

## Significance of anti-glomerular basement membrane antibodies in type 2 diabetic patients

To the Editor

I read the above article by Dr. Noorwali<sup>1</sup> with interest, and I would like to make a few comments. The study evaluated anti-glomerular basement membrane (anti-GBM) antibodies in patients with type-2 diabetes mellitus (DM). The study revealed the presence of antibodies in all the patients with DM. Moreover, anti-GBM antibodies, which seem to appear early on the course of the disease, disappeared once patients developed diabetic nephropathy.<sup>1</sup> These are very interesting findings and have significant implications on the diagnosis of Goodpasture's syndrome which is classically associated with such antibodies. It is, therefore, extremely important to confirm these novel findings.

Anti-GBM antibodies are associated with Goodpasture's syndrome (GPS, also known as anti-GBM disease). The disease is characterized by a rapidly progressive glomerulonephritis and pulmonary hemorrhage. Early diagnosis, and treatment, is of paramount importance for the prevention of the high morbidity, and mortality, that is associated with untreated patients. Since the renal pulmonary-syndrome and the renal biopsy findings (showing crescent formation and linear IgG staining) that are associated with GPS can also occur with a variety of other conditions (for example, Wegner granulomatosis, microscopic polyangiitis, Henoch Schonlein purpura, cryoglobulinemia, connective tissue diseases), diagnosis of GPS is relied up on the findings of serum anti-GBM antibodies.<sup>2</sup> The anti-GBM antibodies that are associated with GPS are directed against the non collagenous part of the alpha-3 chain of type 4 collagen. These antibodies are highly sensitive and specific (>99%) for GPS and, therefore, their presence is taken as diagnostic for the disease.<sup>3</sup> Antibodies to GBM (including antibodies to other parts of type 4 collagen) are not specific for GPS, and are associated with a variety of other conditions (including systemic lupus erythematosus, celiac disease, IgA-nephropathy and other primary glomerulonephritis).<sup>4,5</sup> It is, therefore, important that the findings of anti-GBM antibodies in diabetic patients are confirmed and the nature of the antibodies is elucidated.

I would also like to highlight the following points: 1. In the methods section, it is mentioned that patients with DM used in the study all had >5 years disease duration. However, Figure 1 shows patients with disease duration of <1 year, 1-5 years as well as >5 years. 2. What are the sensitivity and specificity of the

ELISA used in the study? 3. What is the cut off value of the ELISA? 4. What is the nature of the antigen(s) used to coat the ELISA plates? 5. It is mentioned that anti-GBM antibodies correlated with the disease duration. However, Figure 1 shows that the antibodies appear early on the course of the disease and remain elevated until patients develop diabetic nephropathy. 6. It is also mentioned that anti-GBM antibodies can be used as a predictor of glomerulonephritis in patients with type-2 DM. However, this idea is not clear since, as shown in Table 1, all patients presenting with DM develop anti-GBM antibodies. 7. Is the ELISA kit, which is used in the above study, used in the diagnostic Immunology laboratory? 8. Minor point, is the term 'diabetic neuropathy' in Table 1 correct?

In conclusion, it would be important to confirm the novel findings of anti-GBM antibodies in diabetic patients, using a number of additional ELISA preparations, and the nature of the antibodies elucidated. Until the results are confirmed, the findings of anti-GBM antibodies, as detected by specific ELISA, may need to be taken as diagnostic of GPS, a disease, which has been reported to develop in patients with diabetic nephropathy.<sup>6,7</sup>

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### Reply from the Author

No reply was received from the Author.

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