showed significant changes in weight from baseline (59.7 + 17.7kg) to 6 months (59.4 + 9.9kg) to 12 months (63.4 + 17.4Kg), all p<0.001, TSH receptor antibody level from baseline (17.3 + 12.9IU/L) to 12 months (7.1 + 10.8IU/L), NR <1.76IU/L, p<0.001, fT4 levels from baseline (49.9 + 18.1pmol/L) to 6 months (14.3 + 6.9pmol/L) and from baseline to 12 months (11.8 + 2.3pmol/L), NR 8.8-14.4pmol/L, all p<0.001 and TSH levels from baseline (0.011 + 0.009mU/L) to 6 months (1.38 + 1.74mU/L, p=0.001) and from baseline to 12 months (1.80 + 1.72mU/L, p<0.001), NR 0.65-3.70mU/L. After 6 months of treatment, 7 out of 13 ThyPRO scales improved and 9 out of 13 ThyPRO scales improved after 12 months of treatment. Large treatment effects were observed on 2 ThyPRO scales (Hyperthyroid symptoms and Anxiety) while moderate effects were seen in 5 ThyPRO scales (Tiredness, Cognitive complaints, Depressivity, Impaired daily Life and overall QoL) from baseline to 6 months. Large treatment effects were observed on 2 ThyPRO scales (Hyperthyroid symptoms and Anxiety) while moderate effects were seen in 5 ThyPRO scales (Tiredness, Depressivity, Emotional susceptibility, Impaired daily Life and overall QoL) from baseline to 12 months. Small treatment effects were observed in 2 ThyPRO scales (Goiter symptoms and Tiredness) from 6 to 12 months. **Conclusion:** There are significant improvements in many aspects HRQL during the first 6 months of antithyroid drug treatment, with hyperthyroid symptoms and anxiety showing the most improvements throughout the 12 month treatment period. Our results complement clinical monitoring of patients with Graves' disease and provide realistic outcome measures of disease impact and treatment outcomes from the patient's perspective.

Thyroid

FROM HYPO- TO HYPERTHYROIDISM

The Pitfalls of Using Research Grade Immunoassays for Thyroid Health Measurements

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Introduction: Immunoassay technology is subject to matrix interferences that can produce inaccurate results and incorrect conclusions when using samples not previously validated. While many commercially available research grade (RG) immunoassay kits are available, caution should be applied when using RG kits for thyroid health assessments, particularly on samples from pregnant individuals whose blood chemistry is unique to non-pregnant individuals. Question: Do RG immunoassay kits reliably provide precise and accurate measurements of thyroid health biomarkers in serum Standard Reference Materials (SRMs) from pregnant and non-pregnant donors? **Methods:** T4, T3, rT3, Tg and TSH measurements were conducted on SRMs 971, Hormones in Frozen Human Serum, and SRM 1949, Frozen Prenatal Serum, using RG immunoassay kits. When available, performance was assessed against validated FDA approved immunoassays or mass spectrometric (MS) methods. **Results:** RG kits were variable, inaccurate, or imprecise for four of the six biomarkers assessed. RG kit total thyroid hormone measurements overall performed comparably to MS methods, except rT3 measurements, which were twofold greater than mass spectrometric measurements (971M RG mean = 0.51 ng/mL, MS mean = 0.20 ng/mL, p < 0.0001; 971F RG = 0.48 ng/mL, MS = 0.18 ng/mL, p < 0.0001) and had CVs over 30 %. RG kit Tg measurements varied sometimes by as much as tenfold (971M means of 6.50 ng/mL up to 63.3 ng/mL, p < 0.0001; 971F means of 0.350 ng/mL up to 14.5 mg/mL, p < 0.0001). TSH values differed by RG kit manufacturer (971M means of 1.27 μIU/mL up to 1.82 μIU/mL, p < 0.0001; 971F means of 1.36 μIU/mL up to 2.27 μIU/mL, p < 0.0001) and by dilution scheme using the same manufacturer with one case indicating a diagnosis of hypothyroid versus normal TSH levels (1949 non-pregnant undiluted mean = 2325 pg/mL, half dilution mean = 1631 pg/mL, p < 0.0001). **Conclusions:** RG immunoassays are often used for research projects because they do not require expensive equipment and are simple to conducted. However, we demonstrate here that not all kits are accurate for all patient samples. By utilizing a matrix matched SRM with well-defined quantities of thyroid health biomarkers, one can assess method accuracy, making measurements from different methods comparable. Thereby, data can be harmonized to contribute reliable data on thyroid biomarkers to advance the field of thyroid health.

Thyroid

FROM HYPO- TO HYPERTHYROIDISM

What Matters Most to Patients With Thyroid Dysfunction in Malaysia: A Preliminary Qualitative Analysis

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Background: Relatively little is known on the aspects of research that matter most to patients with thyroid dysfunction (TD). We aimed to explore the patients' experience when they were diagnosed and treated for TD, as well as what they needed to improve their care: **Methods:** Qualitative data were obtained online using the Malay language version of the semi-structured qualitative survey in Malaysia, part of the larger research: A CORE OUTCOME SET FOR THYROID DYSFUNCTION. The questionnaires were developed from interactive discussions with patients who have thyroid dysfunction. The responses were analyzed using Braun and Clark's thematic analysis framework guided by the question: What are the perceptions and experiences of thyroid care that matter most to patients with TD? **Results:** Responses from 38 participants, in the 18-60 age range, with TD, were analyzed. Most patients across the spectrum of thyroid dysfunctions experienced emotional

disturbances. These negative emotions were related to the whole spectrum of disease state, the associated treatments, pre-treatment, post-treatment care, and personal aspects of daily life. Uncertainties in medical outcomes were associated with the personal need for further information. Functional psychosocial impairments and socioeconomic disruptions have a strong ability to arouse the anxiety of outcome uncertainties further. Getting treatment and independence in routine daily activities were prioritized while acknowledging treatments may differ in modality and risk of complications. Physician-patient interactions were valued in alleviating concerns and fear. Four salient themes emerged suggesting emotional security, functional ability, self-care (including psychosocial and socioeconomic well-being), and quality of physician-patient relationships were what matters to these participants. **Conclusion:** This insight into the problems of patients with TD underlined the need for quality patient-centered thyroid care and may be enhanced, personalized, and improved through outcomes that mattered most to patients in clinical research/trials, routine clinical practice, and the health system.

Thyroid

THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

A Higher Cutoff for TSI Would Better Predict Recurrence in Patients With Graves' Disease?

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Introduction: GD is an autoimmune disease mediated by immunoglobulins (Igs) that activate TSH receptor (rTSH). Relapse after withdrawal of antithyroid drugs (ATD) can reach 60%. Measurement of TSH receptor antibodies (TRAb) and thyroid stimulating immunoglobulin (TSI) could be an indirect indicator of GD activity. TRAb assays measures thyroid-stimulating, thyroid-blocking and neutral Igs; TSI assays measures only stimulating Igs. Objetive: Evaluate, prospectively, autoimmunity before and after ATD therapy for thyrotoxicosis through TSI measurement. **Methods:** Patients were evaluated at the first visit and at the time of ATD withdrawal. TSH, thyroid hormones, TPO antibody, thyroglobulin antibody, and TRAb were measured using eletrochemiluminescent assays Roche Diagnostics; TSI was determined by chemiluminescent assay Siemens Diagnostics. According to manufacturers, TRAb < 1.75 IU/L and TSI < 0.55 IU/L were negative. **Results:** Sixty-seven patients mean age 45,7±2,45 years, 65 women, were evaluated: 50 at the first visit, 40 (80%) with GD, and 10 (20%) with toxic multinodular goiter (TMNG). TSI diagnostic sensitivity (Sen%) and specificity (Spe%) to diagnose GD were 90% and 100% respectively, similar to that of TRAb, of 89% and 100%. Thirty-six patients were evaluated for recurrence after suspension of ATD (19 of them also had the initial assessment): 21 (58.3%) did not present recurrence in an mean period of 9.5±2.1 months (3-18); and 15 (41.7%) relapsed in 4.4±2.6 months (2-12). In 10/21 patients who did not relapse, and whose TRAb was negative, TSI was positive at low levels, which was responsible for the low Spe% of this test. Assessing possible other cutoff points for the TSI in the recurrence assessment, an adjustment to 1.4 (TSI <1.4 IU/L = negative) raised the Spe% to 86%. **Conclusions:** In this group, TSI and TRAb were equivalent for GD diagnosis. Many clinical factors have been suggested and TRAb measurement is known to be useful for predicting GD relapse because of the active pathogenic role of TRAb. For predicting recurrence, with the proposed cutoff point proposed by the kit manufacturer for TSI, a better sensitivity was obtained when compared with TRAb (93% versus 67%), despite very low specificity (38%); by raising the cutting point to 1.4 specificity could be increased to 86% without reduced sensitivity. A larger sample in needed to support a higher TSI cutoff point in the clinical routine for the assessment of GD recurrence after ATD.

Thyroid

THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

Abnormal Thyroid Function Is Associated With Lymphopenia in Bacterial Sepsis and COVID-19

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Background: Lymphopenia is a key feature of immune dysfunction in bacterial sepsis and COVID-19 patients and is associated with poor clinical outcomes, but the cause is largely unknown. These severely ill patients may also present with thyroid function abnormalities, so-called non-thyroidal illness syndrome (NTIS), and several studies have suggested that TSH, thyroxin (T4) and triiodothyronine (T3) play a crucial role in the homeostatic regulation and function of lymphocyte populations.
Aim: The purpose of this study was to test the hypothesis that abnormal thyroid function correlates with lymphopenia in severly ill patients with bacterial sepsis or COVID-19.
Methods: Retrospective analysis of absolute lymphocyte counts and circulating TSH, T4, FT4, T3, albumin and inflammatory biomarkers was performed in two independent cohorts of bacterial sepsis (n=224) and hospitalized COVID-19 patients (n=35).
Results: Only T3 correlated (rho=0.252, p-value: <0.001) with lymphocyte counts in the bacterial sepsis population and lower concentrations were found in severe lymphopenic compared to non-lympopenic patients (p-value: <0.001; n=56 per group). Severe lymphopenic COVID-19 patients (n=17) showed significantly lower plasma concentrations of TSH, T4, FT4 and T3 (p-value: 0.026, <0.001, 0.001, <0.001, respectively) compared to patients withouth lymphopenia