Evaluating ST2 and REG3α as Biomarkers for Diagnosis and Monitoring of Graft-versus-Host Disease

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Introduction

Allogeneic hematopoietic stem cell transplant (Allo-HCT) is a curative therapy for various hematological disorders; however, acute graft-versus-host disease (aGVHD) remains a significant cause of non-relapse mortality. Although histopathology remains the gold standard for diagnosis, delays in biopsy results can hinder timely management. Recent studies suggest that biomarkers such as suppression of tumorigenicity 2 (ST2) and regenerating islet-derived protein 3 alpha (Reg3a) may assist in early diagnosis and monitoring of aGVHD.

Objectives

This study aimed to investigate the role of ST2 and Reg3a biomarkers in the diagnosis and post-treatment monitoring of aGVHD.

Methods

A prospective observational study was conducted at the Armed Forces Bone Marrow Transplant Center, CMH Rawalpindi, from July 2023 to December 2024. Patients undergoing Allo-HCT for malignancy and beta thalassemia major were included and monitored for clinical signs of aGVHD. ST2 and Reg3a levels were checked at day 0 and 45 of transplant. For patients developing GVHD, pre-treatment and post treatment samples were collected for comparison. Biomarker levels were correlated with clinical outcomes.

Results

A total of number of 15 patients were included, among which 7 patients developed GVHD while 8 patients were considered as controls. At day 0, no significant difference between cases and controls was observed in mean level of ST2 (7504.87 ng/mL vs 3603.41 ng/mL, p=0.19), or in mean level of Reg3a (29.33 ng/mL vs 34.89 ng/mL, p=0.24). However, at day 45, mean level of ST2 was significantly higher in those patients who subsequently developed GVHD (3984.17 ng/mL vs 1742.10 ng/mL, p=0.020) although mean Reg3a level did not show significant difference (29.08 ng/mL vs 32.66 ng/mL, p=0.519).

Comparing levels at onset with post treatment levels in cases, the role of biomarkers in post treatment monitoring was found to be insignificant (ST2: 5900.56 vs 5337.59, p= 0.65, Reg3a: 28.07 vs 23.92, p=0.10).

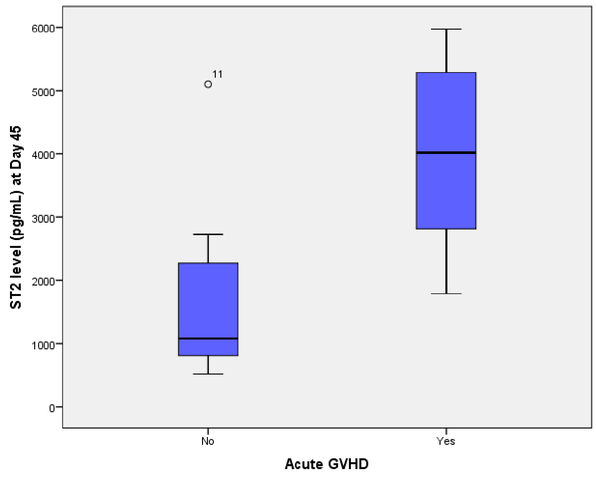


Figure 1: Box plot showing ST2 levels (pg/mL) at Day 45 post-transplantation in patients with and without acute GVHD (aGVHD). The box represents the interquartile range (IQR), the horizontal line within the box indicates the median, and the whiskers denote the minimum and maximum values within 1.5× IQR. An outlier is marked by a small circle.

Conclusion

The ST2 level can be a useful biomarker for predicting acute GVHD. More data with larger cohort is needed to establish clinical utility of ST2 in GVHD prediction and response monitoring

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