



"LYMPOCYTE POPULATION IN CHILDREN AND ADOLESCENTS AFFECTED BY GRAVES' DISEASE. POTENTIAL PREDICTIVE TOOL OF DISEASE SEVERITY"

G. TULI^{1,2}, J. MUNARIN^{1,2}, D. TESSARIS^{1,2}, P. MATARAZZO^{1,2} and L. DE SANCTIS^{1,2}

1. Department of Pediatric Endocrinology, Regina Margherita Children's Hospital, Turin, Italy
2. Department of Public Health and Pediatrics, University of Turin, Turin, Italy



INTRODUCTION

Graves-Basedow disease (GD) is the most common cause of thyrotoxicosis in pediatric age.

Multi-factorial pathogenesis stand on the basis of the autoimmune disorder activation, leading to lymphocyte imbalance that include increased CD4+ and CD8+ subtypes, increased CD4+/CD8+ ratio and B cells dysregulation.

AIM

The aim of this study is to determine the potential prognostic value of lymphocyte population parameters in pediatric GD.

METHOD

Thyroid hormone profile, TRAb titre, lymphocyte population and clinical data of all pediatric subjects (aged <18 y) with new diagnosis of GD were collected.

All of them were referred to the Department of Pediatric Endocrinology of Regina Margherita Children's Hospital in Turin in the period November 2017-April 2021.

RESULTS

The data of 10 subjects (2 males, 8 females; age 11.7 ± 3.47 years old) with newly diagnosed GD in a follow-up period of 2.4 ± 0.8 years are represented in table 1.

Pearson's correlation coefficient between CD4+/CD8+ ratio at diagnosis and fT3 levels and thyroid volume at diagnosis was 0.72 ($p=0.04$) and 0.81 (**$p=0.004$**) respectively.

A positive correlation coefficient was also observed between the CD4+/CD8+ ratio at diagnosis and the TRAb titre at diagnosis and after 6, 12 and 24 months (0.89, 0.89, 0.73 and 0.77; **$p=0.02$, $p=0.01$, $p=0.03$ and 0.04** respectively).

The correlation coefficient of the ATD dose after 6 and 12 months with the CD4+/CD8+ ratio also showed a similar course (0.88 and 0.78, **$p=0.001$ and $p=0.02$** respectively).

Patients with a CD4+/CD8+ ratio above normal (6/10) had higher levels of fT3 at diagnosis (28.77 ± 2.18 vs 13.48 ± 2.19 pmol/L, **$p = 0.03$**) and higher TRAb titre (28.9 ± 11.2 vs 4.88 ± 0.97 , **$p=0.01$**) compared to subjects with normal ratio (4/10).

After 2 years of follow-up, 2/10 patients underwent thyroidectomy, 2/10 had remission of the disease and 6/10 are still being treated with ATD.

The relative risk (RR) of taking a higher daily dose of ATD than maintenance dose (0.1-0.2 mg/kg/daily) and a higher CD4+/CD8+ ratio was 4 and 2.25 at 6 and 12 months from diagnosis respectively. The RR of having a thyroid volume greater than SDS>2 and a higher CD4+/CD8+ ratio was 3.

CONCLUSIONS

Among the parameters of the lymphocyte population, the elevated CD4+/CD8+ ratio appears to be positively correlated with higher fT3 levels and goiter size at diagnosis, higher TRAb titre in the first two years, and higher ATD dose in the first year after the diagnosis.

Thus, this ratio could be considered as a promising predictive tool, together with the other prognostic factors to better manage pediatric GD, even if these preliminary data need to be confirmed over a longer follow-up period and in larger cohorts.

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	Diagnosis	At 6 months	At 12 months	At 24 months
TSH mcUI/ml	0.005 ± 0.001	2.46 ± 0.51	2.8 ± 0.9	2.64 ± 0.66
FT4 pg/ml	55.09 ± 4.7	15.96 ± 5.06	21 ± 1.69	16.18 ± 4.29
FT3 pg/ml	22.58 ± 2.87	6.72 ± 2.27	11.45 ± 5.22	7.61 ± 2.36
TRAb UI/L	18.25 ± 3.49	7.1 ± 2.7	17.7 ± 6.1	10.9 ± 5.8
Thyroid volume SDS	2.98 ± 0.47			
Total lymphocyte count/mcl	2.657 ± 0.7	-	-	-
CD4+/CD8+ ratio	2.19 ± 0.9	-	-	-
ATD dose (mg/kg/day)	0.33 ± 0.1	0.12 ± 0.1	0.23 ± 0.1	0.09 ± 0.001

Table 1. Clinical features of pediatric subjects affected by Graves Disease at onset and in the first two years of follow-up.

CONTACT INFORMATION

Presenting author: Gerdi Tuli (gerdi.tuli@unito.it)

