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THE ROLE OF FREE TRIIODOTHYRONINE TO FREE THYROXINE RATIO IN THE DIFFERENTIAL DIAGNOSIS OF THYROTOXICOSIS: A CROSS-SECTIONAL STUDY

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INTRODUCTION

Accurate diagnosis of thyrotoxicosis, a condition resulting from excessive thyroid hormone activity, is essential for appropriate management. However, access to diagnostic tools such as thyrotropin receptor antibody (TRAb) assays and thyroid ultrasonography remains limited in resource-constrained settings, highlighting the need for cost-effective alternatives. Recent studies suggest that the free triiodothyronine to free thyroxine (FT3/FT4) ratio may serve as a potential biomarker for differentiating the causes of thyrotoxicosis.

METHODOLOGY

This cross-sectional study evaluated the FT3/FT4 ratio in newly diagnosed thyrotoxicosis patients aged ≥18 years recruited from Hospital Tengku Ampuan Rahimah, Hospital Banting, Klinik Kesihatan Pelabuhan Klang, and Klinik Kesihatan Pandamaran between February and December 2025. All participants underwent thyroid function testing (FT3, FT4, and TSH) and autoantibody assessment (TRAb and anti-thyroid peroxidase [anti-TPO]). Diagnostic performance of the FT3/FT4 ratio for Graves' disease was assessed using receiver operating characteristic (ROC) curve analysis.

RESULTS

Fifty-eight patients were included, of whom 58.6% were diagnosed with Graves' disease. Patients with Graves' disease had significantly higher FT3 levels (median 16.8 pmol/L; IQR 10.9–25.7) compared to those with non-Graves' thyrotoxicosis (median 8.3 pmol/L; IQR 5.3–13.5; p <0.001), with similar trends observed for FT4 levels (p <0.001). However, the FT3/FT4 ratio did not differ significantly between groups (p >0.05), with an overall ROC AUC of 0.572, indicating poor discriminatory ability. Subgroup analysis based on FT4 levels improved performance; at FT4 <30 pmol/L, the FT3/FT4 ratio demonstrated 75.0% sensitivity, 91.7% specificity, and 87.5% diagnostic accuracy at a cutoff of 0.3445 (AUC = 0.813; 95% CI: 0.570–1.000; p = 0.069). No significant association was observed between the FT3/FT4 ratio and TRAb or anti-TPO.

CONCLUSION

The FT3/FT4 ratio has limited overall diagnostic utility but may provide adjunctive value in selected biochemical contexts, particularly in settings with limited access to immunological testing.