



## Commentary

### How should one tackle prediabetes in India?

It is estimated that 84 million adults in the USA have prediabetes in 2015<sup>1</sup> and 70 per cent of these persons will develop diabetes in the long term<sup>2</sup>. According to National Urban Diabetes Survey, the estimated prevalence of prediabetes is 14 per cent in India<sup>3</sup>. The question that may be raised is as to how one may identify these individuals, so as to have an early therapeutic impact.

The World Health Organization has defined prediabetes as a state of intermediate hyperglycaemia using two specific parameters, impaired fasting glucose (IFG) defined as fasting plasma glucose of 6.1-6.9 mmol/l (110 to 125 mg/dl) and impaired glucose tolerance (IGT) defined as 2 h plasma glucose of 7.8-11.0 mmol/l (140-200 mg/dl) after ingestion of 75 g of oral glucose load or a combination of the two based on a 2 h oral glucose tolerance test<sup>3</sup>. The American Diabetes Association (ADA) includes haemoglobin A<sub>1c</sub> between 5.7 and 6.4 per cent in addition to IGT of 140-200 mg/dl and uses a lower cut-off value for IFG between 100 and 125 mg/dl<sup>4</sup>.

Since prediabetes is an asymptomatic condition, we need to go the extra mile to identify individuals with prediabetes. In this, the Madras Diabetes Research Foundation-Indian Diabetes Risk Score, which only has three questions and a waist measurement is a relatively simple method to perform<sup>5</sup>.

The next question is as to how one should therapeutically approach those who have been identified with prediabetes. Both lifestyle modification and metformin have been utilized in this group. The ADA has recommended that an intensive diet and physical activity programme for all patients with prediabetes, and that metformin be given to those with additional risk factors such as body mass index of 35 kg/m<sup>2</sup>, age <60 yr or a history of gestational diabetes<sup>6</sup>. Yet another group wherein metformin is recommended is for those with progressively rising A<sub>1c</sub> levels, despite attempts at lifestyle intervention<sup>6</sup>.

The use of metformin for prediabetes although suggested by ADA is not practiced to a great extent. In a retrospective cohort study it was noted that only 3 per cent with prediabetes have been given metformin<sup>7</sup>. In an observational NHANES (National Health and Nutrition Examination Survey) study on 7652 adults with prediabetes, metformin use was only 0.7 per cent<sup>8</sup>. In the Diabetes Prevention Program Outcome study with a 15 yr follow up, the annual incidence of diabetes was approximately 27 per cent lower in the lifestyle arm and 18 per cent lower in those who were randomized to metformin<sup>9</sup>. A substudy of the same looked at a risk prediction model to see which group may benefit the maximum. They found that participants with the highest risk quarter of the several variables were the ones that benefitted with metformin<sup>10</sup>.

In a study by Bantwal *et al*<sup>11</sup> in this issue from Bengaluru, India, 103 individuals with prediabetes based on ADA criteria were randomized into three arms - the standard, intensive lifestyle and intensive lifestyle plus metformin. There was a reduction in the HbA<sub>1c</sub> levels in the medication-based arm; however, weight reduction was noted in all the groups. This weight reduction was similar to the Centers for Disease Control and Prevention (CDC) sponsored National Diabetes Prevention Program in the USA, where 35 per cent of individuals lost five per cent of weight<sup>12</sup>. In a Cochrane review of the 12 randomized control trials with a total of 5238 persons, it was noted that the diet plus physical activity reduced or delayed the incidence of type 2 diabetes mellitus in people with IGT<sup>13</sup>. The current study had a relatively small sample size<sup>11</sup>. The time interval of six months was rather short in duration to observe any transformation in this variable. The study however, emphasized that the benefit of lifestyle modification could result in weight reduction and if metformin was added in our Indian population, it might result in changes in the HbA<sub>1c</sub> level as an additional bonus.

In an earlier study performed in India - the Indian Diabetes Prevention Programme, 531 individuals were randomized into three arms and followed for a median period of 30 months. This study also demonstrated that there was a significant reduction in the incidence of diabetes in Asian Indians with IGT. The number needed to treat one incident diabetes was 6.4 for lifestyle modification and 6.9 for metformin and 6.5 for lifestyle modification and metformin<sup>14</sup>.

In a country like India with a sizeable population of patients with diabetes one needs to reiterate the necessity of identifying prediabetes and plan on lifestyle modification for all individuals. One of the issues that one needs to keep in mind in the lifestyle programmes is the long-term adherence. In a systematic review, it was noted that long-term adherence was an issue, though better than the controls<sup>15</sup>.

It may be rather premature to consider the usage of metformin for such a prevention programme in India, the reason being that with near-universal coverage, there may be a major cost factor involved both for the population at large and the government. With such widespread implementation, there are logistic complexities that may be encountered with such a policy. Moreover, an appropriate 'number needed to treat' to accrue a significant benefit for the population and a cost-benefit figure may be devised only through the implementation of a much larger study.

**Conflicts of Interest:** None.

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