

Performance of an anti-GAGA4 IgM assay in distinguishing multiple sclerosis patients from control groups in a US cohort: a cross sectional retrospective study

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Background: Previous studies have shown that anti-Glc(α-1,4)Glc(α) (GAGA4) IgM antibody enzyme immunoassay (EIA) can distinguish multiple sclerosis (MS) patients from other neurological diseases (OND) and healthy controls (HC).

Objective: To confirm the ability of anti-GAGA4 IgM EIA to differentiate diagnosed MS patients from HC and OND patients positive for other neurological related antibodies in a US cohort.

Methods: Cross-sectional retrospective analysis of frozen sera from a US cohort consisting of 640 MS patients (48.5 ±11.8yrs), 100 HC (39.9±12.3yrs) and 31 OND controls (61.2±16.4yrs) was carried out. Sera with masked identity were diluted 1:1200 and EIA units (EU) of anti-GAGA4 IgM were measured by gMS® Dx Immunoassay (Glycominds, Lod, Israel) and normalized by dividing by the square root of total IgM levels (mg IgM/mL serum). Anti- GAGA4 IgM cutoff level for determining antibody status (positive/negative) was determined at the upper 15 percentile of non-MS controls.

Results: A correction for age was performed since anti-GAGA4 IgM EU/(mg/mL)^{0.5} levels decreased with age (slope coefficient -0.455(EU/(mg/mL)^{0.5}/year), p<0.0001, linear regression). MS patients had significantly higher (p<0.0001, Mann-Whitney U test) levels of anti-GAGA4 IgM (median, 49.0 EU/(mg/mL)^{0.5} than both HC (median, 35.5 EU/(mg/mL)^{0.5}) and OND controls (median, 31.8 EU/(mg/mL)^{0.5}). ROC curve analyses showed that anti-GAGA4 IgM has the ability to discern MS from HC (AUC: 0.70) and MS from OND controls (AUC: 0.83). The cutoff for antibody positivity was set at 57 EU/ (mg/mL)^{0.5}, leading to a sensitivity of 38.8% (95% CI: 35.0-42.7%) for detecting MS patients with a specificity of 84% (95% CI: 75.3-94.6%) for HC and 100% (95% CI: 86.7-100%) for OND controls. Interestingly, anti-GAGA4 IgM levels were slightly increased with longer duration of MS (Spearman's rho=0.08, p=0.04).

Conclusions: We confirmed that the anti-GAGA4 IgM EIA assay can differentiate MS patients from healthy controls and patients positive for other neurological related antibodies.