HEALTH SERVICES LABORATORIES

Comparison of Autoimmune Diagnostic Diabetic Markers of Type-1 Diabetes Miletus

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Introduction

Diabetes miletus is disorder of carbohydrate metabolism char-acterised by hyperglycaemia caused by deficiency, defect or action of insulin and cell resistance. The prevalence of all forms of diabetes miletus in the UK is 3.5-4.5% with about 15% being type 1 diabetes miletus (T1DM) and 85% being type 2 diabetes miletus (T2DM) of which 10% is slowly evolving immune-mediating diabetes (SEIMD). Diabetes affects everyone through out the world and steadily rising .by 3.5-4.5% every year (1,3, 6).

Clinically diagnosis and monitoring of therapy of diabetes is confirmed by measuring blood glucose in the presence of symptoms of diabetes. In asymptomatic people elevated glu-cose level values are repeated with the same test as soon as practicable to confirm the diagnosis (4,5,6).

The revised NICE guideline NG17/18 of diabetes diagnosis and management recommend to consider confirmation with diabetes-specific autoantibody test if the patient have atypical feature of T1DM, suspicion of monogenic diabetes and has implication on threapy. The autoantibody tests have their low-est false negative rate at the time of diagnosis, and that the false negative rate rises after this and using 2 different dia-betes-specific autoantibodies to reduce the false negative rate. Routine diabetes-specific autoantibody testing to confirm type 1 diabetes is not recommended (2,3,4).

The objective of this poster presentation is to compare the specificity, sensitivity and predicative values of the in house indirect immunofluorecence Islet cell antibody (ICA) assay and the referral diabetes ELISA autoantibody assays (Glutamic acid decarboxylase (GAD65), Insulinoma islet antigen-2 (IA-2) and Zinc Transporter (ZnT8) for confirmation of autoimmune diabetes, identify the most accurate assays and verify on automated platform (Agility) to meet the increasing demand of diabetes autoantibody testing of HSL Immunology.

IMAGE 1: Immunology Department at the Halo Building

Method

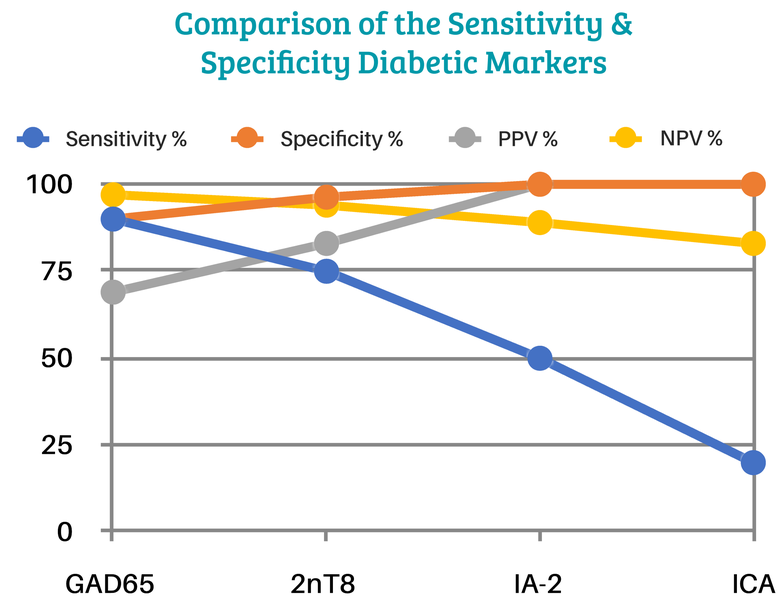
2370 test results of immune-mediating diabetes (T1DM or SEIMD) of patient data extracted from archive of LIMS for review of which 100 samples tested with four autoantibody diabetic markers (in house indirect immunofluorecence anti-body ICA assay and three referral ELISA autoantibody assays (GAD6, IA-2 and ZnT8)) had been identified.

The data of the 100 samples were analysed to calculate and compare sensitivity, specificity and predictive value and select the most accu-rate assays for verification on automated ELISA analyser (Agility) and bring in house samples send to referral laboratory to HSL immunology laboratory following NICE guidelines. and propose pathway of autoantibody diabetic testing.

Results

The data of only 100 samples tested with four pancreatic autoantigens (ICA, GAD, IA-2 and ZnT8) out of 2370 patient samples tested for diabetic autoantibody were analysed. The 29 out of 100 samples tested positive with at least one of the 4 assays of which 9 tested positive with only one assay, while 20 were tested positive with two or more assays.

The 20 immune-mediated diabetes positive and 80 negative samples are used to calculate the sensitivity and specificity of each assays as indicated in Chart-1. From the 100 patient samples 4 ICA, 20 GAD65, 10 IA-2 and 15 ZnT8 ab found tested positive with 20%, 90%, 50% and 75% sensitivity and specificity of 100%, 90%, 100% and 96.3% respectively (see chart below).



Conclusion

With this retrospective data analysis, GADab and ZnT8ab testing are more accurate with comparable sensitivity, specifici-ty and predictive value compared to ICA and IA-2, which is in agreement with other studies (1,2), and the clinical evaluation of the respective kit insert except the low sensitivity rate of ICA IFA assay which might be due to the sample taken late after diagnoses and subjectivity of reading requiring skilled experi-enced staff. ICA is the least sensitive and technically demand-ing assay. Once the verification on the automated platforms (Agility) completed the two best combination (GAD65 and ZnT8 ab) will be used in house to meet the raising demand for testing for autoantibody pancreatic islet beta cell antigen serology markers to confirm T1DM and SEIMD of diabetic patients.

The in house testing will dramatically reduce turn-around time and price of the referred samples without com-promising the quality. The turnaround time of referral sample is 3 weeks, while the in house testing turnaround time is 1-2 days. The combination of GAD and ZnT8 Ab testing increase the diagnosis and predication of T1DM than the other combi-nation of assays.

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