Clinical and Biochemical Heterogeneity of ‘Early Onset’ Type 2 Diabetes Mellitus

Sir,

“Early onset type 2 diabetes is not a single entity but includes at least 3 subtypes- (a) Latent Autoimmune Diabetes in Adults (LADA) (b) Maturity Onset Diabetes in Young (MODY) and, (c) true early onset type 2 diabetes.”

The investigations needed to differentiate these entities such as fasting and stimulated C-peptide levels, islet cell antibodies (ICA), glutamic acid decarboxylase (GAD) antibodies, insulin autoantibodies etc., are not available in majority of the health centres in India. The feasibility of identifying these groups clinically and whether insulin level estimation can be a differentiating factor was investigated.

Sixty clinically “early onset” type 2 diabetic patients in the age group 25 to 40 years and one to sixty consecutive patients with type 2 diabetes aged 50 and above were selected.

Age, sex, age at diagnosis of diabetes, duration of diabetes, onset type (explosive or sub acute) and history of ketosis were recorded. Detailed family history including a three generation family tree was recorded. Specific points for analysis were - history of diabetes among parents (single parent/both parent diabetics), diabetes among siblings, and any autosomal dominant mode of inheritance (history of diabetes in three generations). Weight, height, body mass index (BMI) and waist hip ratio (WHR) were recorded. An ophthalmologist evaluated the optic fundus for diabetic retinopathy. Clinical evidence of peripheral neuropathy was evaluated. Autonomic function was assessed by the three heart rate tests and two blood pressure tests as described by Ewing and Clarke. Fasting and 2-hour postprandial blood glucose estimation was done using glucose oxidase peroxidase method. 24-hour urine protein estimation was done by the turbidimetric method using sulphosalicylic acid. Serum insulin estimation was done using the Radio Immuno Assay Kit from BARC.

Data analysis was done by comparing the early onset (25-40 yrs) and late onset (above 50 yrs) groups. The early onset group was further subdivided into those with and without fasting hyperinsulinemia and compared and is reported here.

On subdividing the early onset group into those with (46 patients) and without hyperinsulinemia (14 patients), significant differences in the age of onset of diabetes, onset type, BMI and WHR were identified among the two subgroups. Age at onset of diabetes was lower in the non-hyperinsulinemic group when compared to those in the hyperinsulinemic group. In the non-hyperinsulinemic group 39.71% of patients had explosive onset of diabetes whereas all patients in the hyperinsulinemic group had insidious onset of diabetes. Thirty-two patients (69.56%) in the hyperinsulinemic group were obese (27.55 ± 1.06kg/m²) whereas none of the patients in the non-hyperinsulinemic group were obese (21.22 ± 2.14kg/m²).

The family history also showed significant differences between the two groups (Table 1). In the hyperinsulinemic group, twenty patients (43.47%) had diabetes in a parent, eight patients (17.39%) were products of conjugal diabetics and 12 patients (26.08%) had positive history of diabetes among siblings. One patient had history of diabetes among three generations suggesting a possible autosomal dominant mode of inheritance. In the non-hyperinsulinemic group, only one patient had positive family history of diabetes. No family history of diabetes could be elicited in 5 patients (10.80%) in the hyperinsulinemic group and 13 patients (92.85%) in the non-hyperinsulinemic group. On comparing complications, the patients in the hyperinsulinemic group had a higher prevalence of retinopathy, nephropathy and neuropathy, but it was not statistically significant. With respect to treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hyperinsulinemic group (n = 46)</th>
<th>Non-hyperinsulinemic group (n=14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>35.24 ± 2.72</td>
<td>31.5 ± 3.73</td>
<td>0.002</td>
</tr>
<tr>
<td>Age at diagnosis (yrs)</td>
<td>33.19 ± 2.58</td>
<td>29.79 ± 3.45</td>
<td>0.002</td>
</tr>
<tr>
<td>Onset type -(Explosive) % % (n)</td>
<td>0</td>
<td>39.71 (5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Duration of diabetes mellitus (yrs)</td>
<td>2.11 ± 0.91</td>
<td>1.34 ± 0.56</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single parent diabetic % (n)</td>
<td>43.47 (20)</td>
<td>7.14 (1)</td>
<td></td>
</tr>
<tr>
<td>Both parents diabetic % (n)</td>
<td>17.39 (8)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Siblings</td>
<td>26.08 (12)</td>
<td>0</td>
<td>0.001</td>
</tr>
<tr>
<td>Autosomal dominant inheritance</td>
<td>2.17 (1)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>10.80 (5)</td>
<td>92.85 (13)</td>
<td></td>
</tr>
</tbody>
</table>
characteristics, all patients were initially on OHA and diet therapy. All 46 patients in the hyperinsulinemic group had good glycemic control with OHA and were non-insulin requiring for glycemic control. In the non-hyperinsulinemic group 6 patients (11%) became insulin requiring after initial therapy with OHA.

To summarize, three clinically and biochemically distinct subgroups could be identified under the broad category of ‘early onset type 2 diabetes’. They were:

- A subgroup who were non-obese,
- had explosive onset of diabetes,
- had significantly low family history of diabetes,
- did not have fasting hyperinsulinemia,
- had low prevalence of complications at diagnosis,
- had poor response to OHA and were insulin requiring in 46% of cases.

This subgroup of patients constitute possibly LADA.

- A subgroup who had higher BMI,
- fasting hyper-insulinemia,
- significant positive family history of diabetes in parents and siblings,
- higher prevalence of complications at diagnosis, and
- were non-insulin requiring for glycemic control.

They constitute possibly the true early onset Type 2 diabetic patients.

- A single case of maturity onset diabetes of young (MODY), who had positive three generation family history, was obese, did not have any microvascular complication, was non-insulin requiring and did not have any markers of insulin resistance like acanthosis nigricans or skin tags.

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Most Common Prescribing Error in Post-Exposure Prophylaxis of HIV/AIDS

*Sir,

The nevirapine is one of the most common available and prescribed drugs in AIDS. However, this drug has absolutely no role in PEP in HIV/AIDS. If prescribed for PEP may lead to serious adverse effects. The same is being emphasized in the present case.

The present case, a 38 year old female, nurse by occupation got percutaneous occupational exposure to blood of an HIV+ve patient four weeks prior to presentation to our hospital. She got deep prick with the needle of syringe which she had used to draw blood sample of the patient while trying to recap the needle. The patient was known to be HIV + ve and he died after few days of this incident. As such, exposure code was 3 and status code was 2 (as per NACO guidelines) which warranted the use of expanded regimen for PEP. The physician attending her prescribed a combination of lamivudine + zidovudine + nevirapine and in the fourth week of prophylaxis she developed a maculopapular rash all over the body (Figs. 1-3) for which she was referred to this hospital. She was advised ELISA for HIV on 22nd day after exposure by attending physician. Guidelines for the investigation after exposure recommend testing at baseline and at interval of 6 weeks, 12 weeks and 6 months after exposure. ELISA for HIV before 4 weeks has no value other than establishing that the exposed individual was negative for HIV at baseline. Although PCR for RNA is not recommended for routine use, this test is of help if we want to detect infection (before ELISA becomes +ve) at early stage. Drug (nevirapine) dechallenge was performed and other two drugs were allowed to continue which improved condition of patient after 4 weeks of dechallenge. Since literature suggests no role of drugs like anti-allergic or corticosteroid in this type of rash hence was no treatment was given in this case also for the rash. The patient is on follow up presently.

In prospective studies the average risk of HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3%. Rationale for HIV PEP include the pathogenesis of HIV infection, particularly the time course of early infection; the biological plausibility that infection can be prevented or ameliorated by using antiretroviral drugs and direct or indirect evidence of the efficacy of specific agents used for prophylaxis. A combination of drugs with activity at different stages in the viral