 to 30 weeks	89	0.9772	1.0652	0.1687	2.4874
>30 to 33 weeks	91	1.0412	1.1018	0.1959	3.0924
>33 to 36 weeks	112	1.1202	1.1036	0.3524	3.0725
>36 weeks to term	113	1.2302	1.3694	0.2477	3.0666

Note: manufacturer's non-pregnant reference interval = 0.35 to 4.94 mIU/L

FT4

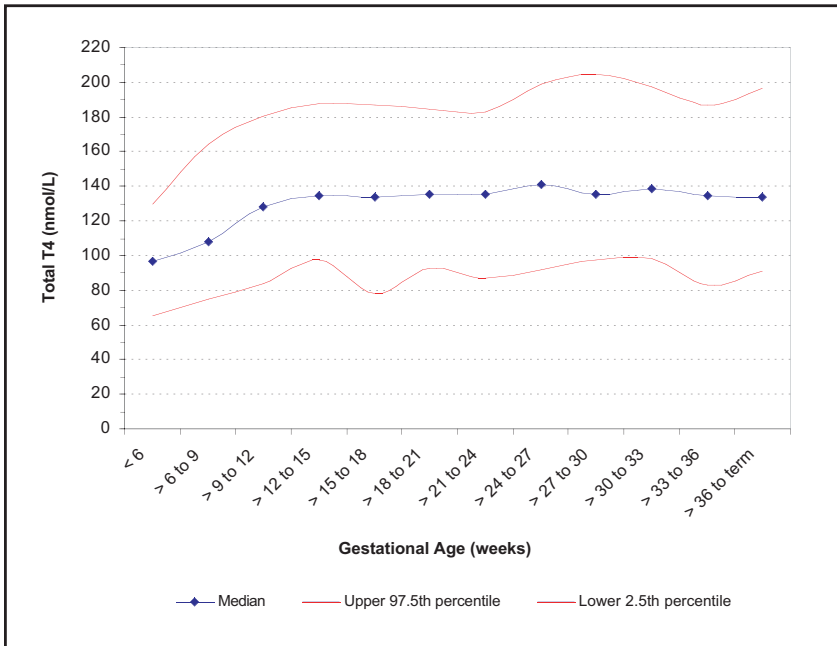


Free T4 (pmol/L)					
Gestational Age	N	Mean	Median	2.5th	97.5th
1st trimester	796	13.95	13.79	10.48	18.31
≤6 weeks	214	13.69	13.71	10.59	17.58
>6 to 9 weeks	296	14.09	13.92	10.54	18.71
>9 to 12 weeks	286	14.01	13.79	10.11	18.96
2nd trimester	530	12.29	12.17	9.49	15.87
>12 to 15 weeks	240	12.89	12.79	10.02	16.34
>15 to 18 weeks	96	12.26	12.23	9.67	15.68
>18 to 21 weeks	86	11.62	11.59	9.83	13.89
>21 to 24 weeks	108	11.54	11.40	8.76	15.14
3rd trimester	504	11.19	11.10	8.57	13.65
>24 to 27 weeks	98	11.53	11.58	9.35	13.82
>27 to 30 weeks	89	11.32	11.24	8.54	13.93
>30 to 33 weeks	91	11.01	10.67	8.60	13.74
>33 to 36 weeks	113	11.03	10.99	8.26	13.64
>36 weeks to term	113	11.11	10.94	9.10	14.01

Note: manufacturer's non-pregnant reference interval = 9.01 to 19.05 pmol/L

Results (cont.)

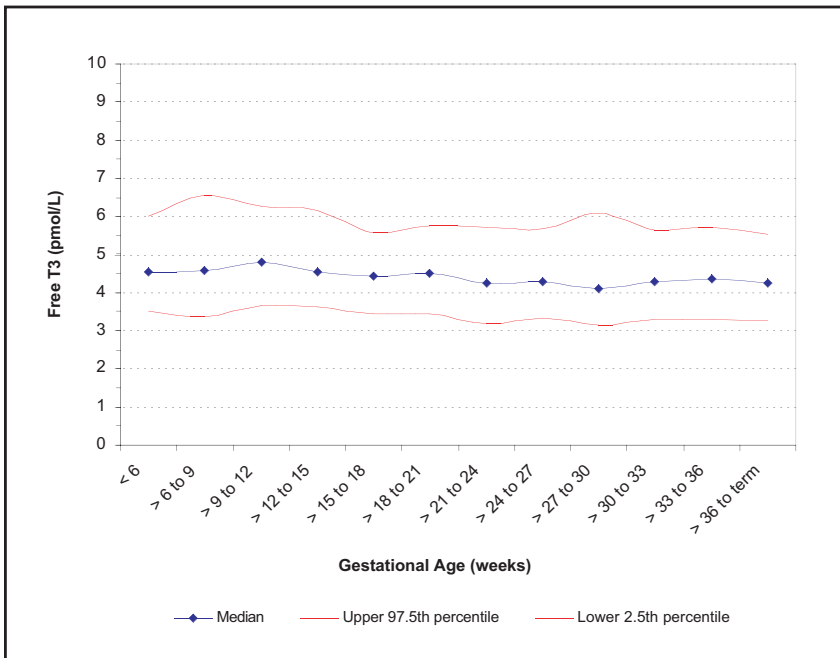
Total T4



Total T4 (nmol/L)					
Gestational Age	N	Mean	Median	2.5th	97.5th
1st trimester	793	114.6	110.6	71.3	171.3
≤6 weeks	212	97.7	96.8	65.5	129.8
>6 to 9 weeks	297	111.7	108.2	75.3	164.5
>9 to 12 weeks	284	130.2	128.1	83.5	180.5
2nd trimester	530	136.2	134.8	94.3	183.3
>12 to 15 weeks	240	136.9	134.6	97.9	187.7
>15 to 18 weeks	96	134.4	133.5	78.4	186.8
>18 to 21 weeks	86	135.9	135.4	92.7	184.7
>21 to 24 weeks	108	136.4	135.2	86.9	182.8
3rd trimester	503	138.0	136.7	93.9	194.0
>24 to 27 weeks	98	141.5	141.1	92.1	199.0
>27 to 30 weeks	89	138.5	135.0	97.4	204.9
>30 to 33 weeks	91	139.9	138.8	98.1	197.6
>33 to 36 weeks	113	134.5	134.8	83.3	187.2
>36 weeks to term	112	136.2	134.1	91.2	196.8

Note: manufacturer's non-pregnant reference interval = 62.7 to 150.8 nmol/L

Free T3

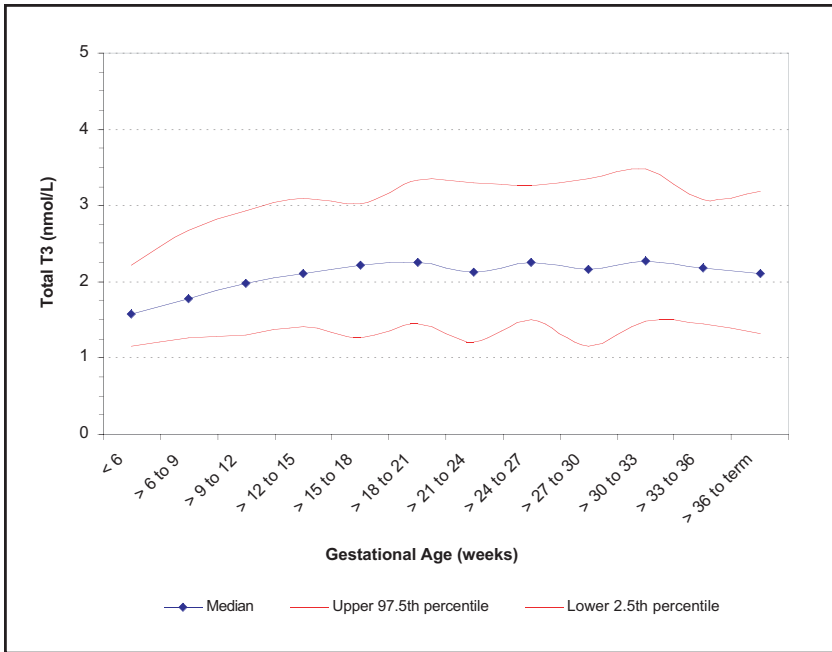


Free T3 (pmol/L)					
Gestational Age	N	Mean	Median	2.5th	97.5th
1st trimester	797	4.73	4.67	3.51	6.25
≤6 weeks	214	4.65	4.55	3.52	6.01
>6 to 9 weeks	297	4.68	4.57	3.37	6.56
>9 to 12 weeks	286	4.85	4.81	3.66	6.25
2nd trimester	530	4.53	4.48	3.39	5.87
>12 to 15 weeks	240	4.66	4.56	3.63	6.17
>15 to 18 weeks	96	4.46	4.44	3.43	5.56
>18 to 21 weeks	86	4.53	4.51	3.46	5.76
>21 to 24 weeks	108	4.28	4.24	3.20	5.73
3rd trimester	504	4.30	4.27	3.31	5.62
>24 to 27 weeks	98	4.36	4.29	3.34	5.66
>27 to 30 weeks	89	4.23	4.12	3.15	6.09
>30 to 33 weeks	91	4.34	4.29	3.29	5.66
>33 to 36 weeks	113	4.36	4.35	3.31	5.73
>36 weeks to term	113	4.24	4.25	3.27	5.55

Note: manufacturer's non-pregnant reference interval = 2.63 to 5.70 pmol/L

Results (cont.)

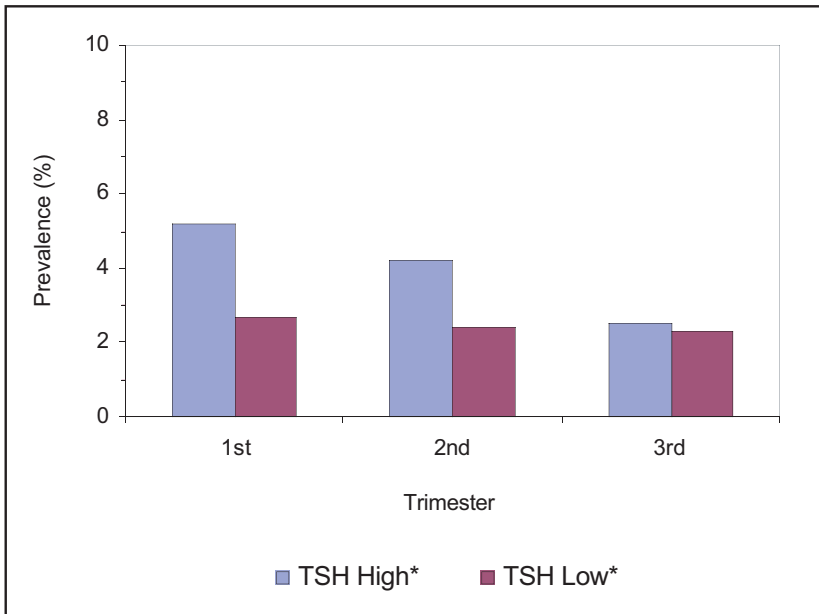
Total T3



Total T3 (nmol/L)					
Gestational Age	N	Mean	Median	2.5th	97.5th
1st trimester	797	1.84	1.78	1.24	2.75
≤6 weeks	214	1.62	1.58	1.15	2.22
>6 to 9 weeks	297	1.82	1.77	1.26	2.67
>9 to 12 weeks	286	2.03	1.98	1.29	2.93
2nd trimester	530	2.17	2.15	1.42	3.21
>12 to 15 weeks	240	2.13	2.10	1.41	3.09
>15 to 18 weeks	96	2.19	2.22	1.26	3.02
>18 to 21 weeks	86	2.26	2.26	1.45	3.34
>21 to 24 weeks	108	2.17	2.13	1.21	3.29
3rd trimester	504	2.21	2.19	1.35	3.19
>24 to 27 weeks	98	2.23	2.26	1.50	3.25
>27 to 30 weeks	89	2.19	2.16	1.16	3.35
>30 to 33 weeks	91	2.30	2.27	1.48	3.48
>33 to 36 weeks	113	2.23	2.18	1.44	3.08
>36 weeks to term	113	2.14	2.11	1.32	3.18

Note: manufacturer's non-pregnant reference interval = 0.89 to 2.44 nmol/L

Prevalence of Elevated or Suppressed TSH by Trimester



* Outside gestational age-specific reference intervals

Conclusions

We have established detailed trimester-specific reference intervals for thyroid hormones assays in TPO-Ab and Tg-Ab negative women on the Abbott ARCHITECT *i2000*_{SR} analyzer.

For some analytes, reference intervals change dramatically throughout pregnancy, and can differ significantly from non-pregnant reference intervals. Using trimester specific reference intervals will aid interpretation of maternal thyroid function tests, and reduce the possibility for sample misclassification.

In our study population, a large number of women (~20%) were positive for TPO-Ab and/or Tg-Ab. A significant percentage of women had elevated (range: 2.5 – 5.2%) or suppressed TSH (1.5 to 2.7%).

Given the association of maternal thyroid dysfunction to adverse outcomes for the mother and child, our data suggest screening of pregnant women for thyroid dysfunction may be justified.