

optic neuropathy or exposure keratopathy and (5) chronic TED greater than 9 months. In our series, we found that teprotumumab was as effective in a wider population of chronic TED patients than included in the clinical trials.

## Thyroid

### THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

#### *The Immune Microenvironment of Hashimoto's Thyroiditis Regulates the Glycosylation Modification of IgG*

Yedi Cao, PhD.<sup>1</sup>, Zhijing Song, PhD.<sup>2</sup>, Yan Gong, MD<sup>1</sup>, Keli Zhao, PhD.<sup>2</sup>, Xue Zhao, PhD.<sup>1</sup>, Youyuan Huang, Bachelor<sup>1</sup>, Chenxue Qu, MD<sup>1</sup>, Yan Li, PhD.<sup>2</sup>, Ying Gao, Doctor MD<sup>1</sup>, Junqing Zhang, MD<sup>1</sup>, Xiaohui Guo, MD<sup>1</sup>.

<sup>1</sup>Peking University First Hospital, Beijing, China, <sup>2</sup>Laboratory of Interdisciplinary Research, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China.

**Objectives:** Elevation of anti-thyroglobulin antibodies that are primarily IgG isotype is a hallmark of Hashimoto's thyroiditis (HT). As for IgG, it bears two conserved repertoire of N-linked glycans attached to its crystallizable fragment (Fc) at the 297 asparagine residue (Asn297). In our previous study, we found that serum TgAb IgG from HT patients exhibits higher glycosylation levels than those observed from healthy controls. Previous studies confirmed that imbalance of Th1/Th2 and Th17/Treg leading to altered immune microenvironment with elevation of certain cytokines was found in the thyroid tissue of HT, including IFN- $\gamma$ , TNF- $\alpha$ , IL-21, IL-17A, IL-6, BAFF, APRIL. Thus, the aim of our study was to investigate the influence of the elevated cytokines on the differentiation process of B cells and the glycosylation levels of IgG. **Methods:** We formed a two-phase culture system in vitro to promote B cells to differentiate to antibody-secreting cells (ASCs). In the process of cell culture, B cells were co-cultured with cytokines as followed: IFN- $\gamma$ , TNF- $\alpha$ , IL-21, IL-17A, IL-6, BAFF and APRIL. Flow cytometry was performed to identify the percentage of plasmablasts (CD38<sup>+</sup>CD27<sup>high</sup>) and plasma cells (CD20<sup>+</sup>CD138<sup>+</sup>). ELISA was used to measure the yield of IgG in culture supernatants. The glycosylation levels of secreted IgG under different stimulation conditions were detected by lectin microarray. **Results:** We found that IL-21, TNF- $\alpha$  and BAFF can significantly promote the differentiation of B cells into ASCs in vitro culture system, and augment the production of IgG to over 4-fold. In addition, cytokines affected the glycosylation modification profile of IgG diversely: 1) IL-21, IL-17A, TNF- $\alpha$ , BAFF significantly increased the glycosylation level of sialic acid of total IgG; 2) IFN- $\gamma$  significantly increased the level of galactose; 3) IL-21, IL-17A, IFN- $\gamma$ , BAFF, and APRIL significantly increased the level of mannose; 4) IL-6 significantly decreased the level of sialic acid, galactose and mannose; 5) IL-17A, IFN- $\gamma$ , TNF- $\alpha$ , BAFF significantly increased the level of GalNAc that was a component of O-Glycan, which only exists in the hinge region of IgG3 subclass. **Conclusions:** The abnormally elevated cytokines in microenvironment participated in the regulation of B cell terminal differentiation process and glycosylation level of IgG, thereby involving in the pathogenesis of AITD.

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### THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

#### *The Potential Impact of the COVID-19 Pandemic on Clinical Management of Thyroid Disorders in Japan.*

Kosuke Inoue, MD, Jaeduk Yoshimura Noh, MD, PhD,

Ai Yoshihara, MD, PhD, Natsuko Watanabe, MD, PhD,

Masako Watanabe, MD, Miho Fukushima, MD, Nami Suzuki, MD,

Ayako Hoshiyama, MD, Takako Mitsumatsu, MD, Ai Suzuki, MD,

Aya Kinoshita, MD, Kentaro Mikura, MD, Ran Yoshimura, MD,

Kiminori Sugino, MD, PhD, Koichi Ito, MD, PhD.

Ito Hospital, Tokyo, Japan.

**Background:** The indirect influence of the coronavirus disease 2019 (COVID-19) pandemic on clinical practice has received great attention. However, the evidence about how the pandemic has affected clinical management of hypothyroidism and hyperthyroidism, two common diseases worldwide, is lacking. We therefore aimed to examine the trends in the number of outpatients with thyroid disorders and their thyrotropin (TSH) levels before and during the pandemic in Japan. **Methods:** This cohort study included all patients aged  $\geq 20$  years who visited Ito Hospital, one of the largest hospitals that specialize in thyroid disorders in Japan, during 2019/1-2020/6. Our outcomes of interest were 1) trends in the aggregated number of visits at the clinic and 2) trends in average TSH levels from January 2019 to June 2020. The trends in TSH according to the clinic visit in early 2020 were assessed utilizing difference-in-difference models controlling for age, sex, and city of residence, stratified by each medication use (i.e., levothyroxine [LT4], antithyroid drug [ATD], potassium iodine [KI], or no medication). **Results:** During 2019/1-2020/6, we observed 517,412 visits at Ito Hospital for thyroid disorders, and the average number of visits per month was significantly decreased for both the first visits (1,995 in 2019 vs. 1,268 in 2020; reduction rate, 36%;  $p < 0.001$ ) and the follow-up visits (29,509 in 2019 vs. 21,959 in 2020; reduction rate, 26%;  $p < 0.001$ ). Among 15,455 patients who had been followed in 2019, we found a higher TSH at the follow-up visits during 2020/4-2020/6 among patients with LT4 who did not visit the clinic during 2020/1-2020/3 than those who did (difference-in-difference [95%CI]=+1.77 [1.25-2.29],  $p < 0.001$ ). We also found decreased trends in TSH among patients with ATD or KI who visited the clinic during 2020/1-2020/3 ( $p < 0.001$  for both categories), but not among patients with no medications ( $p = 0.29$ ). **Conclusions:** In this large cohort in Japan, we found the decreased number of outpatients with thyroid disorders since 2020/1 with a nadir in 2020/4. Using individual-level data, we also found the association between visiting the clinic in early 2020 and TSH control at the following visit among patients with medications. These findings highlight the importance of careful monitoring of patients with medications for thyroid disorders during the COVID-19 pandemic.

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