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A novel approach in defining and predicting steroid resistance in nephrotic syndrome in children

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Objectives: Nephrotic syndrome (NS) is a kidney disease characterized by albuminuria, hyperlipidemia, edema, and hypoalbuminemia. Above 20 % of nephrotic children do not show response to steroid treatment. Recent reports suggest different clinical, genetic and molecular markers to be associated with phenomenon of steroid resistance. However, molecular markers controlling apoptosis have not been studied as a predictors of steroid resistant NS (SRNS) and steroid sensitive NS (SSNS).

Methods:
We analyzed 56 clinical cases of children hospitalized in Pediatric Hospital №7 (Kyiv, Ukraine) with NS (26 SSNS and 30 SRNS). Stepwise logistic regression models use to identify candidates with the potential to be related to have influence of steroid resistance in children with NS. Data processed using GraphPad Prism 9.0 Software for Windows (USA, San Diego, CA).

Results: Arterial hypertension as a candidate among clinical characteristics (β - 0,31, SE 0.15, 95% CI -0.6 to -0.007, $p<0.05$) as a candidate predictive of SRNS. Among basic laboratory factors WBC level (OR: 1.4; OR 95% CI: 1.12–1.85) and RBC level (OR: 1.14; OR 95% CI: 0.38–3.48), serum creatinine (OR: 1.04; OR 95% CI: 0.92–1.14), serum urea (OR: 1.14; OR 95% CI: 0.89–1.49), serum cholesterol (OR: 1.97; OR 95% CI: 1.37–3.18) were found to be a factors defining SRNS. Apoptosis regulating BcL-xL (OR: 1.4; OR 95% CI: 1.17–1.91), Bax (OR: 1.15; OR 95% CI: 1.04–1.37), caspase-3 (OR: 1.66; OR 95% CI: 1.27–2.68) but not caspase-8 (OR: 0.95; OR 95% CI: 0.84–1.05) (AUC: 0.93; SE: 0.03; 95% CI: 0.87-0.99; $p<0.001$) found to be those defining SRNS. In group of transcriptional factors HIF-1alfa selected as a factor defining steroid resistance phenomenon (OR: 1.02; OR 95% CI: 0.98–1.07).

Conclusions: Arterial hypertension, serum creatinine level, serum urea level, serum cholesterol level, WBC and RBC count, BcL-xL, Bax, caspase-3 and HIF-1alfa indentified as candidate biomarkers to predict and define SRNS in pediatric NS.