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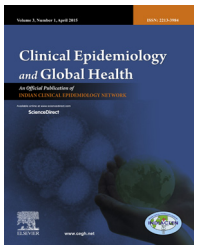

Student's section

Prediction of early response to steroids in nephrotic syndrome patients aged between 2 and 10 years

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ABSTRACT

Objective: The primary objective was to predict onset of remission within 10 days of starting corticosteroid treatment in nephrotic syndrome patients aged between 2 and 10 years (either first episode or first relapse) using clinical and laboratory variables. The secondary objective was to compare changes in CD4 count and percentage among newly diagnosed cases.

Method: Prospective cohort study with a nested case–control design was conducted from September 2009 to August 2010 after institutional ethical clearance. Included were cases aged 2–10 years diagnosed as nephrotic syndrome based on standard clinical and laboratory criteria. Controls were age- and sex-matched healthy subjects recruited from the out-patient's department.

Results: Included were 44 cases (26 newly diagnosed and 16 were first relapse) cases of nephrotic syndrome and 38 healthy age- and sex-matched controls. Variables in the linear regression model predicting remission were sex, presence of tuberculosis, Low-Density Lipoprotein (LDL)/High Density Lipoprotein (HDL) ratio and antihypertensive medication, serum LDL, serum triglyceride, and serum creatinine. CD4 count, CD4%, and CD4% rise were significantly high in first episode of nephrotic syndrome as compared to controls. Serum Very Low Density Lipoprotein (VLDL) was raised in late responders of first episode of nephrotic syndrome.

Conclusion: Female gender, concomitant tuberculosis, and raised serum VLDL delayed onset of remission while use of angiotensin converting enzyme inhibitors in hypertensive patients decreased the duration of proteinuria in cases of nephrotic syndrome in children.

Nephrotic syndrome is an important chronic disease in children. The underlying abnormality in nephrotic syndrome is an increase in permeability of the glomerular capillary wall, which leads to massive proteinuria and hypoalbuminemia. The cause of increased permeability is not well understood, and it is possible that T-cells dysfunction leads to alteration of cytokines, which causes a loss of negatively charged glycoproteins within the glomerular capillary wall. About 80% children with idiopathic nephrotic syndrome show remission of proteinuria following treatment with corticosteroids.[1] Most patients have multiple relapses, placing them at risk for steroid toxicity, systemic infections and other complications.

So a study is needed, which can predict onset of remission after steroid treatment in nephrotic syndrome patients that will guide the physician about the next line of management and hence will prevent overexposure to steroid and its toxicity. It also helps in prognostication and counseling of parents of nephrotic syndrome children because onset of remission after

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7–9 days increases risk of relapse in future.[2] This study also gives us a clue about the pathogenesis of nephrotic syndrome in children, which may help pediatrician to guide the treatment in future by targeting CD4 lymphocytes. We hypothesized that it would be possible to predict onset of remission in nephrotic syndrome patients by using clinical and laboratory variables. Therefore, the primary objective was to develop a prediction model of onset of day of remission for response to steroid using pre-steroid peripheral blood CD4 count, serum lipid levels, total leukocyte counts, and other nonrenal factors (such as age, sex, nutritional status and infections like tuberculosis status, and infections like TB) and renal factors (such as hypertension, hematuria, azotemia and Urinary Tract Infection (UTI) secondary objective was to determine peripheral blood CD4 counts, serum lipid levels with serum protein, and serum albumin before initiation of steroid in nephrotic syndrome patients aged 2–10 years and in age- and sex-matched controls.

1. Materials and methods

This study was conducted from September 2009 to August 2010 among nephrotic syndrome patients admitted in Department of Pediatrics, King George Medical University Lucknow after institutional ethical clearance. A total of 42 cases of nephrotic syndrome and 38 age- and sex-matched controls were recruited in this study (Fig. 1). Cases aged between 2 and 10 years were recruited in our study within 72 h of admission and before intake of steroid. Exclusion criteria for cases were intake of steroid for more than 10 days in last 3 months, having suspected measles infection in last 3 months, and children with clinical suspicion of connective tissue disorders, immunodeficiency disease, or HIV-positive children. Children aged between 2 and 10 years not having suspected renal disease, measles infection, or history of steroid intake for more than 10 days in last 3 months and without clinical suspicion of UTI, connective tissue disorders, and immunodeficiency diseases like HIV were recruited as controls in our study.

Nephrotic syndrome was defined as edema, nephrotic range proteinuria (>40 mg/m^2/h on timed sample, spot albumin to creatinine ratio >2 mg/mg), hypoalbuminaemia (<2.5 g/dl), and hyperlipidemia (serum cholesterol > 250 mg/dl).[3] Blood pressure was measured with the help of sphygnomanometer by auscultatory method. The patients were defined as hypertensive if systolic/diastolic blood pressure was above the 95th percentile for age and sex using normograms. The patients were defined as having pulmonary tuberculosis on the basis of diagnosis made by treating physician-based clinical symptoms, signs, and on X-ray of chest postero-anterior view. Urine protein was estimated in the morning urine sample by dipstic method and graded as nil, 1+, 2+, 3+, and 4+. Informed consent was taken from the parent before recruiting the cases and control in our study. 2 ml venous blood was taken on day 1 in a vacutainer containing EDTA for CD4 count estimation during the morning hours (8 am–12 pm) from both cases and controls. The kit used for estimation of CD4+T lymphocytes was PARTEC CD4 easy count kit. Serum cholesterol was measured by CHOD–POD liquid method. Enzymatic colorimetric (LIQUID) method was used to estimate serum Low-Density Lipoprotein (LDL). Serum High-Density Lipoprotein was measured by direct enzymatic colorimetric method. Triglyceride was measured by GPO–POD (liquid) method. Urinary leucocytes count/hpf. – 10 ml. Urine was taken from both cases and control on day 1 and this sample is first centrifuged, followed by addition of methylene blue on precipitate. With the help of light microscope, urine total leucocytes count was done. It was expressed as total number of cells/hpf. Total leukocyte and %lymphocytes count in blood was calculated through manual method.

For the purpose of analysis, nephrotic syndrome cases who were early responders to steroids were defined as those whose proteinuria became nil within 10 days for at least 1 day.[2] The rest were categorized as late responders. Adequate treatment of nephrotic syndrome patients included 6 weeks daily steroid with dose 2 mg/kg followed by alternate day steroid with dose (1.5 mg/kg for 6 weeks).

Data was collected on a preformed pilot tested structured questionnaire. Data was collected on age, sex, religion, history of consanguinity, family characteristics, anthropometry, history of present complaints, past history, and history of treatment taken. Each patient was examined and findings were noted. Investigations were done on day 1 in both cases and controls. CD4% was calculated by CD4 count divided by Absolute Lymphocyte Count (ALC). ALC was calculated by total leukocyte count (TLC) multiplied by lymphocyte% in differential count. CD4% rise was calculated by 45 minus observed CD4% (presuming 45 as a upper limit of CD4% in normal children).

1.1. *Statistical analysis*

Since this was a pilot study, formal sample size calculation was not done a priori. We committed to take all cases of nephrotic syndrome, which fulfilled the inclusion criteria during our study period because of short duration of study and low incidence of disease in study population. Distribution of all outcome and potential explanatory variables was assessed. The data was analyzed by using SPSS16 version. Univariates comparison between cases and controls was done using chi-

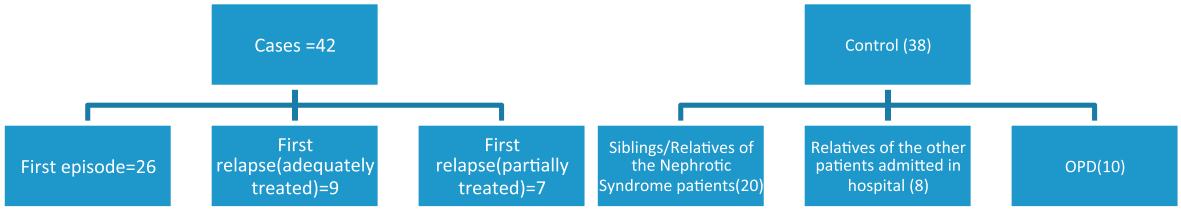

Fig. 1 – Flow diagram of recruited cases and control.

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