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# Diabetes-Associated Autoantibodies Among Young Diabetes Mellitus Patients in Malaysia

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## ABSTRACT

**Introduction:** Diabetes-associated autoantibodies (DAA) is the hallmark of T1DM and LADA which are frequently tested in young diabetes patients. It was noted that up to 10-15% of patients with initial diagnosis of T2DM also exhibit DAA. Regardless of the classification, the presence of DAA suggests an underlying islet autoimmunity which lead to progressive pancreatic β-cell failure. There is limited data reported on DAA in young diabetes patients in Malaysia. This study aims to determine the frequency of DAA positivity and its association with demographic and clinical characteristics among this cohort. **Methods:** A retrospective study using secondary data obtained from Allergy and Immunology Research Centre, Institute for Medical Research, Malaysia. This study included 194 diabetes patients who were diagnosed before the age of 40 years old and tested for GADA, ICA, IA2A and IAA. **Results:** From 194 patients, 91 (46.9%) were positive for least one of the following DAA: ICA (79, 40.7%), GADA (61, 31.4%), IA2A (37, 19.1%) and IAA (9, 4.6%). Multiple positivity was higher (73.6%) compared to single positivity. Highest combination of double positivity was ICA+GADA (54, 59.3%) and triple positivity was ICA+GADA+IA2A (25, 27.5%). Simultaneous positivity of four autoantibodies was seen in only one (1.1%) patient. ICA, GADA and IA2A were associated with age group and ethnicity (all $p < 0.001$). Only IA2A was associated with gender ($p = 0.012$). **Conclusions:** GADA, ICA ad IA2A are more significant in young Malaysian diabetes patients. IAA has a very low frequency in this studied population.

**Keywords:** Diabetes mellitus, Islet cell antibodies, Anti-GAD, Anti-IA2, Anti-insulin

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## INTRODUCTION

Prevalence of diabetes mellitus in Malaysia is among the highest in the world. It was reported to be 17.5% in 2015, almost 6% increment from the last 10 years (1). As reported world-wide, the incidence of diabetes is increasing especially in adolescent and young adults (2–4). Diabetes-associated autoantibodies (DAA) are produced following autoimmune β-cell injury and are frequently tested in young DM patients. Apart from confirming type 1 diabetes mellitus (T1DM), it helps to differentiate T1DM from type 2 diabetes mellitus (T2DM) especially with non-typical or overlapping phenotypes (5).

Islet cell cytoplasmic antibodies (ICA), glutamic acid decarboxylase antibodies (GADA), insulinoma-associated-2 autoantibodies (IA2A) and insulin autoantibodies (IAA) are four commonly measured diabetes autoantibodies. Although the appearance of these autoantibodies does not follow a distinct pattern, the presence of multiple autoantibodies is highly predictive of T1DM (6). Diabetes-associated autoantibodies were also found to be positive in up to 10-15% of patients initially diagnosed with T2DM (7–9). This subgroup of patients are classified as latent autoimmune diabetes in adults (LADA). LADA is also called as double diabetes or type 1.5 diabetes as it has features of T2DM with positive DAA. LADA with multiple autoantibodies was shown to progress into β-cell failure earlier than those with single autoantibody positivity (10).

Identifying the presence of DAA enables proper classification of diabetes and is clinically relevant for management. Positive autoantibodies indicates ongoing β-cell injury and earlier needs for insulin treatment compared to those with absent autoantibodies (11). This group of patients is likely to respond poorly to oral hypoglycaemic agents which results in poor blood glucose control (12). An ideal therapeutic aim in autoimmune diabetes would be at protecting the residual β-cell mass and function (13). The prevalence of DAA are reported to be different with different cohort of

patients (14). Till date, it is still unclear whether specific combinations of different autoantibodies is associated with certain forms of diabetes or carries certain risks (6).

There are many studies involving DAA but the information on young diabetes patients in Asia, particularly in Malaysia is limited (15,16). This study aims to determine the presence of four classical DAA (ICA, GADA, IA2A and IAA) and their association with demographic and clinical characteristics among young DM patients in Malaysia.

## MATERIALS AND METHODS

This is a retrospective study using data collected from Allergy and Immunology Research Centre (AIRC), Institute for Medical Research, Malaysia which is the reference laboratory for specialised autoimmune tests. The study included 194 patients (111 females and 83 males) who were diagnosed with DM before the age of 40 years old with varying disease duration. All patient samples were analysed for the four classical DAA (GADA, ICA, IA2A and IAA). The relevant demographic and clinical characteristics (age, ethnicity, gender, disease duration and HbA1c level) were obtained from the laboratory request forms. The results of DAA testing were collected from the laboratory information system (LIS) in AIRC. This study protocol was approved by the Malaysia Ministry of Health ethics committee (NMRR-16-757-30464).

Anti-glutamic acid decarboxylase (GADA), anti-islet cell (ICA), anti-insulinoma associated antigen 2 (IA2A) and anti-insulin (IAA) were assayed by enzyme-linked immunosorbent assay (ELISA) (MEDIPAN Medizym®, Germany). The cut-off positivity was according to manufacturer's recommendation which were 5 IU/ml for GADA, 1.0 for ICA, 10 IU/ml for IA2A and 18 IU/ml for IAA.

Statistical analysis was performed with Social Package for Social Science Version 25.0. The associations were tested using Chi-square test or Fisher's exact test. Comparison between groups were analysed using Mann-Whitney U test and Kruskal-Wallis test. The correlations were analysed using Pearson's correlation coefficient test. The level of significance was set at $p$ value of less than 0.05.

## RESULTS

The overall demographic characteristics of patients are shown in Table I. In summary, 91 (46.9%) patients aged between 10 to 20 years old. Only 21 (10%) patients aged below 10 years old. Most were of Malay ethnicity, 129 (66.5%) with slight female predominance, 111 (57.2%). Majority of patients, 144 (74.2%) were diagnosed of having DM in less than a year and 184 (94.8%) had raised HbA1c level.

**Table I: Demographic and clinical characteristics of young diabetes patients in Malaysia**

| Demographic and clinical characteristics | | Patients (n = 194) | |
|---|---|---|---|
| | | Frequency (n) | Percentage (%) |
| **Age Group** | <10 years | 21 | 10.8 |
| 19.14 ± 8.413[a] | 10-20 years | 91 | 46.9 |
| (years) | 20-30 years | 57 | 29.4 |
| | >30 years | 25 | 12.9 |
| **Gender** | Male | 83 | 42.8 |
| | Female | 111 | 57.2 |
| **Ethnicity** | Malay | 129 | 66.5 |
| | Chinese | 26 | 13.4 |
| | Indians | 29 | 14.9 |
| | Others | 10 | 5.2 |
| **Disease duration** | < 1 year | 127 | 65.5 |
| 22.30 ± 46.08[a] | 1 - 5 years | 43 | 22.2 |
| (months) | > 5 years | 24 | 12.4 |
| **HbA1c level** | ≤ 6.5% | 11 | 5.7 |
| 11.40 ± 2.96[a] | > 6.5% | 183 | 94.3 |
| (%) | | | |

[a] Mean ± SD

### Positivity of diabetes autoantibodies and their combination

Among 194 patients, 91 (46.9%) had at least one positive DAA. ICA was found to be positive in up to 79 (40.7%) of patients, followed by GADA, 61 (31.4%) and IA2A, 37 (19.1%). IAA was found to be positive in only 9 (4.6%) patients (Table II). Among patients with positive autoantibodies, 24 (26.4%) had single positivity compared to multiple positivity, 67 (73.6%). For double positivity, combination of ICA + GADA was the highest as seen in 54 (59.3%) patients. Triple positivity of DAA was found to be highest with ICA + GADA + IA2A combination in 25 (27.5%) of patients. Simultaneous positivity of four autoantibodies was observed in only one (1.1%) patient.

**Table II: Diabetes-associated autoantibodies and their combinations in young diabetes patients with positive autoantibodies**

| DAA or its combination | Patients with positive DAA (n=91) | |
|---|---|---|
| | Frequency (n) | Percentage (%) |
| ICA | 79 | 86.8 |
| GADA | 61 | 67.0 |
| IA2A | 37 | 40.7 |
| IAA | 9 | 9.9 |
| ICA + GADA | 54 | 59.3 |
| ICA + IA2A | 33 | 36.3 |
| ICA + IAA | 5 | 5.5 |
| GADA + IA2A | 27 | 29.7 |
| GADA + IAA | 4 | 4.4 |
| IA2A + IAA | 1 | 1.1 |
| ICA + GADA + IA2A | 25 | 27.5 |
| ICA + GADA + IAA | 3 | 3.3 |
| ICA + IA2A + IAA | 1 | 1.1 |
| GADA + IA2A + IAA | 1 | 1.1 |
| ICA + GADA + IA2A + IAA | 1 | 1.1 |
| ICA / GADA / IA2A / IAA | 91 | - |

DAA, diabetes-associated autoantibodies; ICA, islet cell cytoplasmic antibodies; GADA, glutamic acid decarboxylase antibodies; IA2A, insulinoma-associated-2 autoantibodies; IAA, insulin autoantibodies; "+" indicates simultaneous positivity; "/" indicates at least one positivity

### Association of diabetes autoantibodies

Diabetes-associated autoantibodies were found to be associated with demographic characteristics (Table III). ICA, GADA and IA2A were associated with age group and ethnicity (all p < 0.001). However, only IA2A was associated with gender (p = 0.012). All the autoantibodies were neither associated with disease duration nor HbA1c level.

**Table III: Association of diabetes-associated autoantibodies with demographic and clinical characteristics of young diabetes patients**

| | Patients (n = 194) | | | |
|---|---|---|---|---|
| | **ICA** | **IAA** | **GADA** | **IA2A** |
| **Positivity n (%)** | 79 (40.7%) | 9 (4.6%) | 61 (31.4%) | 37 (19.1%) |
| **Age** | | | | |
| < 10 | 18 | 3 | 16 | 12 |
| 10 - 20 | 32 | 3 | 26 | 13 |
| 20 - 30 | 22 | 2 | 15 | 9 |
| > 30 | 7 | 1 | 4 | 3 |
| $X^2$ (df)[a] | 20.56 (3) | NA | 23.32 (3) | NA |
| *p* value | **< 0.001** | 0.183[b] | **< 0.001** | **< 0.001**[b] |
| **Gender** | | | | |
| Male | 30 | 5 | 25 | 9 |
| Female | 49 | 4 | 36 | 28 |
| $X^2$ (df)[a] | 1.26 (1) | NA | 0.12 (1) | 6.36 (1) |
| *p* value | *p*=0.262 | *p*=0.501[b] | *p*=0.731 | **p=0.012** |
| **Ethnicity** | | | | |
| Malay | 40 | 6 | 21 | 12 |
| Chinese | 14 | 1 | 12 | 9 |
| Indians | 15 | 2 | 15 | 12 |
| Others | 7 | 0 | 3 | 4 |
| $X^2$ (df)[a] | 15.92 (3) | NA | 11.44 (3) | NA |
| *p* value | **0.001** | 0.915[b] | **0.001** | **< 0.001**[b] |
| **Disease duration** | | | | |
| < 1 year | 46 | 7 | 41 | 29 |
| 1 - 5 years | 21 | 2 | 12 | 5 |
| > 5 years | 12 | 0 | 8 | 3 |
| | 3.10 (2) | NA | 0.33 (2) | 3.38 (2) |
| | 0.213 | 0.770[b] | 0.848 | 0.184 |
| **HbA1c level** | | | | |
| ≤ 6.5% | 76 | 8 | 60 | 37 |
| > 6.5% | 3 | 1 | 1 | 0 |
| $X^2$ (df) | NA | NA | NA | NA |
| *p* value | 0.598[b] | 0.287[b] | 0.463[b] | 0.350[b] |

DAA, diabetes-associated autoantibodies; ICA, islet cell cytoplasmic antibodies; GADA, glutamic acid decarboxylase antibodies; IA2A, insulinoma-associated-2 autoantibodies; IAA, insulin autoantibodies
[a] Chi-square test [b] Fisher's exact test

### Comparison of diabetes autoantibodies level

Levels of ICA, GADA and IA2A were significantly higher in patients below 10 years old compared to other age groups. Levels of ICA (p = 0.002) and GADA (p = 0.005) were significantly higher in Chinese compared to Malays whereas ICA (p = 0.001) was significantly higher in Indians compared to Malays (Table IV). There were no significant difference between DAA levels with disease duration and HbA1c.

**Table IV: Comparison of diabetes-associated autoantibodies levels with demographic and clinical characteristics of young diabetes patients**

| | Median (IQR) | | | |
|---|---|---|---|---|
| | **ICA (ratio)** | **IAA (U/mL)** | **GADA (IU/mL)** | **IA2A (IU/mL)** |
| **Age** | | | | |
| < 10 years | 14.86 (11.20) | 2.11 (8.90) | 107.14 (243.40) | 72.76 (198.54) |
| 10 – 20 years | 0.49 (2.75) | 2.06 (2.40) | 2.87 (6.13) | 0.69 (4.98) |
| 20 – 30 years | 0.66 (4.38) | 1.86 (2.74) | 2.47 (5.45) | 0.01 (7.50) |
| > 30 years | 0.42 (1.71) | 1.77 (5.04) | 2.86 (3.84) | 0.52 (1.49) |
| df[a] | 3 | 3 | 3 | 3 |
| *p* value | **< 0.001** | 0.685 | **< 0.001** | **0.007** |
| **Gender** | | | | |
| Male | 0.48 (2.83) | 1.81 (2.54) | 3.01 (15.55) | 0.01 (1.09) |
| Female | 0.60 (5.82) | 2.02 (2.92) | 2.78 (17.25) | 1.04 (13.34) |
| *Z*-statistic[b] | -1.149 | -1.234 | -0.591 | -2.433 |
| *p* value | *p*=0.136[b] | *p*=0.217[b] | *p*=0.555[b] | **p=0.015**[b] |
| **Ethnicity** | | | | |
| Malay | 0.43 (1.80) | 2.02 (2.55) | 2.77 (4.43) | 0.08 (3.13) |
| Chinese | 1.77 (16.55) | 1.70 (2.62) | 4.29 (248.22) | 0.65 (80.15) |
| Indians | 4.21 (14.13) | 1.85 (4.54) | 10.64 (93.49) | 0.66 (144.57) |
| Others | 1.68 (7.51) | 3.44 (4.45) | 2.84 (5.85) | 4.15 (94.12) |
| df[a] | 3 | 3 | 3 | 3 |
| *p* value | **< 0.001** | 0.714 | **0.023** | <0.130 |
| **Disease duration** | | | | |
| < 1 year | 0.51 (8.24) | 1.85 (2.63) | 2.92 (15.53) | 0.77 (7.79) |
| 1 - 5 years | 0.88 (6.21) | 2.19 (2.66) | 2.45 (13.10) | 0.01 (3.10) |
| > 5 years | 0.99 (2.70) | 1.83 (3.84) | 3.52 (26.03) | 0.69 (2.05) |
| df[a] | 2 | 2 | 2 | 2 |
| *p* value | 0.592 | 0.387 | 0.113 | 0.120 |
| **HbA1c level** | | | | |
| ≤ 6.5% | 0.48 (2.75) | 2.46 (14.28) | 3.24 (4.56) | 1.02 (7.66) |
| > 6.5% | 0.54 (7.67) | 1.86 (2.89) | 2.87 (16.07) | 0.54 (7.22) |
| *Z*-statistic[b] | -0.007 | -1.443 | -0.169 | -0.188 |
| *p* value | 0.995[b] | 0.149[b] | 0.866[b] | 0.851[b] |

DAA, diabetes-associated autoantibodies; ICA, islet cell cytoplasmic antibodies; GADA, glutamic acid decarboxylase antibodies; IA2A, insulinoma-associated-2 autoantibodies; IAA, insulin autoantibodies
[a] Kruskal-Wallis test [b] Mann-Whitney U test

### Correlation of diabetes autoantibodies

Higher levels of DAA were seen in younger patients. All four autoantibody levels were inversely correlated with age (Table V).

## DISCUSSION

The classification of diabetes mellitus is not as straight forward as previously thought. Although they are mainly

**Table V: Correlation of diabetes-associated autoantibodies with age**

| | Age | |
|---|---|---|
| | r[a] | p value |
| ICA | -0.172 | 0.016 |
| IAA | -0.152 | 0.034 |
| GADA | -0.186 | 0.010 |
| IA2A | -0.213 | 0.003 |

ICA, islet cell cytoplasmic antibodies; GADA, glutamic acid decarboxylase antibodies; IA2A, insulinoma-associated-2 autoantibodies; IAA, insulin autoantibodies
[a] Spearman's rank correlation coefficient

classified into T1DM and T2DM, diabetes mellitus is more a spectrum of heterogenous disease (17). Certain clinical features of T2DM such as overweight and acanthosis nigricans are seen in up to 12-14% of T1DM patients (18). Increasing prevalence of obesity in children and adolescent has made identifying the types of diabetes challenging (19,20). The proportion of patients who were clinically T2DM, but later found out to be adult-onset T1DM or LADA falls in between 6.5-15% (21). DM with underlying autoimmune mechanism imposes different clinical and public health implications. Testing for DAA is not only for confirming T1DM and LADA, but is also helpful for ascertaining the classification of diabetes mellitus with mixed phenotypes. Presence of DAA indicates continuous injury that will progress into β-cell failure and future needs of insulin administration (18,22).

Diabetes-associated autoantibodies was found to be positive in 91 (46.9%) young (40 years old and below) Malaysians with diabetes mellitus, regardless of the form. ICA has the highest frequency of positivity which was seen in 76 (40.7%) patients, followed by GADA in 61 (31.4%) patients. Generally, ICA and GADA were positive in 70-80% of T1DM and 10-20% of T2DM (23–25). ICA was the first autoantibodies recognised to be associated with autoimmune form of diabetes mellitus back in 1970s (26–28). Subsequent studies had revealed that ICA are heterogeneous and target multiple antigens including GAD65, IA-2 and IA-2β. GADA which is directed against GAD65 was shown to be part of positive ICA reaction (6,26). According to the Islet Autoantibody Standardization Program (IASP), they recommend four types of DAA measurement which are GADA, IA-2A, IAA and zinc transporter 8 autoantibody (ZnT8A) (29,30). ICA has been very useful and is still measured in some laboratories including in Malaysia, but many have opted for autoantibodies to specific proteins of the islet cells. As reported by Decochez *et al.*, (37) and our current study, it can be concluded that ICA and GADA positivity are almost similar in frequency.

IA-2A was only found in 37 (9.1%) patients which is not in agreement with a study conducted by Ong *et al.* on Singaporean adult-onset diabetes. That study concluded that IA-2A is more prevalent than GADA in Asian cohort compared to Caucasian (14). However, inconsistent findings on IA2A were found in the following studies (23,31). IA-2A was noted to be of lower prevalence compared to GADA in a study conducted by Trisorus *et al.* on Thai juvenile-onset T1DM (23), but an opposite finding was found from another study by Anderson *et al.* carried out in Sweden population (31). Buzzetti *et al.* concluded that IA2A appearance was associated with DM patients of high BMI, which phenotypes were similar to T2DM (21). It is suggesting that a different mechanism of DM pathogenesis might be involved in this group of patients.

Presence of multiple DAA is associated with more rapid progression of β-cell failure (32). It is also more significant and better at predicting the risk of developing T1DM as compared to single autoantibody positivity. However, these autoantibodies are not completely independent of each other and they are shown to have age relationship (6). In our study, there were 67 (73.6%) patients who had multiple autoantibodies. Double positivity was found to be highest with ICA + GADA combination that was in 54 (59.3%) patients. Triple positivity was found to be the highest with ICA + GADA + IA2A combination that was in 25 (27.5%) patients. Simultaneous positivity of four autoantibodies was observed in only one (1.1%) patient. Multiple DAA positivity is reported to be more commonly seen in T1DM children below 10 years old (33) and prevalence significantly decrease along the disease duration (22). A study in elderly with T2DM demonstrated that majority tend to have single DAA positivity (34).

In this study, ICA, GADA and IA2A were shown to be associated with age group. Their levels were significantly higher in children less than 10 years old as compared to older age groups. Previous studies have found that the positivity of DAA varies with age of onset. GADA and IA2A were shown to significantly decrease along disease duration (22,35). Our study did not show association of IAA with age. This finding might have been contributed by the low number of patients that aged below 10 years old (10.8%) and the overall low IAA positivity in this cohort (4.6%). IAA positivity inversely correlated with age and is rare in adults. Its positivity decreases from 50-60% in T1DM patients aged less than 10 years old to only 10% in above 30 years old. This is in contrast to IA2A positivity which gradually decreases following disease duration and GADA positivity which is shown to be the most consistent regardless of age (36,37). GADA was also shown to be persistently positive in about 35% of LADA patients after 3 years (38).

There was no significant difference in the number of young DM patients according to gender in our cohort. However, IA2A was found to be associated with gender and its level was significantly higher in females. Several studies have reported GADA and IA2A to be more frequent in females, but the significant higher levels were only seen in GADA (22,36,39,40).

The prevalence of DAA varies in different populations.

These differences were seen within the same continents such as among the European countries as reported in studies by Garnier *et al*. on a large French cohort (47), by Decochez *et al*. on Belgian population (37) and by Anderson *et al*. on Swedish population (31). Such differences were also seen among different ethnicities in Asians as reported by several studies on DM patients in China (7), Thailand (18, 23), Korea (35), Taiwan (22) and Malaysia (16). We found that ICA to be significantly higher in Malaysian Chinese compared to Malays and Indians. GADA on the other hand was only significantly higher in Chinese compared to Malays. Our finding is in contrast to a study among adult Singaporean cohort which concluded that GADA is less prevalent in Asian compared white European cohort (14).

GADA was found to be present in 77.1% of multi-ethnic DM patients between 12 to 40 years old from China, India, Malaysia and Singapore as reported in a study by Thai *et al*. (15). Other studies on paediatric and young DM patients in Thailand, Taiwan and Korea also found similar percentages of GADA positivity which were in between 65.0% to 75.0% (18,22-23,35). However, GADA positivity in Malaysian young DM patients were lower as seen in our study (31.4%) which also agrees to what was reported by Nazaimoon *et al*. in year 2000 (33.8%) (16).

The frequency of positive IAA is the lowest in our study and it does not associate with all the demographic and clinical characteristics studied. Wang *et al*. have concluded that IAA is often the first autoantibody detected in children at diagnosis (41). This finding was also supported by Larrson *et al*. and Bosi *et al*. (42,43). Although insulin is regarded to be a highly specific antigen of β-cells, IAA measures both antibodies against endogenous and exogenous insulin and becomes clinically insignificant after insulin treatment is initiated (44,45).

We found no relationship between the levels of DAA and HbA1c. This finding is in agreement with a study looking at the association between GADA and clinical severity of fulminant T1DM where GADA was shown to be correlated with blood pH and ketone bodies, but not HbA1c (46). Another study also concluded that GADA and IAA levels were not correlated with HbA1c levels (35).

Another interesting part is that more than half of this study cohort were negative for all four DAA tested. As reported in previous studies, it can be concluded that not all autoimmune DM patients will be tested positive for the currently available DAA assays (14-16,22-24,47). They might produce autoantibodies against other not tested epitopes such as ZnT8. Anti-ZnT8 was found to be positive in 5-10% of T1DM patients (47–49) and 3-12% of LADA patients whom initially diagnosed as T2DM with negative GADA and IA2A (38). There is also possibility of the autoantibodies to be directed at other islet cell epitopes that are yet to be discovered. Another possibility is that these young DM patients are truly having earlier than usual onset of T2DM (19) or having rarer monogenic disorders of DM like maturity-onset diabetes of the young (MODY) (50).

Our study has a few limitations. We did not classify the diagnosis of diabetes according to the classification. Rather, the data was analysed in relation to young DM patients of less than 40 years old in general. It is also of note that the sensitivity of ELISA techniques varies among different kits and reports. This might explain the differences in the findings among different studies. The different positivity cut-off values could also contribute to these variation. The strength of this study is that it analysed the four classical DAA in young DM patients from all over Malaysia, thus representing the multi-ethnic Asian population in this country.

Information on different frequency of DAA in local population provides useful reference for selection of types of DAA to be tested. Taking the most common DAA to be present and cost into consideration, a superior DAA combination can be determined. GADA is islet cell protein specific, in contrast to ICA but has almost similar positivity rate with the latter. IA2A is also substantial as its positivity rate is more than half of GADA frequency in studied population. IAA positivity on the other hand is very low in Malaysian young DM patients. Apart from GADA and IA2A, it might be beneficial to consider other specific autoantibodies such as anti-ZnT8 in order to increase the detection rate of autoimmune DM. Additional study is needed to assess the performance of a new DAA combination in this population.

## CONCLUSION

Autoimmune diabetes mellitus has a distinct pathological mechanism and is best detected by measuring the diabetes-associated autoantibodies. Serum ICA, GADA and IA2A are significantly associated with certain demographic and clinical characteristics of young Malaysian DM patients. Serum IAA on the other hand has a very low frequency and is less useful in detecting autoimmune DM in studied population.

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