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*Original Article*

# Clinical research on maternal platelet parameters and indicators of coagulation function in complication of preeclampsia-eclampsia

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**Abstract:** Objective: To study the change trend of maternal platelet parameters and indicators of coagulation function and their correlation with posterior reversible encephalopathy syndrome (PRES) in preeclampsia-eclampsia. Method: 320 cases of preeclampsia-eclampsia and normal full-term pregnancy women in Fujian Provincial Maternity and Children's Hospital from June 2011 to June 2017 were retrospectively analyzed and divided into three groups. 64 cases of women with PRES as PRES group, 128 cases of pregnant women with head normal MRI examination as preeclampsia group, and 128 cases of normal full-term pregnancy and childbirth women as normal group. Clinical information, relevant laboratory parameters and imaging examination results from three groups were collected. Results: The content of PLT, PCT, and INR were decreased, PDW, TT, FDP, and D-dimer were increased, while the ratio of PLT/MPV was decreased in PRES group. There was statistically significant difference compared with pre-eclampsia group and normal group ($P<0.05$). Area under curve (AUC) of operating characteristic after subjects being diagnosed by PLT/MPV ratio was 0.703 ($P<0.01$). The best diagnostic cut-off point was 12.38, the sensitivity was 46.88%, and the specificity was 87.89%. Conclusion: There is a certain correlation in maternal platelet parameters, indicators of coagulation function and PRES. PLT/MPV provides a certain predictive value for PRES. In clinical practice, early detection, diagnosis and treatment of PRES can be achieved with laboratory parameters, so as to improve perinatal maternal and infant outcomes.

**Keywords:** Posterior reversible encephalopathy syndrome, preeclampsia, platelet parameters, indicators of coagulation function

Posterior reversible encephalopathy syndrome (PRES) was first discovered and proposed by Hinchey [1] in 1996, and named by Casey [2] in 2000. There are many causes of PRES, among which the most common ones are preeclampsia or eclampsia, malignant hypertension, and immunosuppression [3]. Preeclampsia or eclampsia pregnant women are considered a high-risk group of this disease, and some critical conditions may endanger the life of mothers and children, which lead to adverse perinatal outcomes. Therefore, it is particularly important for early detection, diagnosis and strengthening symptomatic treatment. In our research, the differences in platelet count, mean platelet volume, PLT/MPV ratio and indicators of coagulation function among preeclampsia or eclampsia combined with PRES patients, pre-eclampsia or eclampsia non-combined with PRES patients, and normal full-term pregnant women were compared to analyze their correlation with PRES and their predictive value.

## Materials and methods

### *Subjects of investigation*

320 cases of preeclampsia-eclampsia and normal full-term pregnancy women in Fujian Provincial Maternity and Children's Hospital from June 2011 to June 2017 were retrospectively analyzed and divided into three groups. 64 cases of women with PRES were assigned to PRES group, 128 cases of pregnant women with head normal MRI examination were

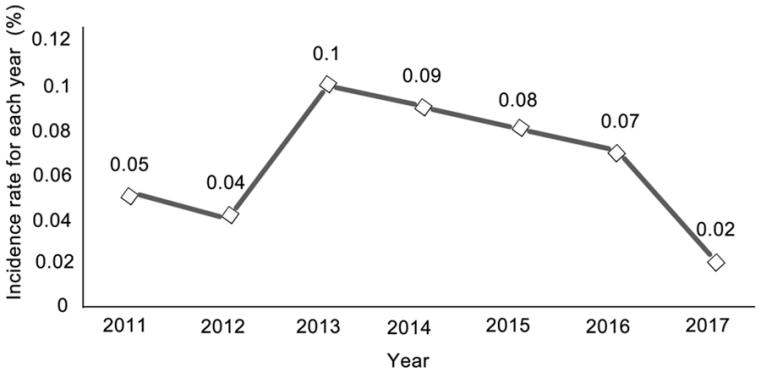


**Figure 1.** The curve graph of PRES incidence rates from 2011 to 2017.

assigned to preeclampsia group, and 128 cases of normal full-term pregnancy and childbirth women were assigned to normal group. There was no statistically significant difference (P>0.05) in age, number of pregnancies and birth among three groups.

*Methods on investigation*

Clinical data of three groups of women were collected, including: (1) general information: age, education level, body mass index (BMI), blood pressure, the number of pregnancy and birth, etc. (2) results of auxiliary examinations during pregnancy: blood routine examination, coagulation function, blood lipid, liver function, renal function, albumin, 24-hour urine protein, fundus retinal examination, head MRI examination, etc. All the data above were retrospectively analyzed and compared for the differences in platelet count (PLT), mean platelet volume (MPV), platelet volume (PCT), platelet distribution width (PDW), thrombin time (TT), fibrinogen degradation products (FDP), PLT/MPV ratio and coagulation function indexes among three groups.

*Criteria of diagnosis*

The diagnosis of RPES was mainly based on Jennifer E criteria [4]: (1) patients with a history of preexisting conditions or specific medications, such as hypertension, blood pressure fluctuations, immunosuppression, autoimmune diseases, renal dysfunction, preeclampsia, and eclampsia, etc; (2) the clinical manifestations were mental disorder, headache, seizures or visual impairment, which attack acutely or subacutely; (3) craniocerebral imaging showed vasogenic edema changes with white matter at the back of both sides of the brain; (4) symptoms mostly or completely disappeared in imaging exam after treatment; (5) exclusion of other diseases. Diagnostic criteria of preeclampsia and eclampsia were based on Williams Obstetrics (24th edition).

*Statistical methods*

SPSS 21.0 statistical software was used to analyze the data. The researched data were tested for normality and those that conformed to the normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± SD). Univariate ANOVA was selected for the difference comparison among three groups, and independent sample t test was used for comparison between two groups to clarify the differences between the groups. Frequency, percentage were used to express the qualitative data, chi-square test was used for the differences between groups detection, and binomial logistics regression analysis was used for influencing factors analysis of posterior reversible encephalopathy. P<0.05 was used as the statistically significant difference standard.

## Results

*Curve graph of PRES incidence rates*

This research analyzed 64 cases of childbirth women with posterior reversible encephalopathy syndrome in our hospital from June 2011 to June 2017. Out of 92710 cases of total delivery at the same term, the incidence of posterior reversible encephalopathy syndrome was 0.07%. The incidence rate of PRES from 2011 to 2017 was statistically analyzed, respectively, and the graph of incidence rates for each year was drew (See **Figure 1**). The results showed that the incidence rate of posterior reversible encephalopathy syndrome in our hospital was increased from 2012 (0.04%) to 2013 (0.1%), and declined since 2013. From the year of 2013 to 2016, the rate of posterior reversible encephalopathy syndrome was reduced by 0.01% each year, and the rate was 0.02% in 2017.

**Table 1.** Comparison of general clinical data ($\bar{x}$ ± SD)

| Group | Age (years) | BMI (Kg/m$^2$) | Number of pregnancy (n) | Number of birth (n) | Hospital gestational age (week) |
|---|---|---|---|---|---|
| Normal | 29.62±4.73 | 25.73±2.85 | 2.06±1.18 | 0.48±0.59 | 39.60±0.86 |
| Preeclampsia | 29.30±5.11 | 28.71±3.89[b] | 2.00±1.24 | 0.35±0.56 | 35.63±3.32[b] |
| PRES | 29.73±5.62 | 28.43±4.76[b] | 2.34±1.42 | 0.48±0.62 | 34.86±3.94[b] |
| P | 0.822 | 0.000[a] | 0.190 | 0.158 | 0.000[a] |

Note: a: P < 0.05 overall comparison; b: P < 0.05 compared with the normal group.

**Table 2.** Comparison of platelet parameters ($\bar{x}$ ± SD)

| Group | PLT (×10$^9$/L) | MPV (fL) | PLT/MPV | PCT (%) | PDW (%) |
|---|---|---|---|---|---|
| Normal | 223.15±49.65 | 9.98±1.64 | 23.32±7.69 | 0.23±0.12 | 13.97±2.97 |
| Preeclampsia | 198.45±63.52[b] | 11.17±1.57[b] | 18.59±7.89[b] | 0.21±0.06[b] | 14.98±3.10[b] |
| PRES | 163.50±67.16[b,c] | 11.33±2.00[b] | 15.49±8.55[b,c] | 0.17±0.06[b,c] | 16.81±3.25[b,c] |
| P | 0.000[a] | 0.000[a] | 0.000[a] | 0.000[a] | 0.000[a] |

Note: a: P < 0.05 overall comparison; b: P < 0.05 compared with the normal group; c: P < 0.05 compared with preeclampsia group.

**Table 3.** Comparison of coagulation function indicators ($\bar{x}$ ± SD)

| Group | PT (s) | APTT (s) | TT (s) | INR | FDP (μg/mL) | FIB (g/L) | D-dimer (mg/L) |
|---|---|---|---|---|---|---|---|
| Normal | 11.42±0.83 | 31.03±18.67 | 16.13±1.12 | 0.93±0.06 | 6.36±3.73 | 4.26±0.96 | 2.06±1.37 |
| Preeclampsia | 11.39±2.43[b] | 29.86±4.75[b] | 16.60±1.15[b] | 0.90±0.07[b] | 8.40±7.59[b] | 4.57±4.89[b] | 2.52±2.58[b] |
| PRES | 11.35±1.09[b] | 29.67±5.16[b] | 17.49±2.42[b,c] | 0.88±0.09[b,c] | 13.94±13.26[b,c] | 4.67±0.91[b] | 4.04±3.96[b,c] |
| P | 0.000[a] | 0.000[a] | 0.000[a] | 0.000[a] | 0.000[a] | 0.000[a] | 0.000[a] |

Note: a: P < 0.05 overall comparison; b: P < 0.05 compared with the normal group; c: P < 0.05 compared with preeclampsia group.

*Analysis of general clinical data and laboratory indexes of all pregnant women*

*Comparison of general clinical data of pregnant women:* There were no statistically significant differences in age, number of pregnancies and births among the three groups (P>0.05). The BMI of pregnant women in the PRES group and the preeclampsia group was significantly higher, while the gestational weeks were significantly reduced compared with the normal group. The difference was statistically significant (P<0.05) (See **Table 1**).

*Comparison of platelet parameters in pregnant women:* Both PLT and PCT of pregnant women in the PRES group and the preeclampsia group were decreased, while PDW was increased, comparing with the preeclampsia group and the normal group. The difference was statistically significant (P<0.05). PLT/MPV was significantly lower in the preeclampsia group than that of the normal group (P<0.05) (See **Table 2**).

*Comparison of coagulation function indicators in pregnant women:* PT, APTT and INR in PRES group and preeclampsia group were all decreased, while TT, FIB, FDP and D-dimer were all increased, with statistically significant difference (P<0.05) compared with the normal group. Compared with the preeclampsia group, the INR of pregnant women in the PRES group was decreased, and the TT, FDP, and D-dimer were increased with statistically significant differences (P<0.05). However, there was no statistically significant differences of PT, APTT, and FIB in PRES group and preeclampsia group (P>0.05) (See **Table 3**).

*Assessment results of PRES were predicted by PLT/MPV ratio:* Correlation analysis of platelet parameters, coagulation function indicators and the occurrence of PRES was conducted on patients in the PRES group. Multivariate logistic regression analysis showed that PLT/MPV was correlated with PRES (P<0.05). PLT/MPV is a protective factor of PRES (OR=0.943). The greater PLT/MPV is, the lower the risk of PRES

**Table 4.** Logistics regression analysis of PRES influenced factors

| Independent variable | B | S.E. | Wald | P | Exp (B) | 95% CI |
|---|---|---|---|---|---|---|
| PLT/MPV | -0.058 | 0.023 | 6.220 | 0.013 | 0.943 | 0.901-0.988 |
| PT | 0.609 | 0.247 | 6.054 | 0.014 | 1.838 | 1.132-2.984 |
| D-dimer | 0.193 | 0.073 | 6.986 | 0.008 | 1.213 | 1.051-1.399 |
| Creatinine | 0.044 | 0.014 | 9.491 | 0.002 | 1.045 | 1.016-1.075 |
| LDH | 0.004 | 0.001 | 12.003 | 0.001 | 1.004 | 1.002-1.006 |

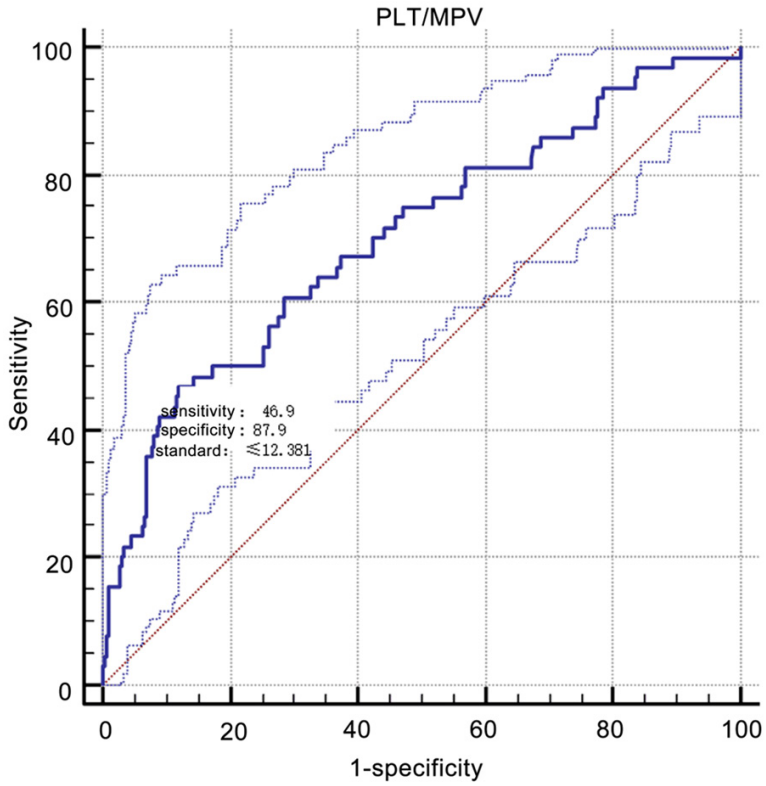


**Figure 2.** ROC curve of PLT/MPV ratio predicting PRES.

is (See **Table 4**). The ROC survival curve was used to analyze the predictive value of PLT/MPV ratio for PRES. The results showed that the area under the ROC curve (AUC) was 0.703 (P<0.01), the optimal diagnostic cut-off point was 12.38, the sensitivity was 46.88%, and the specificity was 87.89% (See **Figure 2**).

*Comparison of clinical symptoms between PRES group and preeclampsia group:* Common symptoms appeared in pregnant women with reversible posterior encephalopathy syndrome including headache, visual impairment, disturbance of consciousness, and seizures. Analysis and comparison of the clinical symptoms of pregnant women in PRES group and preeclampsia group showed that the incidence of headache, visual impairment and convulsion in PRES group was significantly higher than that of preeclampsia group, and the difference was statistically significant (P<0.05) (See **Table 5**).

*MRI results of pregnant women with reversible posterior encephalopathy:* MRI results of 64 cases of pregnant women with PRES in this research showed that the reversible posterior encephalopathy lesion occurred in the parietal lobe was 52 cases (81.25%), occipital lobe was 46 (71.88%), frontal lobe was 31 (48.44%), temporal lobe was 17 (26.56%), basal ganglia region was 24 (37.50%), white matter of paraventricular cerebra was 7 (10.94%), brain stem was 3 (4.69%), cerebellum, pons, thalamus, midbrain was 2 cases (4.68%) respectively. Most lesions on MRI were isosignal or hyposignal on T1WI, hypersignal on T2WI and FLAIR, isosignal or slightly hypersignal on DWI, and obvious hypersignal on ADC.

## Discussion

PRES is reversible in clinical and imaging studies, so early diagnosis and early treatment are critical, and delayed diagnosis and treatment may lead to PRES irreversible damage. Closely monitor the platelet parameters, coagulation function indicators of preeclampsia-eclampsia pregnant women will help to timely discover the occurrence of PRES, and carry out intervention and treatment, so as to improve maternal-fetal prognosis.

**Table 5.** Comparison of clinical symptoms between PRES group and preeclampsia group [n (%)]

| Group | Dizzy | Headache | Visual impairment | Convulsion | Conscious disturbance |
|---|---|---|---|---|---|
| Preeclampsia | 44 (34.4%) | 42 (32.8%) | 23 (18.0%) | 1 (0.8%) | 0 (0.0%) |
| PRES | 30 (46.9%) | 38 (59.4%) | 21 (32.8%) | 22 (34.4%) | 1 (1.6%) |
| Chi-square | 2.814 | 12.386 | 5.322 | 45.666 | 2.010 |
| P | 0.093 | 0.000* | 0.021* | 0.000* | 0.156 |

Note: *: p<0.05.

*Clinical manifestations of PRES*

Posterior reversible encephalopathy syndrome (PRES) is an acute onset disease which develops rapidly. It is a clinical imaging syndrome including headache, visual impairment, consciousness disorders, and epileptic seizure manifestations. In addition, functional defects, tinnitus, and acute vertigo also often appear [5]. Investigation showed that the incidence of headache and visual impairment was higher, about more than 60% in pregnant women with severe preeclampsia or eclampsia combined with RPES [6]. In this study, Our research showed that the incidence of posterior reversible encephalopathy syndrome was 0.07%. Among them 38 (59.4%) pregnant women experienced headache, 30 (46.9%) had dizziness, 21 (32.8%) had visual impairment, 1 (1.6%) had consciousness impairment, and 22 had (34.4%) convulsions in the RPES group. There were statistically significant differences in headache, visual impairment and convulsion between the preeclampsia and eclampsia groups. Therefore, the occurrence of PRES needed to be alerted when pregnant women had the above symptoms.

*Laboratory examination of PRES*

Platelet parameters mainly contain PLT, MPV, PCT and PDW, etc. The PLT value of most normal pregnant women is in the normal range. The main pathophysiological mechanism of pre-eclampsia is systemic arteriolar spasm and vascular endothelial injury. The damage of vascular endothelial cells in patients with preeclampsia leads to aggregation and consumption of platelets, which further makes platelets decline. There is a non-linear correlation between platelet count and platelet volume in normal people. The large platelets are newly formed in bone marrow and have metabolic activity. The increased platelet volume suggests active bone marrow hyperplasia, while the small platelets are senescent platelets with poor coagulation function. Studies researched by Freitas LG [7] showed that the value of PLT and PCT were decreased in patients with severe preeclampsia, while MPV and PDW were increased, comparing with normal pregnant women. Doğan K [8] found that PLT, MPV, PLT/MPV were significantly different between preeclampsia and normal pregnant women, and PLT/MPV could be used as a predictive indicator of preeclampsia. Our research indicated that the changes of PLT, MPV, PDW and PLT/MPV in patients with PRES were more obvious. The rate of PLT/MPV was significantly reduced, and the difference was statistically significant. Results of multivariate analysis showed that there was a correlation between PLT/MPV and PRES (P=0.013). The greater rate of PLT/MPV was, the lower the risk of PRES was. ROC curve analysis of the rate of PLT/MPV predicted that the optimal cutoff point for diagnosis of PRES was 12.38, sensitivity was 46.88% and specificity was 87.89%. It suggested that PLT/MPV could be used as an observational predictor of PRES.

PT, APTT and FIB are important indicators of coagulation function. Feng yan [9] showed that PT, TT and APTT were significantly declined, while FIB was significantly increased in patients with hypertension during pregnancy compared with normal pregnancy. The trend of decreased PT and increased FIB became more and more obvious when the disease aggravated. This study considered that vascular endothelial injury occurred much easily in patients with hypertension during pregnancy, thus causing high blood coagulation. With the development of the disease, this clinical change would be more and more obvious. Han L [10] showed that the concentration of D-dimer in plasma of patients with preeclampsia, especially severe preeclampsia, was significantly higher than that of normal pregnant women. The results of this research showed that PT, APTT were obviously

declined and FIB was significantly increased in PRES patients and preeclampsia-eclampsia patients without PRES. However, there was no statistically significant in patients. It indicated that PT, APTT, and FIB can be used as predictors and evaluation indicators of preeclampsia-eclampsia, but predict whether combined with PRES needs a further research.

*Imaging examination of PRES*

PRES is a clinical imaging syndrome, and its characteristic changes in imaging are the important basis for the disease diagnosis. Among them, MRI is the best auxiliary examination method for PRES diagnosis. The typical imaging changes are the symmetrical patchy abnormal signal shadows of white matter in posterior hemispheres of both hemispheres, which are mostly reversible after active treatment. Most of the lesion sites were located in the posterior cerebral circulation blood supply area, namely white matter under bilateral parietal occipital cortex. We found that frontal lobe, temporal lobe, brainstem, basal ganglia, thalamus and pons were involved with the increase of case reports and the deepening understanding of this disease [11]. MRI results of 64 cases of patients with PRES in this research showed that the lesion occurred in the parietal lobe was 52 cases (81.25%), occipital lobe was 46 (71.88%), frontal lobe was 31 (48.44%), temporal lobe was 17 (26.56%), basal ganglia region was 24 (37.50%), white matter of paraventricular cerebra was 7 (10.94%), brain stem was 3 (4.69%), cerebellum, pons, thalamus, midbrain was 2 cases (4.68%), respectively. It was generally consistent with the reported literature. FLAIR imaging technology is the most sensitive examination to recognize white matter edema. It can show cortical and subcortical lesions and is very sensitive to small lesions, which is of great significance for early diagnosis. DWI and ADC sequences can distinguish angiogenic edema from cellular edema, which is helpful for the diagnosis and prognosis of PRES.

In conclusion, platelet parameters and coagulation function indicators can be used as predictors of preeclampsia-eclampsia combined with PRES. Cranial MRI is the best auxiliary examination method for PRES diagnosis. In clinical practice, the monitoring of platelet parameters and coagulation function indicators should be strengthened, and cranial MRI check should be carried out timely, which was benefit for early detection and diagnosis of PRES.

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## Disclosure of conflict of interest

None.

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## References

[1] Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, Pessin MS, Lamy C, Mas JL and Caplan LR. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996; 334: 494-500.

[2] Casey SO, Sampaio RC, Michel E and Truwit CL. Posterior reversible encephalopathy syndrome: utility of fluid-attenuated inversion recovery MR imaging in the detection of cortical and subcortical lesions. AJNR Am J Neuroradiol 2000; 21: 1199-1206.

[3] Shankar J and Banfield J. Posterior reversible encephalopathy syndrome: a review. Can Assoc Radiol J 2017; 68: 147-153.

[4] Fugate JE and Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol 2015; 14: 914-925.

[5] Granata G, Greco A, Iannella G, Granata M, Manno A, Savastano E and Magliulo G. Posterior reversible encephalopathy syndrome--insight into pathogenesis, clinical variants and treatment approaches. Autoimmun Rev 2015; 14: 830-836.

[6] Kurdoglu Z, Cetin O, Sayın R, Dirik D, Kurdoglu M, Kolusarı A, Yıldızhan R and Guler Sahin H. Clinical and perinatal outcomes in eclamptic women with posterior reversible encephalopathy syndrome. Arch Gynecol Obstet 2015; 292: 1013-1018.

[7] Freitas LG, Alpoim PN, Komatsuzaki F, Carvalho Md and Dusse LM. Preeclampsia: are platelet count and indices useful for its prognostic? Hematology 2013; 18: 360-364.
[8] Doğan K, Guraslan H, Senturk MB, Helvacioglu C, İdil S and Ekin M. Can platelet count and platelet indices predict the risk and the prognosis of preeclampsia? Hypertens Pregnancy 2015; 34: 434-442.
[9] Feng Y and Xu JJ. Correlation analysis of the changes of coagulation function and platelet parameters with the severity of hypertension during pregnancy. Maternal and Child Health Care of China 2016; 31: 947-948.
[10] Han L, Liu X, Li H, Zou J, Yang Z, Han J, Huang W, Yu L, Zheng Y and Li L. Blood coagulation parameters and platelet indices: changes in normal and preeclamptic pregnancies and predictive values for preeclampsia. PLoS One 2014; 9: e114488.
[11] MO BC, Zhang ZL, Liu ZH, et al. The clinical manifestations and features of MRI of the atypical posterior reversible encephalopathy syndromes (PRES). Chinese Journal of CT and MRI 2015; 13: 27-29.