# Study on Changes of the Concentration of Some Indicators of the Serum Iron Test in Patients with Nephrotic Syndromein Vietnam

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## Abstract

**Background:** In nephrotic syndrome (NS), the excessive and prolonged loss of protein in the urine reduces albumin blood and leads to many other changes such as dyslipidemia, blood clotting disorders, and disorders of hematopoietic components. In NS, the more persistent and persistent decrease in albumin in the blood, the more apparent these disorders, including disorders of iron, transferrin and ferritin in serum. The objectives of the study were to: Determine serum iron, transferrin and ferritin concentrations and Investigate the relationship between iron, transferrin and ferritin concentrations and serum albumin in NS patients.

**Methodology:** Cross-sectional descriptive research method. Convenient and controlled sample selection of 68 NS patients without kidney failure, aged 16 years and over, hospitalized for treatment at Internal Department of Hue University of Medicine and Pharmacy Hospital, Vietnam.

**Results:** The average serum iron concentration is 8.9 μmol/L, of which at low level, the rate is 30.9%; In 100% of cases, the serum transferrin concentration is lower than normal, the average concentration is 0.68 mmol/L; the average elevation of ferritin in serum was 610.3 pmol/L, of which at high level accounted for 67.6% (46 patients). Serum albumin concentrations are positively correlated with iron and transferrin, but negatively with serum ferritin.

**Conclusion:** In NS, the serum ferritin concentration is elevated and inversely correlated with the serum iron, transferrin, and albumin concentration.

***Keywords:*** *Concentration, serum iron, nephrotic syndrome.*

## Introduction

Nephrotic syndrome (NS) is a common problem in glomerular diseases. The disease often recurs many times and can lead to kidney failure if not treated and taken care well. Currently, the diagnosis and determination of NS are no longer difficult, however, the pathogenesis mechanism and the disorders caused by nephrotic disease still have many problems that need attention. In NS, the loss of protein in urine is much and prolonged, it reduces blood protein and leads to many other changes such as dyslipidemia, clotting disorders, disorders of blood-forming components,….In NS, the greater the decrease in blood albumin, the more pronounced these disorders are, including disorders of iron, serum transferrin and ferritin[(1),(2)(3),(4)]. In normal people, the daily requirement of iron is about 0.5-1mg, the main source of iron is from foods of animal and plant origin. All iron in the body is about 4g, of which 65% is in Hb, 15-30% is stored in the endothelial inter-retinal system and liver parenchymal cells in the

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form of ferritin. Iron is an important component in the synthesis of hemoglobine and myoglobine; Iron plays an important role in oxidative energy production, oxygen transport, mitochondrial respiration and inactivating harmful oxygen radicals. Ferritin has been identified as a predictor of the development and progression of atherosclerosis.

In NS, iron deficiency and ferritin stagnation in the body will cause iron deficiency anemia, affecting the metabolic activity of cells, causing glomerular fibrosis leading to impaired kidney function, making the process of Treatment and prognosis of patients with NS become more complicated[4],[5],[6].

Quantification of serum ferritin levels provides an indication of the body's total iron stores, thereby assessing the prognosis of anemia in patients with NS; however, research on the changes in iron components in NS has not been given adequate attention, while this disorder may contribute to worsening kidney disease and worse prognosis.To find out this problem, we study the topic "*Study on changes of the concentration of some indicators of the serum iron test in patients with nephrotic syndrome*". Objectives of the study:

Determine of serum iron, transferrin and ferritin in adults with NS patients.

Investigate the relationship between iron, transferrin and ferritin levels and serum albumin in patients with NS patients.

## Subjects and Methodology

**Research Subjects:** We selected a convenient sample of 68 NS patients without kidney failure from May 2019 to May 2020, aged 16 years and over, hospitalized for treatment at Internal Department of Hue University of Medicine and Pharmacy Hospital, Vietnam. Criteria for diagnosis of NS include: proteinuria ≥ 3.5 grams/24 hours; blood protein <60 grams/L and blood albumin <30 g/L, increased blood cholesterol and total edema [7].

- Criteria for the exclusion of NS patients not included in the study are patients with one of the following diseases:

+ Endocrine disorders, hypertension, hepatitis, liver failure, kidney failure, rheumatoid arthritis.

+ Blood diseases.

+ Acute and chronic infections.

+ Pregnant women.

+ Cases of alcoholism.

+ The cases are being treated for NS.

Patient has been transfusion or lipid-rich products. Patients are taking vitamin B12, taking iron-containing drugs, oral contraceptives and some drugs that alter serum iron levels.

**Research Method:** Research method according to cross-sectional descriptive method.

Patients are carried out clinical examination and tests to diagnose NS, eligible for inclusion in the research group.

Tests are conducted on Cobas analyzers, at Labo of Hue University of Medicine and Pharmacy Hospital, a reputable and reliable hospital. Before the test, instruct patients to eat normally, not to eat or drink foods containing high amounts of iron. All tests are done when the patient first arrives in the hospital, has blood drawn in the morning and has not eaten.

Quantification of serum iron, ferritin and transferrin concentrations by immunoturbidity measurement.

Normal values of serum iron, transferrin and ferritin concentrations

| Type | Normal Value |
|---|---|
| Serum iron | 5,83-34,5 µmol/l |
| Serum transferrin | 2-3,6 mmol/l |
| Serum ferritin in men | 30-400 pmol/l |
| Serum ferritin in women | 15-150 pmol/l |

Test for serum protein, serum albumin and proteinuria at the same time as serum iron, ferritin and transferrin.

- Processing data according to the method of medical statistics, Excel 2007.

## Research Results

### General characteristics of the subject of the study group:

**Table 1. General characteristics of the subject of the study group**

| General characteristics \ Rate | | Male | | Female | | Total | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| Age | <30 | 32 | 47.0 | 6 | 8.8 | 38 | 55.8 |
| | 30-50 | 8 | 11.8 | 7 | 10.3 | 15 | 22.1 |
| | >50 | 11 | 16.2 | 4 | 5.9 | 15 | 22.1 |
| | $\bar{X}$CI 95% | 24 (27.7-37.6) | | 42 (28.5-46.1) | | 33.4 (29.1-37.6) | |
| Occupation | Officer | 21 | 30.9 | 5 | 7.3 | 26 | 38.2 |
| | Farmer | 19 | 27.9 | 8 | 11.7 | 27 | 39.7 |
| | Homemaker | 11 | 16.2 | 4 | 5.9 | 15 | 22.1 |
| Area | Urban | 24 | 35.3 | 9 | 13.2 | 33 | 48.5 |
| | Rural | 27 | 39.7 | 8 | 11.8 | 35 | 51.5 |
| **Total** | | **51** | **75** | **17** | **25** | **68** | **100** |

Male accounted for 51 patients (75%), female 17 patients (25%), the difference is statistically significant with $p<0.05$. The average age of the study team is 33.4. Occupation in agriculture accounts for 39.7% and in rural areas 51.5%.

### Test results of the study group:

**Table 2. Results of biochemical tests of the study group**

| Test results | | Rate | | Overall average |
|---|---|---|---|---|
| | | n | % | |
| **Serum protein** *(gram/L)* | <40 | 7 | 10.3 | **44.4** *CI 95%: 43.2-45.6* |
| | 40-60 | 61 | 89.7 | |
| **Serum albumin** *(gram/L)* | <20 | 62 | 91.2 | **16.4** CI 95%: 15.7-17.1 |
| | 20-40 | 6 | 8.8 | |
| **Proteinuria** *(gram/24 hours)* | 3.5-5 | 12 | 17.6 | **9.7** *CI 95%: 8.4-11.5* |
| | 5-10 | 30 | 44.1 | |
| | >10 | 26 | 38.2 | |
| **Serum iron** *(µmol/L)* | Low | 21 | 30.9 | **8.9** *CI 95%: 8.1-9.7* |
| | Normal | 47 | 69.1 | |
| | High | 0 | 0.0 | |
| **Serum transferrin** *(mmol/L)* | Low | 68 | 100 | **0.68** *CI 95%: 0,64-0.72* |
| | Normal | 0 | 0.0 | |
| | High | 0 | 0.0 | |
| **Serum ferritin** *(pmol/L)* | Low | 0 | 0.0 | **610.3** *CI 95%: 521.9-699.2* |
| | Normal | 22 | 32.4 | |
| | High | 46 | 67.6 | |

The Serum albumin<20 grams/L accounts for 91.2% (62 cases), the average concentration was 16.4 grams/L. Proteinuria concentration was mainly over 5 grams/day, accounting for 82.3% (56 cases), the average concentration was 9.7 grams/day.

The serum iron concentration at a low level <5.83 µmol/l, accounting for 30.9%, the average concentration was 8.9 µmol/L. In 100% of cases, the serum transferrin concentration was lower than normal, the average concentration was 0.68 mmol/L. Serum ferritin at high levels accounted for 67.6% (46 patients), average concentrations were 610.3 pmol/L.

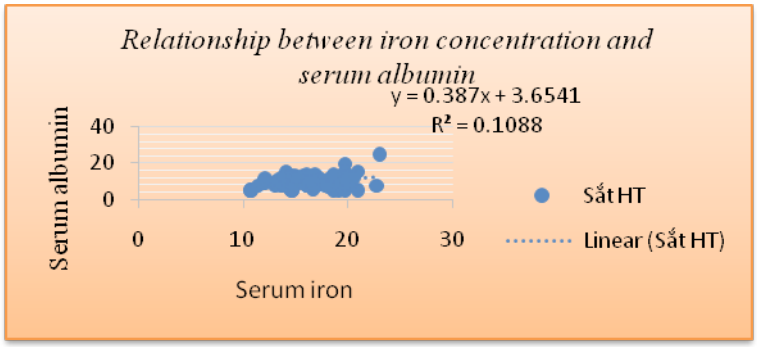


**Figure 1. Relationship between iron concentration and serum albumin**

There is a moderatepositive correlation between the iron concentration and serum albumin, through the linearregression equation y = 0.387x+3.6541 and the correlation coefficient r = 0.34, with a difference of p <0.05

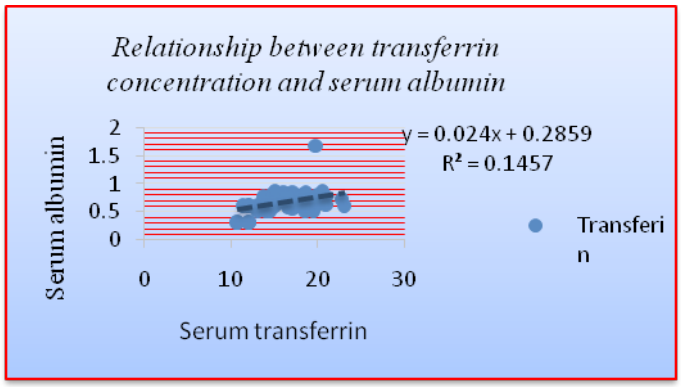


**Figure 2. Relationship between transferrin concentration and serum albumin**

There is a moderate positive correlation between the concentration of transferrin with serum albumin, using a linear regression equation of y = 0.024x+0.2859 and correlation coefficient r = 0.38, with difference p <0.05.

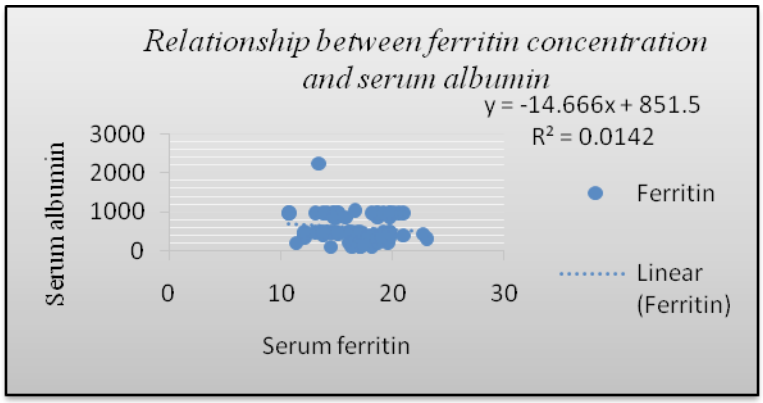


**Figure 3. Relationship between ferritin concentration and serum albumin**

There is a moderate negative correlation between the average ferritin concentrations with serum albumin, through linear regression equation y = -14.666x+851.5 and the correlation coefficient r = 0:38, with the difference p <0.05.

## Discussion

Iron is an important component in the synthesis of hemoglobine and myoglobine, in addition iron also participates in some redox enzymes such as catalase, peroxydase and cytochrome.In NS the loss of transferrin in the urine is sufficient to reduce the serum transferrin concentration, the decrease in transferrin concentration can lead to iron deficiency and iron deficiency anemia. For ferritin has been identified as a predictor of the development and progression of atherosclerosis and is often elevated in NS[3],[4],[5], iron deficiency will cause iron deficiency anemia and affect the metabolism of cells due to a deficiency of iron-containing enzymes, but iron overload in the body also causes iron stagnation in the tissuessuch as heart, liver, endocrine glands, atherosclerosis, ...In NS the greater the decrease in serum albumin, the more pronounced these disturbances. Therefore, in NS, prolonged disturbance of iron, transferrin and ferritin factors will make treatment more difficult and the prognosis of NS becomes worse [2],[8].

The changes in serum iron, transferrin and ferritin concentration through data in Table 3.2 showed that up to 21 patients had lower than normal iron serum concentration (<5.83 µmol/l), accounting for 30.9%; The average serum iron concentration was 8.9 µmol/L. Iron deficiency in NS is a risk factor for kidney damage. In the body of macrophages that release iron periodically during the day with the highest iron release in the morning and lowest in the afternoon, it is important to consider the timing of the test, however the iron test in our study was to draw blood in the morning so this is a reflection of the highest iron concentration of the patient[1].

The correlation between transferrin synthesis and hepatic albumin synthesis suggests that transferrin synthesis is a component of the overall response to protein synthesis in patients with NS. This suggests that the therapeutic approach to maximize the serum transferrin concentration in nephrotic patients is primarily based on a reduction in proteinuria[1],[2]. Data in Figure 3.2 show that, in 100% of cases, NS had a lower than normal serum transferrin concentration, the highest serum transferrin concentration was 1.68 mmol/L, the lowest was 0.32 mmol/L and the average concentration was 0.68 mmol/L. This shows that in NS, the more proteinuria is lost, the lower the serum transferrin, and the higher the risk of iron deficiency anemia.

Ferritin is a high molecular weight protein that reflects the level of iron reserves in the body, but can also increase responsiveness in some acute illnesses. Increased serum ferritin in NS patients has been associated with loss of proteinuria[1]. The results of the study data in Table 3.2 also showed that the serum ferritin concentration increased 67.6% (46 patients), there was no case at low level and the average concentration was 610.3 pmol/L. This is also consistent with the result of excessive proteinuria loss in our patient group. Increased serum ferritin indicates the degree of cardiovascular risk in NS, especially in cases of dyslipidemia. Compared with the study of Nguyen Tran Kien[9], the rate of ferritin increase in NS is 58%, which is lower than our study, which may be explained by our patient group has blood albumin is too low.

Regarding the relationship between the iron concentration and serum albumin, the results in Figure 3.1 show that there is a moderate positive correlation between the iron concentration and serum albumin, with a linear regression equation of y = 0.387x+3.6541 and the correlation coefficient r = 0.34, the difference is statistically significant with p <0.05. Regarding the concentration of transferrin with serum albumin, the results in Figure 3.2 show that, there is a moderate positive correlation between the transferrin concentration and serum albumin concentration with a linear regression equation of y = 0.024x+0.2859 and the correlation coefficient r = 0.38, the difference is statistically significant with p <0.05. Regarding the concentration of ferritin and serum albumin, the results in Figure 3.3 show that, there is a moderate negative correlation between the concentration of ferritin and serum albumin and the linear regression equation is y = -14.666x+851.5 and the correlation coefficient r = 0.38, the difference is statistically significant with p <0.05. Thus in NS serum albumin concentration positively correlated with iron concentration and transferrin, but negatively correlated with serum ferritin concentration.

## Conclusion

Through the study of serum iron, transferrin and ferritin concentrations of 68 NS adult patients without

renal impairment, aged 16 years and over, we reach the following conclusions:

The average concentration of serum iron and transferrin is lower than normal, especially transferrin concentrations, while serum ferritin concentrations are often elevated in NS patients.

The serum albumin concentration positively correlated with iron concentration and transferrin, but negatively correlated with serum ferritin concentration.

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## References

1. Amanda J. W. Branten Dorine W. Swinkels Ina S. Klasen Jack F. M. Wetzels.Serum ferritin levels are increased in patients with glomerular diseases and proteinuria. Nephrology Dialysis Transplantation 2004; 19:2754-60
2. Branten AJ, Swinkels DW, Klasen IS, Wetzels JF. Serum ferritin levels are increased in patients with glomerular diseases and proteinuria. Nephrol Dial Transplant 2004; 19:2754-60.
3. Nakanishi T, Kuragano T, Nanami M, et al. Importance of ferritin for optimizing anemia therapy in chronic kidney disease. Am J Nephrol 2016; 32:439-46.
4. Se Jin Park, MD; Jae Il Shin, MD. Complications of nephrotic syndrome. Korean Journal of Pediatrics 2011; 54: 322-28.
5. Iorember F, & Aviles D. Anemia in nephrotic syndrome: approach to evaluation and treatment. Pediatric Nephrology 2017; 32:1323-30.
6. Prinsen BH, de Sain-van der Velden MG, Kaysen GA, Straver HW. Transferrin synthesis is increased in nephrotic patients insufficiently to replace urinary losses.J Am Soc Nephrol 2001; 12:1017-25.
7. Charles Kodner. Diagnosis and Management of Nephrotic Syndrome in Adults. Am Fam Physician 2016; 93: 479-85.
8. Moftah Mohamed Rabeea, Nayera Mahmoud Al-Akkad, Gamal Zakariya El-Morsi, Ahmed Elsayed Darwish. Evaluation of Serum Iron and Transferrin in Idiopathic Nephrotic Syndrome Patients Attending Al-Hussein Pediatric Nephrology Clinic. The Egyptian Journal of Hospital Medicine 2019; 74:1036-46.
9. Nguyen Tran Kien, Do Gia Tuyen. Study on changes in serum ferritin levels and related factors in primary nephrotic syndrome in adults. Medical Information 2011; 1:21-24.