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American Society for Reproductive Medicine 2015 Annual Meeting
October 17 to 21, 2015 • Baltimore, Maryland

Title:

DO ELEVATED TSH LEVELS PREDICT EARLY PREGNANCY LOSS IN ART PATIENTS?

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Objective:

Infertility related to ovulatory dysfunction is commonly associated with thyroid disorders such as hypothyroidism. A number of studies have observed increased miscarriage rates in patients with hypo- and hyperthyroidism, but the basis of this association remains unclear. While the manufacturer-listed normal range TSH is 0.5-5 mIU/L, recent literature suggests that optimal management of the infertile woman involves maintaining levels 0.5-2.5 mIU/L. We sought to evaluate the link between an abnormal TSH and miscarriage rate in a cohort of in vitro fertilization (IVF) patients.

Design:

Retrospective cohort study.

Materials and Methods:

Serum thyroid stimulating hormone (TSH) levels were routinely tested in patients participating in IVF cycle(s) (July 2002 – April 2014). Study patients were restricted to those with a TSH measurement within 2 weeks of the IVF cycle start date. Patients were stratified by oocyte age, binned as A <35, B [35-38), C [38-41), D [41-43) and E ≥43 yo, and TSH level, binned as (0-0.5], (0.5-2.5], (2.5-5], (5-9], and (9-23) mIU/L. Patients with TSH (0.5-2.5] were the reference "euthyroid" group. Patients were followed until pregnancy loss or delivery. After a positive pregnancy test, miscarriages were modeled by oocyte age and TSH level bin. Model was assessed by chi-square of ANOVA with significance at $p < 0.05$.



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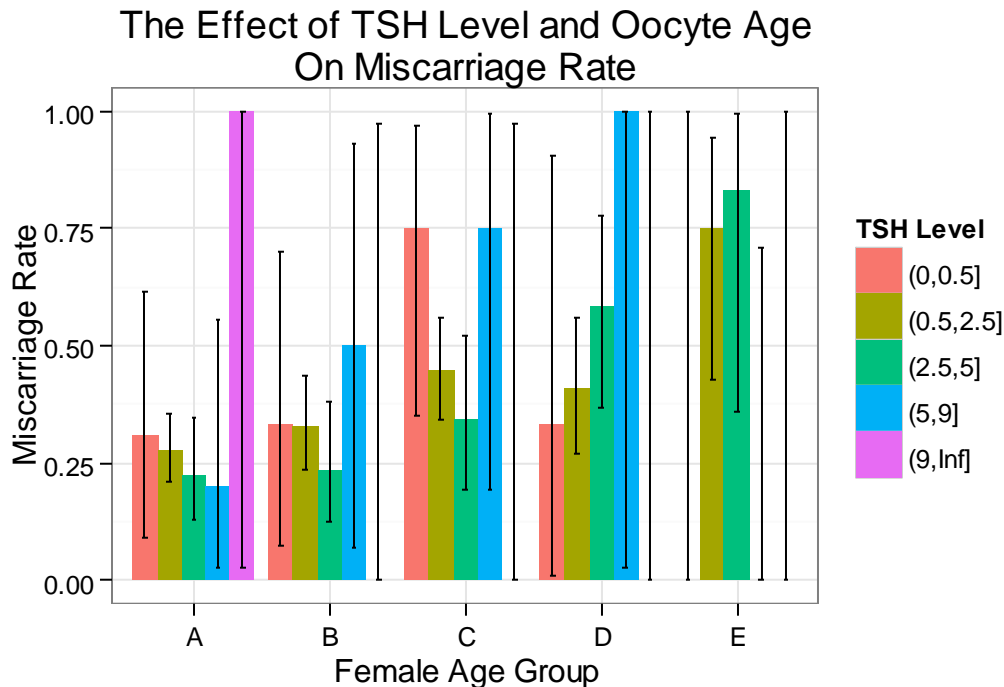
Results:

Couples (n=1140) who completed 1208 fresh autologous IVF cycles were evaluated. In patients aged 22.4-47.1 yo, TSH was abnormally elevated (>5 mIU/L) or suppressed (≤ 0.5 mIU/L) in 46/1208 and 65/1208 cycles, respectively. Treatment resulted in 632 pregnancies, 526 clinical pregnancies and 410 deliveries (multiple births counted as one). Increasing oocyte age was associated with significantly increased miscarriage rates in groups C-E ($p < 0.001$) but not B ($p = 0.40$) compared with age group A, with increasing effect strength with age. The miscarriage rate was not statistically different across all TSH bins compared with euthyroid patients ($p > 0.30$ for all groups) after adjusting for oocyte age.

Conclusions:

While other studies have suggested an increased miscarriage rate in patients with subclinical hypothyroidism, patients with confirmed pregnancies treated in routine infertility care with IVF in this analysis appeared to deliver at comparable rates regardless of recent TSH levels. While maternal hypothyroidism during pregnancy are known to cause multiple complications, including preeclampsia, pre-term delivery cardiac and neurological defects, patients should not be discouraged from pursuing assisted reproductive treatment. In order to better counsel and plan infertility treatment, further corroborating research is needed to define the miscarriage risk in patients with thyroid disorders.

Support: None





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Female Age	TSH Level	# Cycles	# Patients	# BPs	Miscarried	Miscarriage Rate	
						Mean	95% CI
A	(0,0.5]	30	30	13	4	0.31	[0.09-0.61]
A	(0.5,2.5]	248	243	158	44	0.28	[0.21-0.36]
A	(2.5,5]	105	105	63	14	0.22	[0.13-0.34]
A	(5,9]	12	12	10	2	0.20	[0.03-0.56]
A	(9,23]	3	3	1	1	1.00	[0.03-1.00]
B	(0,0.5]	12	12	9	3	0.33	[0.07-0.70]
B	(0.5,2.5]	158	156	91	30	0.33	[0.23-0.44]
B	(2.5,5]	70	70	47	11	0.23	[0.12-0.38]
B	(5,9]	10	10	4	2	0.50	[0.07-0.93]
B	(9,23]	1	1	1	0	0.00	[0.00-0.98]
C	(0,0.5]	14	14	8	6	0.75	[0.35-0.97]
C	(0.5,2.5]	167	164	89	40	0.45	[0.34-0.56]
C	(2.5,5]	81	80	35	12	0.34	[0.19-0.52]
C	(5,9]	11	11	4	3	0.75	[0.19-0.99]
C	(9,23]	2	2	1	0	0.00	[0.00-0.98]
D	(0,0.5]	6	6	3	1	0.33	[0.01-0.91]
D	(0.5,2.5]	121	117	49	20	0.41	[0.27-0.56]
D	(2.5,5]	48	47	24	14	0.58	[0.37-0.78]
D	(5,9]	8	8	1	1	1.00	[0.03-1.00]
D	(9,23]	0	0	0	0		[0.00-1.00]
E	(0,0.5]	4	4	0	0		[0.00-1.00]
E	(0.5,2.5]	67	66	12	9	0.75	[0.43-0.95]
E	(2.5,5]	26	26	6	5	0.83	[0.36-1.00]
E	(5,9]	2	2	3	0	0.00	[0.00-0.71]
E	(9,23]	0	0	0	0		[0.00-1.00]