Yonsei Medical Journal
Vol. 37, No. 2, 1996

Iron Related Indices in Iron Deficiency Anemia of Geriatric Korean Patients

Jong Hwa Lee, Jee Sook Hahn, Seung Moo Lee*, Jeong Ho Kim*, and Yun Woong Ko

The purpose of this study was to compare iron related indices in patients with iron deficiency anemia and chronic causative diseases between geriatric older than 65 years and adult, nongeriatric younger than 65 years groups. Iron deficiency anemia (IDA) cases with chronic disorders from Youngdong Severance hospital from June, 1991 to April, 1994, older than 65 years (17 cases), and younger than 65 years (29 cases) were analysed with iron related indices. Mean hemoglobin was 7.8 ±2.2 g/dl in geriatric IDA and 8.0±1.8 g/dl in adult IDA without significant diffenence. RDW value was 19.5±2.6 in geriatric IDA and 18.4±3.2 in adult IDA with no significant difference. Serum iron and transferrin saturation between geriatric IDA were 22.7±12.3 ug/dl, 6.7±4.1% and 28.6±16.6 ug/dl, 7.1±4.4% in adult IDA with no significant difference, but TIBC was significantly lower (P=0.011)in geriatric IDA than in adult IDA patients (357.2±83.2, 413.6±54.0 ug/dl). In normal elderly people, serum ferritin was 152.5±95.4 ng/ml in male and 111.1± 54.1 ng/ml in female with range 19.8~367.7 ng/ml in male and 11.7~238.7 ng/ml in female and was higher than that of normal adult in both sexes (147.0±108.0, 35.3± 20.5 ng/ml) (P=0.045). Serum ferritin in geriatric IDA was 13.8±11.8 ng/ml and 5.7±4.0 ng/ml in adult IDA with significant difference(P =0.001). The Upper margin for geriatric IDA was 37 ng/ml with 95% confidence interval. In the diagnosis of geriatric IDA with causative diseases, we should consider that TIBC does not increase and the upper margin for serum ferritin is suggested to increases up to 37 ng/ml.

Key Words: Iron deficiency anemia, iron related indices, geriatric population

Because our life expectancy has been elongated, the geriatric population is increasing in number recently in Korea. Various data from geriatrics are needed but few studies are available in this field of medicine in Korea.

Anemia is one of the most frequent conditions in geriatric clinics and IDA is especially frequent with various causes, so an exact diagnosis for this condition is thought to be very important for the management of geriatiric diseases. We have assessed the serum iron, total iron binding capacity and serum ferritin with bone marrow studies for the diagnosis of iron deficiency anemia with cauative diseases in the geriatric and nongeriatric population to ascertain the differences between the two groups.

Received November 14, 1995
Accepted March 29, 1996
Department of Internal Medicine and Clinical Pathology, Yonsei University College of Medicine
Address reprint requests to Dr. J.H. Lee, Department of Internal Medicine, Yong In Severance Hospital, Yongin, Kyunggi-do 449-800, Korea

MATERIALS AND METHODS

From June 1991 through April 1994, 46 patients with iron deficiency anemia (Hemoglobin<12 g/dl) by chronic disorders: 17 geriatric cases who were more than 65 years old, 29 nongeriatric adult cases who were all less

than 65 years old and normal control 64 cases (elderly 39, nonelderly adult 25 cases) who were examined in health clinic without any abnormalities at Youngdong Severance hospital, Yonsei University in Seoul, Korea were analysed. Their age in geriatric study group ranged from 65 to 81 with a median age of 77 years. And there was a male to female sex ratio of 0.9:1 in the geriatric study group (Table 1).

Using venous blood samples in the morning, serum iron and unsaturated iron binding capacity was measured by colorimetry and serum ferritin using a chemofluorescent technique. Bone marrow aspirate was stained by Prussian blue to assess iron stores. Student's t test was used to compare the variables and to assess the significance of the differences between groups using SPSS/PC+.

A P-value less than 0.05 was considered to be statistically significant.

RESULTS

Serum ferritin levels in normal nonelderly adults and normal elderly subjects

Serum ferritin levels in 39 normal elderly people over 65 years are shown in Table 2 with a mean ± standard deviation of 134.5±91.8 ng/ml and were higher than that of normal

Table 1. Age and sex distribution of normal subjects and patients with iron deficiency anemia with chronic disorders

Age(yrs)		Male	Female	Total
Normal nonelderly adult (<65)		12	13	25
Normal elderly (≧65)		22	17	39
I	Nongeriatric adult(<65)	9	20	29
	Geriatric(≧65)	8	9	17
D	65~69	0	3	3
	70~74	3	3	6
	75~79	2	2	5
A	80~84		1	3
	Total	17	29	46

Geriatric IDA median age: 77 years (M: 77.5, F: 72)
Nongeriatric adult IDA median age: 40 years (M: 29, F: 40)

Table 2. Serum ferritin in normal nonelderly adult and normal elderly subjects

Age group (yrs)	Serum ferritin (ng/ml)		
	Male	Female	Total
<65	147.0±108.0	35.3±20.5	88.9±93.8
(n=25)	(10.9~239.9)	(8.3~114.5)	
≥65	152.5±95.4	111.1±54.1	134.5±91.8*
(n=39)	(19.8~367.7)	(11.7~238.7)	

*: P=0.045 When the normal elderly group were compared with the normal nonelderly adult group.

Table 3. Hemoglobin in normal elderly and patients with iron deficiency anemia with chronic disorders

		Hbg(g/dl)		
		Male	Female	Total
Normal nonelderly adult	(12/13)	15.5±1.0	12.6±1.3	14.0±11.1
Normal elderly	(22/17)	14.9±0.7	12.9±0.5	14.0±1.3
Nongeriatric adult IDA	(9/20)	7.6±1.9	8.1±1.8	8.0±1.8
Geriatric IDA	(8/ 9)	8.5±2.3	7.1±2.1	7.8±2.2*

*: P=0.712 When compared geriatric IDA with nongeriatric adult IDA(/)=M/F

Table 4. Red cell distribution width in normal elderly and patients with iron deficiency anemia with chronic disorders

	RDW		
	Male	Female	Total
Normal nonelderly adult	13.5± 0.7	12.8± 0.7	13.2±0.8
Normal elderly	12.7± 0.2	12.4± 0.5	12.6±0.6
Nongeriatric adult IDA	19.0±10.0	18.1±10.6	18.4±3.2
Geriatric IDA	19.5± 5.5	19.5± 9.0	19.5±2.6*

*P: 0.214 When compared geriatric IDA with nongeriatric adult IDA

Table 5. Serum iron in adult and geriatric IDA with chronic disorders

	Serum ion (μg/dl)		
	Male	Female	Total
Normal nonelderly adult	121.5±17.7	111.0±59.4	116.3±36.3
Normal elderly	91.8±34.9	92.0±33.3	91.9±31.6
Nongeriatric adult IDA	30.2±21.2	27.9±14.6	28.6±16.6
Geriatric IDA	26.3±15.1	20.0± 9.0	22.7±12.3*

*P: 0.32 When compared geriatric IDA with nongeriatric adult IDA

nonelderly adult in both sexes (P=0.045).

Hemoglobin levels

The mean hemoglobin level in geriatric patients over 65 years of age with iron deficiency anemia with chronic disorders was 7.8 ± 2.2 g/dl. No significant difference was noted when compared with that of nongeriatric adult patients less than 65 years (P=0.712) (Table 3).

Red cell distribution width (RDWs)

The mean RDW in geriatric patients with iron deficiency anemia with chronic disorders over 65 years was 19.5±2.6 and showed no significant difference when compared to that of nongeriatric adult patients less than 65 years (P=0.214) (Table 4).

Serum iron levels

The mean serum iron in geriatric patients

Table 6. Total iron binding capacities in adult and geriatric IDA with chronic disorders

	TIBC(μg/dl)		
	Male	Female	Total
Normal nonelderly adult	355.5±13.4	320.5±113.8	338.0±69.2
Normal elderly	286.8±41.3	294.5± 25.5	290.6±32.1
Nongeriatric adult IDA	393.3±35.4	422.7± 59.0	413.6±54.0
Geriatric IDA	344.9±94.4	368.1± 75.9	357.2±83.2*

*P: 0.011 When compared geriatric IDA with nongeriatric adult IDA

Table 7. Transferrin saturation in adult and geriatric IDA with chronic disorders

	Transferrin saturation(%)		
	Male	Female	Total
Normal nonelderly adult	34.5±3.5	33.5±6.4	34.0±4.2
Normal elderly	31.3±8.3	31.0±9.2	31.1±8.1
Nongeriatric adult IDA	7.6±5.4	6.9±4.0	7.1±4.4
Geriatric IDA	8.3±5.3	5.4±2.2	6.7±4.1*

*P:=0.964 When compared geriatric IDA with nongeriatric adult IDA

Table 8. Serum ferritin in adult and geriatric IDA with chronic disorders

	Serum ferritin(ng/ml)		
	Male	Female	Total
Normal nonelderly adult	147.0±108.0	35.3±20.5	88.9±93.8
Normal elderly	152.5± 95.4	111.1±54.1	134.5±91.8
Nongeriatric adult IDA	5.0± 2.7	6.1± 4.5	5.7± 4.0
Geriatric IDA	18.9± 14.6	9.2± 6.3	13.8±11.8*

*P:=0.001 When compared geriatric IDA with nongeriatric adult IDA

with iron deficiency anemia with chronic disorders over 65 years was 22.7±12.3 ug/dl and had no significant difference when compared with that of nongeriatric adult patients less than 65 years (P=0.32) (Table 5).

Total iron binding capacities (TIBCs)

The mean TIBC in geriatric patients with iron deficiency anemia with chronic disorders over 65 years was 357.2±83.2 ug/dl and was significantly lower than that of nongeriatric adult patients who were less than 65 years (P=0.011) (Table 6).

Transferrin saturation (%)

The mean transferrin saturation percentage in geriatric patients with iron deficiency anemia with chronic disorders over 65 years was 6.7±4.1% and had no significant difference when compared with that of nongeriatric adult patients less than 65 years (P=0.964) (Table 7).

Table 9. Causative diseases and serum ferritin in iron deficiency anemia

Causative diseases	No of case		Serum ferritin (ng/ml)	
	≧65	<65	≧65	<65
Gastric cancer	6	4	14.6	5.3
Gastric ulcer	1	0	4.6	–
Gastric erosion	1	0	10.6	–
Duodenal ulcer	0	2	–	6.1
Colon cancer	2	2	9.0	6.1
Anal bleeding	0	2	–	4.3
Other GI bleeding	2	1	8.9	2.8
Uterine cancer	0	2	–	4.3
Uterine myoma	1	1	4.9	19.3
Menorrhagia	1	5	9.7	7.2
Malnutrition	1	0	12.6	–
Others	2	10	34.6	4.9
Total	17	29	13.8±11.8	5.7±4.0

Table 10. Serum ferritin and red cell indices in normal elderly and geriatric IDA with chronic disorders

Serum ferritin (ng/ml)	0~12	13~45	46~74	75~99	100~299	≧300
No. of cases	12	12	5	2	23	2
(M/F)	(4/18)	(8.4)	(1/4)	(1/1)	(13/10)	(2/0)
No. of IDA	11	5	1	0	0	0
Hb(g/dl)	7.3	12.2	12.5	13.5	14.0	14.7
MCV(fl)	65.6	84.5	8.77	93.1	92.8	88.9
RDW	19.0	16.1	13.1	13.0	12.1	12.5

Serum ferritin level

The mean serum ferritin in geriatric patients with iron deficiency anemia over 65 years was 13.8±11.8 ng/ml and was significantly higher when compared with that of nongeriatric adult patients less than 65 years ($P=0.001$) (Table 8).

The upper limit of serum ferritin level in geriatric patients with iron deficiency anemia with chronic disorders over 65 years was 37ng /ml with 95% confidence interval and higher than that of nongeriatric adult patients less than 65 years (20 ng/ml).

Serum ferritin levels in the causative diseases

Table 9 shows serum ferritin levels as they relate to the causative diseases. Chronic bleeding from the gastric cancers (6 cases) were the leading cause in patients over 65 years and also chronic bleeding from the gastric cancers (4 cases) were the leading cause in patient less than 65 years old.

There were no significant differences between causative diseases.

Changes of red cell indices with serum ferritin levels

Each of the changes of red cell indices with serum ferritin levels in geriatric patients with iron deficiency anemia with chronic disorders and normal eldery over 65 years are as in Table 10. Almost all of iron deficiency anemias are found in less than 12 ng/ml of serum ferritin, but up to 74 ng/ml there could be found iron deficiency anemia. MCVs are decreased below normal when serum ferritin level getting less than 12 ng/ml, RDWs increased significantly when serum ferritin level dropped below 45 ng/ml.

DISCUSSION

Life expectancy has increased recently in Korea and the geriatric population is increasing in number. As the geriatric population is increasing, welfare for old ages has been a problematic affair and medical care is very important for this age group. In many developed countries, geriatric studies are ongoing and many of these study results are of use to geriatric clinics. But in Korea, studies for old ages are still in the primitive stage and we have only few studies on geriatric disease.

Anemia is a clinical condition frequently encountered in the elderly. Iron deficiency anemias (IDA) are frequently developed second to anemia of chronic disorders. We want to know the differences of iron related indices in iron deficiency anemia with chronic disorders in the geriatric group compared to that of the nongeriatric adult group. Though the incidene of IDA in geriatric group is lower than that of nongeriatric adult group, Guyatt *et al.* (1990) reported as 36.3% of anemias in the elderly next to the anemia of chronic disorder (43.6%). The exact diagnosis of IDA in the elderly makes it possible for adequate treatments and detection of underlying disease is also very important. Bone marrow study is definite in confirmation of IDA, but such invasive study is uncomfortable for use in old ages. Therefore noninvasive studies such as access of iron related indices are highly available.

In our study, mean hemoglobin level in geriatric IDA was 7.8±2.2 g/dl, belong to moderate degree of anemia and in female patients, mean hemoglobin was 7.1 g/dl and was lower than that of male patients (8.5 g/dl). In the normal elderly people, the female group had lower hemoglobin level and it was consistent with the results from our previous study (Lee *et al.* 1993). It was though that no specific treatment for menstrual bleeding in their premenopausal period would lower hemoglobin levels in their old age in geriatric females.

Mean RDW value was 19.5±2.6 and was higher than that of normal elderly but not higher than that of the nongeriatric IDA group. RDW represents the degree of red blood cell anisocytosis and this is a very useful index for the diagnosis of IDA (Kwon *et al.* 1988), helping us predict the state of iron deficiency during the development of anemia (McClure *et al.* 1985). This can also be used for follow up in the treatment of IDA (Kim *et al.* 1992). We can also use this index in the elderly for the previous diagnosis, treatment and follow up of IDA.

Serum iron level was higher in males than in females both in geriatric and nongeriatric groups and it was similar to the data from foreign countries (Powell and Thomas, 1969). Serum iron levels for geriatric IDA were not lower than that of nongeriatric IDA but in normal elderly it was lower than that of normal nonelderly adult and these were consistent with foreign data (Powell and Thomas, 1969).

TIBC level was inclined to be lower in males than in female both in the geriatric and the nongeriatric groups, and this was not consistent with foreign reports (Powell and Thomas, 1969). TIBC level in geriatric IDA was 357.2±83.2 ug/dl and was lower than that of the nongeriatric IDA group (413.6±54.0 ug/dl) with significant difference ($P=0.011$), and this was consistent with foreign reports that geriatric IDA had a lower TIBC level than that of the nongeriatric group (MacLennan *et al.* 1973). It was thought that decreased TIBC in the aged was because of nutritional defects,

decreased serum protein by chronic disorders, lower level of tranferrin that transfer iron (Weeke and Krasilnikoff, 1972). Other factors affecting TIBC are being studied and continue to be reported (Awad *et al.* 1982).

Mean tansferrin saturation was 6.7±4.1% in geriatric IDA without significant difference compared to nongeriatric IDA (7.1±4.4%). This was lower than Patterson's report (11%) (Patterson *et al.* 1985).

Mean serum ferritin level in normal elderly was 134.5±91.8 ng/ml and was higher than that of the normal adult group. In geriatric IDA it was 13.8±11.8 ng/ml and also higher than nongeriatric adult IDA with significance (P=0.001) especially in male patients.

Jacobs and Worwood (1975) report that the serum ferritin concentration appears to reflect reticuloendothelial storage of iron fairly accurately and the assay of serum ferritin in those with iron deficiency provides a useful and convenient method of assessing status of iron stores. However, the serum ferritin may be elevated and may be misleading in the setting of acute and chronic inflammation, or liver disease (Bentley and Williams. 1974), so measurement of red blood cell ferritin could provide an accurate method of marrow iron store (Balaban *et al.* 1993). Serum level was suggested 20~250 ng/ml in normal adult males and in normal females, 10~150 ng/ml. In our study in normal aged male was 152.5 ng/ml and 111.1 ng/ml in normal aged female, and it were smilar to Loria's report (Loria *et al.* 1979) that normal aged male was 170.8 ng/ml, normal aged female 140.2 ng/ml, and lower level in normal female was thought to be due to decreased iron store in premonopausal period by menstrual bleeding.

Usually in the diagnosis of IDA in adult, the serum ferritin level is considered lower than 10~12 ug/ml but in our study, in the geriatric group it was increased to 37 ng/ml. This was similar to Patterson's 45 ug/ml (Patterson *et al.* 1985), though Holyoake *et al.* (1993) found iron deficiency anemia in the range of 46~75 ng/ml, and we could find 1 case like that. In our study serum ferritin level in normal elderly was higher than normal nonelderly adult with significance. Cook *et al.* (1976) report that increased serum ferritin is present in elderly population, Loria *et al.* (1979) also report increasd serum ferritin levels in both sexes, and the cause of the shift was suggested to be a physiological normal event. Finch and Huebers (1982) report that in normal males, serum ferritin started to increase at the age of 15 years from 30 ng/ml stifly to 94 ng/ml until the age of 30 years then to 124 ng/ml above 45 years, and tended to rise steadily with aging. In normal females, up to 50 years it stayed constantly 30 ng/ml but post menopausely increased up to 89ng/ml then slowely increased with aging.

REFERENCES

Awad MO, Breford AV, Grindulis KA, Montgomery RD, Sammons HG: Factors affecting the serum iron binding capacity in the elderly. *Gerontology 28: 125-131, 1982*

Balaban EP, Sheehan RG, Demian SE, Cox JV, Frenkel EP: Evaluation of bone marrow iron stores in anemia associated with chronic disease. *Am J Hematol 42: 177-181, 1993*

Bentley RP, Williams P: Serum ferritin concentration as an index of storage iron in rheumatoid arthritis. *J Clin Pathol 27: 786-788, 1974*

Cook JD, Finch CA, Smith NJ: Evaluation of the iron status of a population. *Blood 48: 449-453, 1976*

Finch CA, Huebers H: Perspectives in iron metabolism. *N Engl J Med 306: 1520-1528, 1982*

Guyatt GH, Patterson C, ALI M, Singer J, Levine M, Turpie I, Meyer R: Diagnosis of iron deficiency anemia in the elderly. *Am J Med 88: 205-209, 1990*

Holyoake TL, Stott DJ, McKay PJ, Hendry A, MacDonald JB, Lucie NP: Use of plasma. ferritin concentration to diagnose iron deficiency in elderly patients. *J Clin Pathol 46: 857-860, 1993*

Jacobs A, Worwood M: Ferritin in serum. *N Engl J Med 292: 951-956, 1975*

Kim SC, Ko YW, Lee SJ, Min YH, Hahn JS: The RDW response during iron therapy in iron deficiency anemia. *Korean J Hematol 27: 15-21, 1992*

Kwon HM, Lee JH, Lee ST, Hahn JS, Ko YW: Diagnostic significance of RDW and MCV in iron deficiency anemia and anemia of chronic disorders. *Korean J Hematol 23: 408-416, 1988*

Lee JH, Kim JH, Lee SJ, Hahn JS, Ko YW, Kim BS, Song KS: A study on hemoglobin level in geriatric population. *Korean J Hematol 28: 89-95, 1993*

Loria A, Hershko CK, Konijn MA: Serum ferritin in an elderly population. *J Gerontol 34: 521-524, 1979*

MacLennan MJ, Andrews GR, Macleod C, Caird FI: Anaemia in the elderly. *Q J Med 52: 1-13, 1973*

McClure S, Custer E, Bessman D: Improved detection of early iron deficiency in nonanemic subjects. *JAMA 253: 1021-1023, 1985*

Patterson C, Turpie ID, Benger AM: Assessment of iron stores in anemic geriatric patients. *J Am Geriatr Soc 33: 764-767, 1985*

Powell DEB, Thomas JH: The iron binding capacity of serum in elderly hospital patients. *Gerontol Clin 11: 36-47, 1969*

Weeke B, Krasilnikoff PA: The concentration of 21 serum proteins in normal children and adults. *Acta Med Scand 192: 149-155, 1972*