

## Background and Objective

- Neonates born to mothers with Graves' disease are at risk to develop hyperthyroidism due to placental transmission of TSH-receptor antibodies.
- Neonatal hyperthyroidism should be effectively diagnosed and treated to prevent severe complications of this disease (cardiac symptoms, poor weight gain, severe neurological manifestations).
- The objective of this study was to describe the post-natal follow-up of neonates born to women with Graves' disease.

## Methods

- 33 neonates (17 ♀, 52%) born to 32 women (1 twin pregnancy) referred to our hospital between 2006 and 2015 were included in this study.
- Symptoms of hyperthyroidism, thyroid function tests, TSH-receptor antibodies (TRAK) titres were collected during the follow-up.
- Data are reported in median [Q1-Q3] values. Data were analyzed using Wilcoxon tests.

## Results

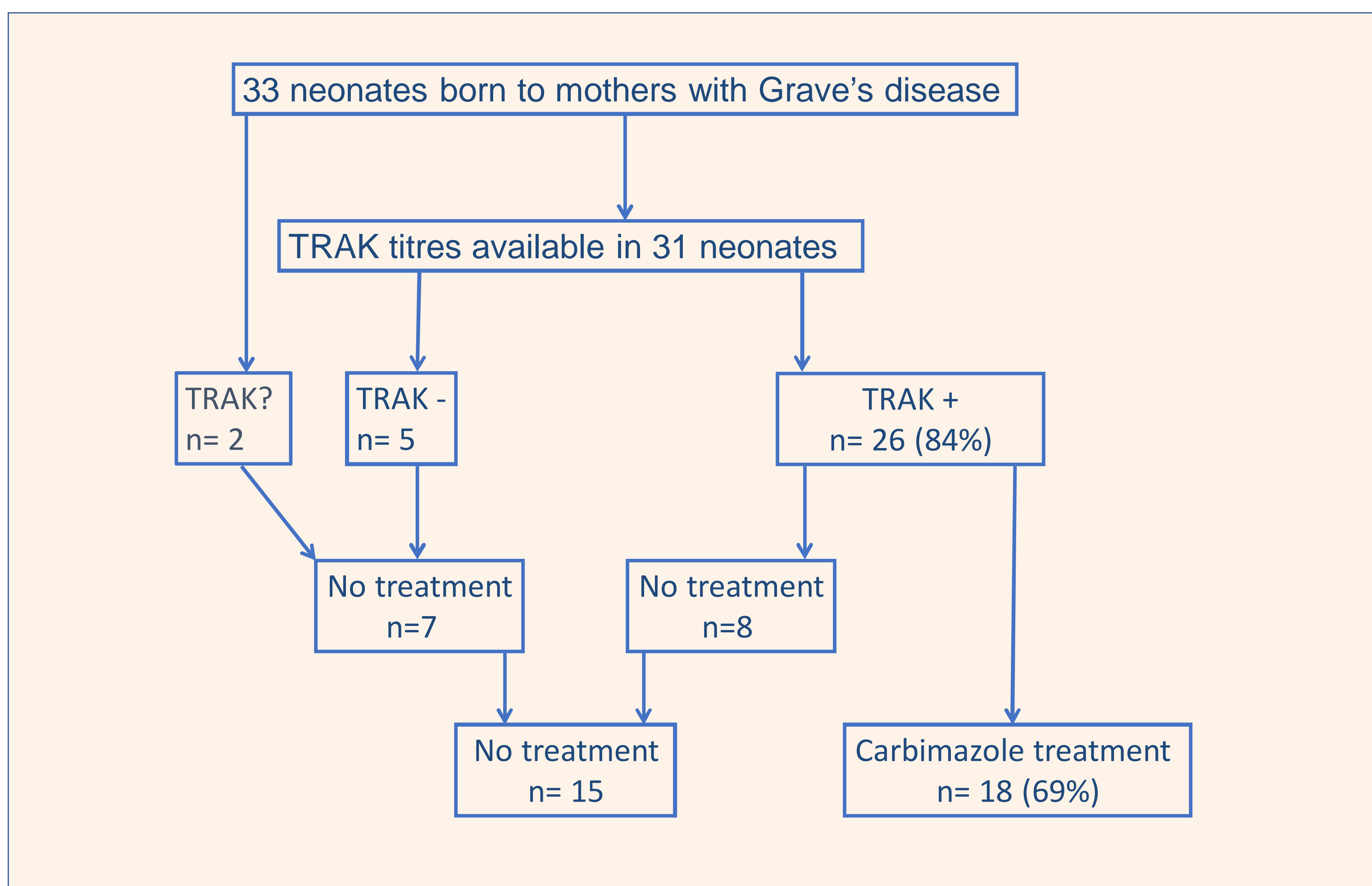
### Mothers

- Maternal Graves' disease was diagnosed before pregnancy in 23 (74%) women at the age of 26 (22-33) yrs.
- Seven(22%) women have had thyroidectomy and/or IRA therapy, 24 (75%) women were treated with anti-thyroid drugs (ATD, 21 received PTU).
- At the last trimester of pregnancy or at birth, TRAK titres were available in only 22 (68%) women and were positive in 22 (95.5%).

### Newborns

- Median GA was 38 (37-39) weeks, 7 neonates were born preterm and 3 were SGA.
- Birth parameters (weight, length, HC) did not differ significantly between the newborns who required ATD and those who did not.
- 3 neonates had birth defects: hexadactily, biventricular dilatation, unilateral kidney hypoplasia with ureteral duplication.
- 14 neonates had goiter and 2 exophthalmia.
- 26/31 neonates (84.8%, 2 missing data) were TRAK+ within the first 10 days. Median TRAK titres were 10.9 (5.8-19.5) UI/l (normal values <1,5UI/l) (see figure1).

Figure1: Flow chart of the patients

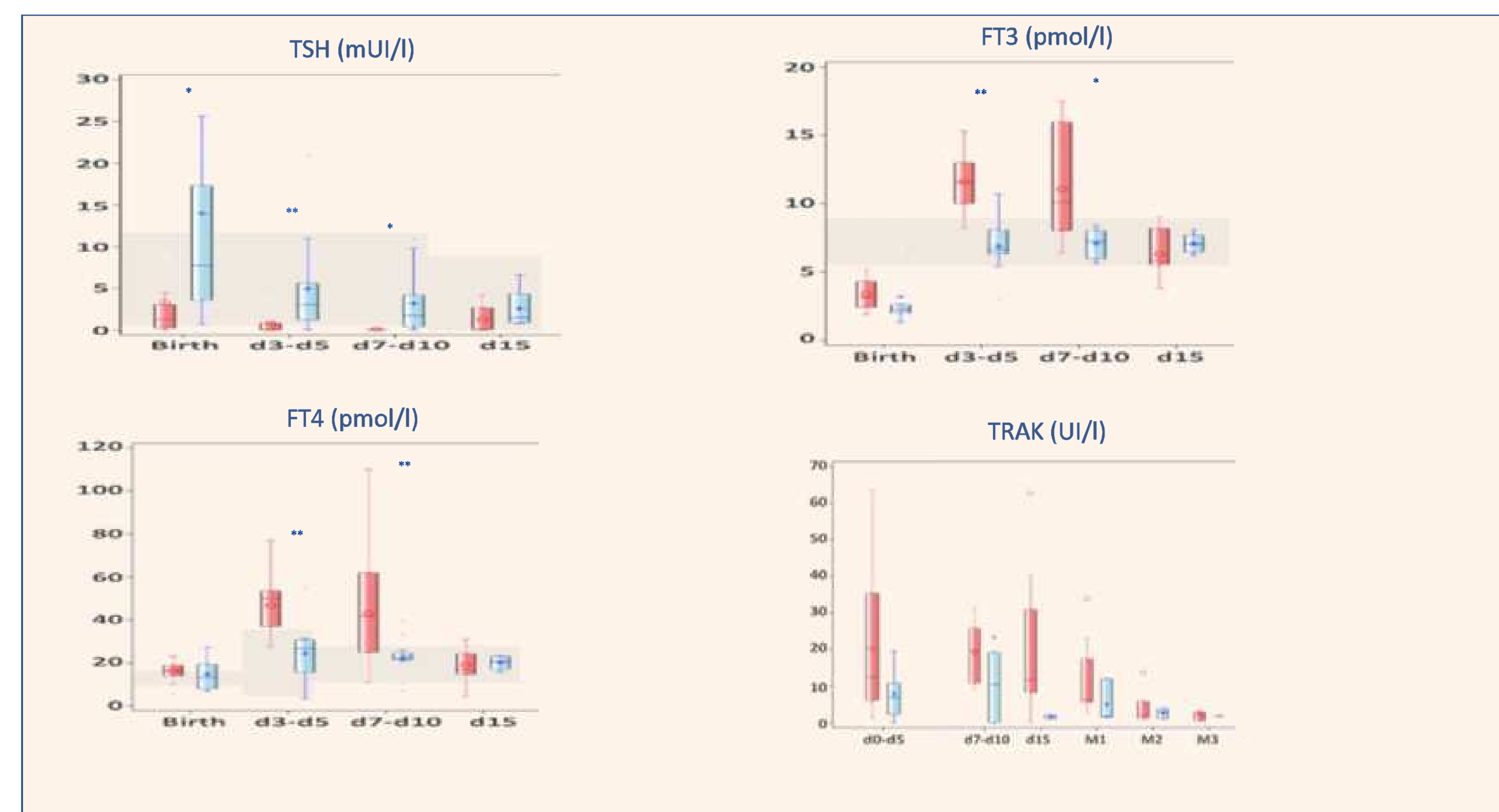


## Results

### Newborns

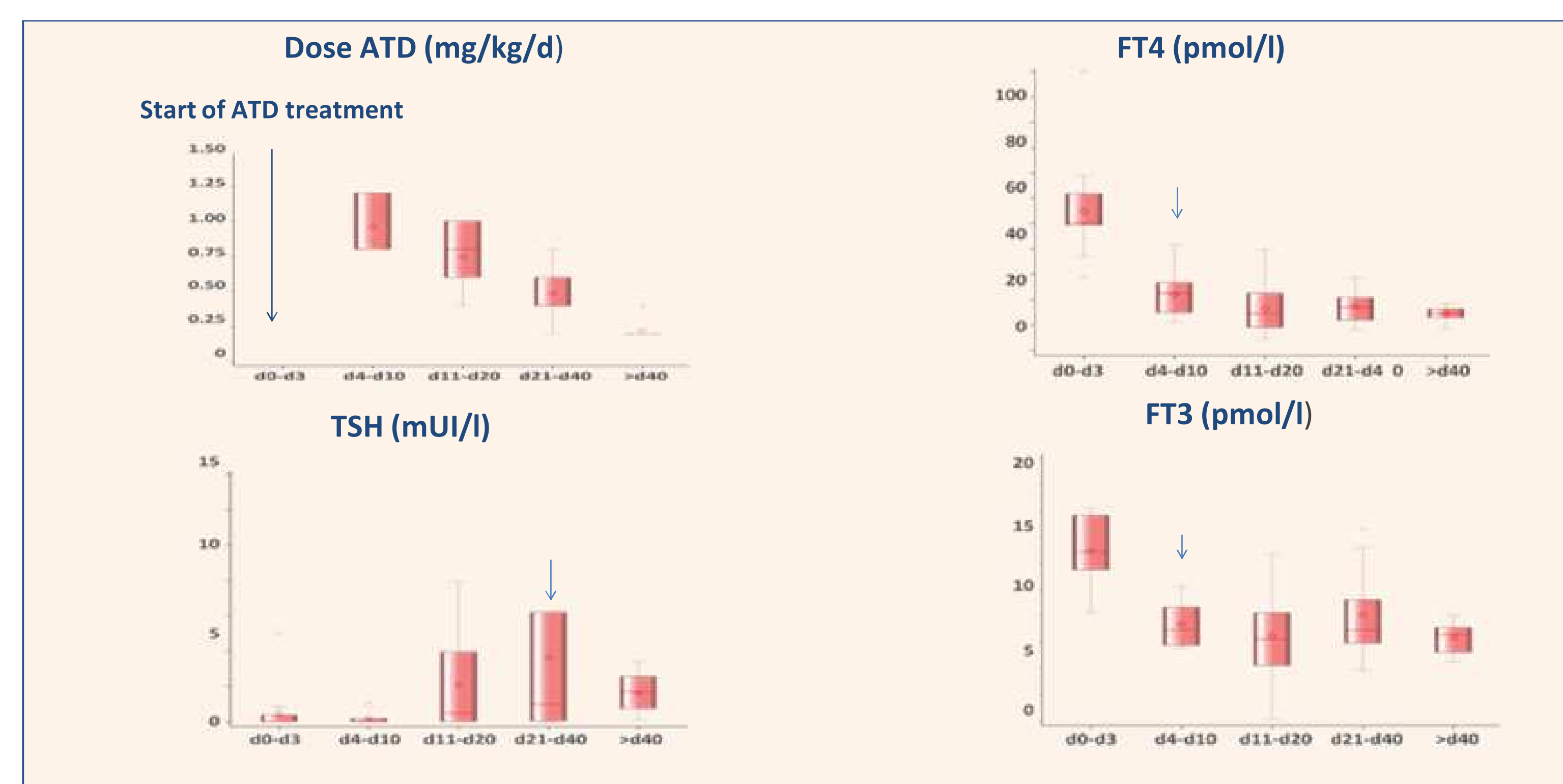
- 18 (54.5%) had overt hyperthyroidism requiring ATD and 15 did not require ATD.
- At birth, median TSH was significantly lower in the treated group [TSH: 1.3 mUI/l (0.2-3.1)] than in the untreated group [7.7mUI/l (3.6-17.3)- p=0.02].
- At post natal D3-D5, thyroid function tests differed significantly between the 2 groups (treated group vs untreated group): TSH: 0.1 (0.0-0.9) vs 3 (1.2-5.7) mUI/L (p<0,05)- FT4: 50 (37-54) vs 26.8 (15.5-30.6) pM/( p<0,01) - FT3: 11.6 (10.0-13.0) vs 6.6 (6.3-8.1) pM/L (p<0,01).

Figure 2 - Table 1: Changes in TSH, FT4, FT3 and TRAK levels during the first 15 post natal days in the treated (Red bars) and untreated groups (Blue bars). Grey areas represent normal values for CA. \*p<0,05 \*\*p<0,01.



	Birth	D3-D5	D7-D10	D15
<b>TSH</b>	1.3(0,2-3,1)* 7.74 (3.6-17.3)	0,1(0,03-0,9) ** 3.0 (1.2-5.7)	0,03(0,01-0,08)* 1.7 (0.4-4.2)	0,1(0,04-2,7) 1.5 (0.9-4.3)
<b>FT4</b>	16.4(13.9-19.0) 13.2 (7.9-19.5)	50.0(37.0-53.7) ** 26.8(15.5-30.6)	41.6(24.9-62.0)** 22.0(21.2-24.7)	16.7(14.6-24.5) 20.8(17.1-23.2)
<b>FT3</b>	3.1 (2.4-4.3) 2.3 (2.0-2.6)	11.6 (10.0-13.0)** 6.6 (6.3-8.1)	10.1 (8.0-16.0)* 7.3 (6.0-8.1)	6.2 (5.5-8.2) 7.0 (6.5-7.7)
<b>TRAK</b>	12.4 (6.0-35.4) 6.8 (2.2-10.9)		19.7 (10.8-25.8) 10.5 (0.0-19.2)	11.7 (8.2-31.0) 1.6 (1.0-2.2)

Figure 3: Changes in ATD doses and TSH, FT4, FT3 levels during treatment.



- Carbimazole was initiated at the age of 4.5 (3.0-8.0) days, at a baseline dose of 0.8 (0.6-1.0) mg/k/d for a duration of 1.9 (1.3-2.5) months. Treatment was well tolerated.
- 10 babies (55%) received beta-blockers and 7 combined treatment with L-Thyroxin.
- FT4 and FT3 normalized within the first week of treatment: FT4: 22,7 pmoles/l (14.9-26.8); FT3: 6.9 pmoles/l (5.8-8.7).
- Median TSH normalized within the 3<sup>rd</sup> week of treatment: TSH:1,0 mUI/l (0.04-6.2).
- TRAK titers were negative after a median duration of follow-up of 2.5months.
- 1 patient developed craniostenosis.

## Conclusion

- In this study, a high proportion of babies born to mothers with Graves' disease and TRAK+ at birth developed hyperthyroidism requiring anti-thyroid drug.
- ATD was effective to control hyperthyroidism rapidly and was well tolerated.
- Larger prospective studies are needed to determine factors associated with the occurrence of HT requiring treatment among TRAK+ newborns.
- A tight collaboration between obstetricians and paediatric endocrinologists is needed during pregnancy and at birth to optimize the monitoring of at risk fetuses and newborns.