Editorial

CLINICAL UTILITY OF BETA 2 MICROGLOBULIN MEASUREMENT

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Beta 2 microglobulin ($\beta 2$ M) is a light chain of Class I Histocompatibility Locus Antigen (HLA) with 99 amino acids. It is homologous to CH₃ domain of human Immunoglobulin. It migrates in Beta 2 region on electrophoresis and has a molecular weight of 11.8 kilodalton (K da). It was first isolated from human urine.

$\beta 2$ M is located on the exterior of plasma membranes of all nucleated cells, attached non-covalently to the heavy chain of HLA. Small amounts of $\beta 2$ M are shed into body fluids regularly, the main source of circulating $\beta 2$ M being the cells of immune system and liver. Approximately 150 to 200 mg of $\beta 2$ M is produced per day. Its serum concentration varies from 1 to 2 mg/L. Plasma levels of $\beta 2$ M are elevated either due to immune system activation or due to decreased renal clearance. $\beta 2$ M in body fluids is estimated by RIA or ELISA technique. In the past two decades knowledge of its biochemistry and physiology have been well exploited to use it as diagnostic and prognostic marker in a number of diseases involving immune system and kidney.

One of the significant areas in which $\beta 2$ M is measured is for the management of patients on renal dialysis. Plasma $\beta 2$ M increases in long term dialyzed patients. This rise collaborates with impairment of excretion and degradation by inefficient kidneys and also with increased synthesis of protein during standard dialysis.

Serum $\beta 2$ M is elevated in malignancies such as multiple myeloma, leukaemia, lymphoma and other lymphoproliferative disorders. It is one of the

most powerful tool for assessing the prognosis and response to treatment of patients with multiple myeloma. Indeed, $\beta 2$ M alone can predict outcome as well or better than many prognostic markers used previously in patients with multiple myeloma. A value of 6 mg/L is reported critical for survival. When this is used in conjunction with either Serum albumin or haemoglobin, the resultant prognostic information is far superior to that of any available prognosticators for multiple myeloma staging [1]. Serum $\beta 2$ M levels behave similarly in patients with diffuse large cell lymphoma. In patients on chemotherapy the presence of elevated serum $\beta 2$ M has been considered as a bad prognostic marker. Its value as an early indicator of relapse in this disease is well established [2]. $\beta 2$ M appears to correlate with tumor stage in patients with Hodgkin's disease as well. Elevated levels of this polypeptide predicts a less favourable prognosis.

Chronic Lymphatic Leukemia (CLL) and Immunocytoma (IC) are remarkably heterogeneous with regard to their clinical course. Given the increase of treatment options for CLL & IC, additional parameters are needed to decide which patient may benefit from early and intensified treatment. It has been shown that serum $\beta 2$ M is an independent predictor of disease progression free survival, in patients with CLL & IC in early disease stages [3].

Normal $\beta 2$ M levels in CSF are very low. A rise above 1.8 mg/L is associated with leptomeningial leukemia and lymphoma. However, the test is not very specific. Levels of $\beta 2$ M in CSF increase in

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HIV infected individuals, and the raise is proportional to the duration of infection. It has been recommended as a parameter for prognostication of neurological disease in HIV.

β 2M is produced in parotid glands of primary Sjogren's syndrome. Consequently β 2M increases in saliva of these patients. Though the sensitivity of this test is around 50 per cent it may be used as a supplementary diagnostic test in Sjogren's syndrome.

Normally 95 per cent of β 2 M is filtered through the glomerulus and 99.9 per cent filtered β 2 M is reabsorbed by proximal tubules. Increased urinary excretion of β 2 M is observed as a result of diminished tubular reabsorption when the proximal tubules are damaged. Consequently, it is used as a parameter of renal proximal tubular function.

Cadmium is widely used in industry, causing exposure of the workers and environmental pollution because of its presence in the biosystems. β 2M excretion in urine is widely used as a marker of cadmium toxicity. Mortality rates increase proportionately with the amount of β 2M excretion in urine.

Although an increase in urinary β 2M level is reported to be very useful for the diagnosis of tubulointerstitial involvement, urinary β 2M does not always provide evidence of absence of tubulointerstitial changes in normal range. Suzuki et al reported that the immunological study of renal β 2M deposition is more reliable than urinary β 2M in identifying renal dysfunction and renal injury [4].

Sodarblam et al reported that pleural fluid β 2 M was 86 per cent specific at 91 per cent sensitivity in the diagnosis of Rheumatoid arthritis. They opined that pleural fluid β 2M along with thymidine kinase could be used as a marker to differentiate Rheumatoid arthritis and Tubercular pleural effusions [5].

As a part of continuous search for surrogate markers for diagnosis and management of AIDS patients, in an article that appeared in this issue, Rao et al proposed serum β 2M level as the most useful surrogate marker for prognostication of disease progression in HIV infected patients. They found markedly elevated Serum β 2M in all HIV patients irrespective of the stage of disease and the

levels were proportionately higher in advanced cases. Similar findings were reported from other parts of the world as well [6]. While, it is true that β 2 M may be elevated in HIV patients, current life conditions of the patient must be taken into consideration for interpretation of results, as β 2 M is known to be high in non-HIV infected needle users and many other disease conditions. Further, analysis of data from Veterans Affairs Committee study on AIDS while confirming HIV RNA level and CD4 count taken together as valid predictor of HIV disease progression, did not find any correlation of β 2 M with disease progression [7]. Trials to use it as a surrogate marker in monitoring therapeutic effects in AIDS have not yielded positive results.

The value of estimating β 2M seems to be its cost effectiveness and simplicity of procedure. While, considering its usefulness as diagnostic or prognostic tool, we will be well advised to remember that it is one among a long list of surrogate markers. Using a cost effective combination of surrogate markers appears to be the right proposition for our set up.

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