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Mini Review

# Prediction of Renal Damage in Children with Henoch-Schönle in Purpura Based on Machine Learnings

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## ABSTRACT

Henoch-Schönlein Purpura (HSP) is one of the most common systemic vasculitis in childhood. When HSP involves the kidney and causes different degrees of renal damage such as hematuria and proteinuria, it is called Henoch-Schonlein Purpura Nephritis (HSPN). HSPN is the most common secondary glomerular disease in children. Early and accurate diagnosis of HSPN is very important for patient prognosis and individualized treatment. Renal biopsy is the gold standard for the diagnosis of HSPN. However, due to its invasive nature, it is difficult for parents and children to accept it. As a result, some patients have extremely serious renal lesions at the time of diagnosis. Many researchers are committed to studying whether simple clinical data can be used to predict HSP renal damage, so as to help clinicians diagnose HSPN early and efficiently, in order to avoid the occurrence of HSPN or reduce its severity. At present, the research on machine learning in clinical disease prediction has been relatively common; we will review the application of machine learning in children's HSPN.

**Keywords:** Henoch-Schönlein purpura; Renal impairment; Random forest; Machine learning; Prediction

## INTRODUCTION

Henoch-Schönle in Purpura (HSP) is a common systemic vacuity in childhood. IgA-based immune complex deposition can be seen in skin, kidney, digestive tract and other histopathology, also known as IgA Vasculitis (IgAV). When HSP involves the kidney and causes different degrees of renal damage such as hematuria and proteinuria, it is called Henoch-Schönle in purpura Nephritis (HSPN). Renal damage and its severity are the key factors that determine the prognosis of HSP. It is reported that about 15% to 20% of children with HSPN will eventually develop into chronic renal failure, seriously threatening the health and quality of life of children [1]. Therefore, early diagnosis of HSPN has important clinical significance for optimizing individualized treatment and determining prognosis, which makes it an important medical research direction to explore the high risk factors and active prevention and treatment of renal damage in HSP.

## EPIDEMIOLOGY AND PATHOLOGY

The incidence of HSP is high in preschool and school-age children. At present, the direct cause of HSP is not clear. Most scholars believe that it is related to infection, drug or food allergy, vaccination, dust mites, mosquito bites and other inducing factors. It can also be secondary to some tumors, which may become allergens, act on individuals with genetic susceptibility, induce autoimmune response, lead to capillary inflammatory changes, and then result in HSP. Our understanding of its pathogenesis can be divided into four categories: deposition of immune complex and abnormal cellular immunity, abnormality of cytokines and inflammatory mediators, coagulation and genetic factors. At present, it is believed that abnormal glycosylation of IgA1 may be the main mechanism of HSPN. Abnormal glycosylated IgA1 circulating immune complex cannot enter the liver and be cleared, but deposited in glomerular Mesangial area, it will cause Mesangial cell proliferation and inflammatory reaction, resulting in immunopathological damage of renal tissue [2].

## DIAGNOSIS AND TREATMENT

The current criteria for HSP are those of EULAR/PRINTO/PRES: in a child with (round or oval and retiform) purpura predominantly on the lower limbs, the diagnosis is made if at least one of the following 4 criteria is present: (1) abdominal

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pain; (2) presence of IgA on histology; (3) arthritis or arthralgia;(4) renal impairment [3]. According to "Evidence-based Guideline for Diagnosis and Treatment of Purpura Nephritis (2016)" by the Nephrology group of pediatric branch of Chinese Medical Association, the diagnostic criteria of HSPN were proposed as: hematuria and/or proteinuria occurred within 6 months of the course of HSP. Hematuria definition: gross hematuria or hematuria with more than 3 red blood cells/high-power field (HP) under microscope 3 times within 1 week. Proteinuria definition: Meet any of the following: 3 routine urine tests within 1 week qualitatively indicate positive urine protein; 24 h quantitative urine protein >150 mg or urine egg/creatinine (mg/mg) >0.2; Urinary microalbumin was higher than normal for 3 times within 1 week [4].

The clinical manifestations of children with Henoch-Schönle in purpura nephritis are not completely consistent with the degree of renal pathological injury, and the latter can more accurately reflect the degree of lesion and long-term prognosis. When there is no condition to obtain the results of pathological diagnosis, the corresponding treatment scheme can be chosen according to its clinical classification. The 2021 Updated Kidney Disease: Improving Global Outcomes (KDIGO) has proposed recommended guidelines for the treatment of glomerular diseases [5]. KDIGO's recommendation for the treatment of HSPN is to give Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Antagonist (ARB) when proteinuria continues to exceed 0.5 g~1.0 g/(d 1.73 $m^2$), and to give glucocorticoid for 6 months if urinary protein remains>1 g. DGFR>50 ml/(min 1.73 $m^2$). When more than 50% of the glomeruli have crescent formation, with or without deterioration of renal function, methylprednisolone shock plus cyclophosphamide. Hormones, immunosuppressants (such as cyclophosphamide, mycophenolate mofetil, cyclosporine A, Tripterygium wilfordii, etc.), ACEI, plasma exchange and tonsillectomy are also suitable for the treatment of HSPN.

## MANAGEMENT RECOMMENDATIONS

For children with HSP, there is a risk of kidney damage within 6 months or even 12 months after the onset of the disease. Therefore, there are the following management suggestions for children with HSP: (1)Patient should exercise actively to enhance resistance and to reduce infection(especially upper respiratory tract infection); (2)Patient should actively look for various pathogenic factors that cause the disease, and try to remove allergens; (3)conduct regular urine tests, strengthen follow-up of children, in order to grasp the progress of the disease, timely intervention, and prevent the occurrence of renal damage.

## APPLICATION OF MACHINE LEARNING IN PREVENTING HSPN

As a part of digital medicine, machine learning is widely used in modern public health care model, in which the two most beneficial aspects are disease diagnosis and outcome prediction. The disease early warning model based on machine learning and medical big data is beneficial to the early diagnosis, risk early warning, prognosis and data management of the disease, and is of great significance to clinical work [6]. In machine learning, this method is called supervised learning, which refers to the technique of training the model on a series of features related to the known results. In the field of medical research, this may mean training a model to link a person's characteristics (for example, age, weight, allergic status, etc.) to a result (for example, HSPN within six months). Once the algorithm is successfully trained, it will be able to predict the results when applied to new data. Clinically, we mainly rely on urine test, renal function test and renal biopsy to judge the occurrence of renal damage in children with HSP. However, due to the relatively high risk of renal biopsy, low acceptance of children and parents, lag of routine urine test and other shortcomings, in recent years, a large number of scholars have devoted themselves to studying the high risk factors of renal damage in HSP and the methods of preventing renal damage to make up for the deficiency in clinical treatment. At present, a variety of prediction models have been established for the risk of HSPN, and the prediction indicators are mainly focused on epidemiological characteristics, clinical symptoms and laboratory examination, which is of great significance for early intervention and prevention of disease progress.

Before machine learning was introduced and widely used, most of our applications in clinical medical data processing and analysis were statistical techniques. For example, logical regression is a classical linear regression analysis model, which can better analyze the quantitative relationship between disease and risk factors. However, a single machine learning method often leads to over-fitting, which makes it difficult to deal with a large number of unbalanced data sets in clinic. In order to make up for this deficiency, integrated learning based on multiple decision trees came into being, such as RandomForest, XGBoost, GBDT and so on. Tree classifiers are used to obtain better prediction results and higher operational efficiency. The combined Stacking model constructed in the model fusion is the learning of the next model from the previous model, which can optimize the final result. They have higher accuracy, sensitivity and specificity.

At present, most of the researches on risk models are retrospective models, which are not satisfied with the time-limited information, which limits the clinical application value of risk prediction models. In order to solve this problem, it is a good choice to embed the model into the clinical Electronic Medical Record system (EMR).EMR is the product of information technology and network technology in the medical field, which integrates multi-disciplinary information, quality control in the whole process, and has the ability of information early warning and prompting. In clinical practice, we can put the model online to EMR, incorporate patient information into the model, and monitor the relevant predictive indicators. When the medical record and doctor's order information changes, the predicted value changes in real time according to the change of the predictive index. When the urine test results are updated in the medical record system, the predicted value is presented at an interface, and the standard of renal damage depends on the urine test. Following the urine test results, not only the risk can

be intuitively indicated, but also the predicted value can be compared with the urine test results. if the predicted value has a large deviation, actively adjust the model parameters. When the predicted value exceeds the set threshold, early warning and prompts are issued: (1) pop-up windows appear in the doctor's order system in the form of critical values to issue warnings; (2) pop-up real-time assessment forms of risk factors, combined with time-limited information according to the scores of different prediction indicators, targeted intervention can be carried out. The establishment of this model of the combination of machine learning and medical big data, compared with a single machine learning, by providing early warning and operable feedback to monitor the clinical prescription information, can better fit the clinical actual situation, can actively carry out intervention treatment, achieve good performance, and may prevent the adverse results of renal damage in Henoch-Schönlein Purpura in the clinical environment.

## CONCLUSION

Machine learning based on cross-section to predict children's HSPN has obvious advantages of simplicity, low cost and non-invasive. It can arouse doctors' attention to renal damage causedby HSP in an intuitive form of data analysis, and early evaluate the possible risk factors of HSP in clinic, so as to assist in early diagnosis and prevent or delay the occurrence of renal damage. It is expected that the combination of machine learning and medical big data can provide new ideas for risk prediction and clinical intervention of Henoch-Schönle in Purpura nephritis in children.

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