

## **SUMMARY**

Minimal change nephrotic syndrome is the most common form of the nephrotic syndrome occurring in children. The etiology and underlying defects in the glomerulus remain largely unknown. In recent years, several of the newly discovered cytokines have been implicated in the pathogenesis of renal disease. Their exact role, however, remains obscure.

The current study was designed to evaluate the role of the cytokines interleukin-1 $\beta$ , interleukin-6, tumor necrosis factor and the urinary protein  $\beta$ 2-microglobulin in the children affected by minimal change nephrotic syndrome.

Our study comprised 80 children. They were divided into 4 groups:

1. Twenty children suffering from minimal change nephrotic syndrome for the first time.
2. Twenty children who recently had nephrotic syndrome and are now in remission for less than three months.
3. Twenty children having a relapse of the disease, they were examined before reinstitution of therapy.
4. Twenty healthy children were included as a control.

The children were subjected to a thorough clinical examination to make sure they met the criteria for the study. A set of laboratory investigation was performed to assess the renal function (blood urea, serum creatinine), in addition to the complete blood picture. Specific tests for serum interleukin-1 $\beta$ , interleukin-6, tumor necrosis factor and urinary  $\beta$ 2-microglobulin were performed using the ELISA technique. The results were tabulated and subjected to several statistical tests including the F test, Kruskal-Wallis test and multiple logistic regression analysis.

Our clinical data have revealed a tendency toward elevated systolic and diastolic blood pressures in the first presentation, remission and relapse groups, contrary to most previous studies, which found hypertension only in the minority of patients.

Our study revealed a significant rise in the level of interleukin-1 $\beta$  in the first presentation group, the remission group and the relapse group. Similar results were obtained for serum interleukin-6. As for serum tumor necrosis factor, only the first presentation and the relapse groups had a significant rise over the control. The urinary levels of  $\beta$ 2-microglobulin were significantly higher in the first presentation and relapse group too.

Multiple logistic regression was used to find out factors that predict the different groups. Tumor necrosis factor was found to be reliable in predicting remission cases liable to relapse. On the other hand, remission cases which are not yet immunologically stable could be predicted by the high level of interleukin-1 $\beta$  and interleukin-6. Cases in first presentation that are likely to go into remission easily could be predicted by lower levels of tumor necrosis factor and lower systolic blood pressure.

This study revealed:

1. Interleukin-1 $\beta$ , interleukin-6 and tumor necrosis factor are important pathogenic factors in minimal change nephrotic syndrome.
2. The patients in clinical remission could still have immunologic abnormalities and should be monitored by measurement of serum cytokines
3. The levels of the cytokines can be used as prognostic factors to determine which patients are likely to respond to treatment quickly, and to predict the patients which are likely to have relapses of the disease.

4. The definition of remission should be revised to include the return of the levels of interleukin-1 $\beta$  and interleukin-6 to normal.
5. A clinical trial of prolonged steroid therapy in patients in remission but have high level of interleukin-1 $\beta$  and interleukin-6 should be performed to find out if this regimen can ward off relapse.