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ORIGINAL ARTICLE

Mitochondrial Ferritin in Erythroid Cells from patients with Myelodysplastic Syndrome

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ABSTRACT

Background: The Myelodysplastic syndrome (MDS) is extremely fatal illness whither anaemia is insensitive to any medical management.
Aim: In present research, effect of levels of ferritin in serum lying on prospects and continued existence was scrutinize in MDS subjects with no previous record of blood transfuse.
Study design: Retrospective.
Methods: These cases (MDS) were alienated into two groups, according to their serum ferritin levels. Sample size of 58 cases of MDS calculated according to online service "Select Statistical Services Ltd" comparing two means.
Results: The time of endurance mean was 5.09 years ± 4.8 months. Median ferritin levels of serum ferritin were 358 ng /ml. The plasma ferritin level is related with higher rate of mortality with levels as 500 ng/ml. The ROC part for Serum ferritin was 0.721 by means of a cut-off range of 401; susceptibility and explicitness. were 71.7% and 69.1%, correspondingly) P=0.002. In attendance were 33 subjects with value of ferritin is ≥ 500 ng/ml. Patients with serum ferritin values ≥ 500 ng/mL had lower survival expectancy. Ferritin ≥ 500 ng/mL be related with seven folds augmented death rates (P = 0.001).
Practical Implication: In MDS iron chelation is not well-known, for that reason the overall survival is not good. The iron chelation might encompass a favorable outcome on survival of MDS.
Conclusion: Even though 1000ng/ml ferritin value in the beginning of chelation therapy is adequate, reduced survival expectancy will be associated with high levels of serum ferritin.
Keywords: Myelodysplastic syndrome, ferritin, chelation, ring sideroblast, isoniazid, penicillamine

INTRODUCTION

Myelodysplastic Syndrome (MDS) is designated as mixed cluster of disorders begins from stem cell origin in hematopoietic clone. In MDS presenting scenarios reduced number and dysfunction of erythrocytes production, platelets and granulocytes of mature level which causes higher risk of producing anemia, bleeding tendency, and infections[1].The most predictable finding in MDS is acute myeloid leukemia (AML) transformation that account for 10–20% of these cases. In 80% of cases throughout the diagnosis anemia is the most frequent cytopenia in MDS[2]. The only treatment option in 40% of subjects may be standard packed cell volume (PCV) transfusions which also lead to increased risk of developing secondary iron overloads. In MDS three major predictive forms are using: first Revised (IPSS-R), International Prognostic Scoring System, second was WHO prognostic scoring system WPSS and third form is (MDACC) MD Anderson Cancer Center[3].

In these form percentage of bone marrow blast, cytopenia, genetics karyotyping using this parameter meant for (PCV) transfuse, age and performance score. In MDS research studies to one side beginning as of prognostic scoring systems like later age, performance score poor, severe anaemia, absolute neutrophil count decrease count of platelets, PCV transfusion reliance, greater than before ferritin levels in serum, and fibrosis of bone marrow, an predictive value of other experimental data have also been investigated on the other hand, integration in that data in scientific practical is yet unknown[4].

Serum ferritin is renowned predictor for iron load and in inflammation and it can be exaggerated as an acute phase reactant in acute infection, inflammation, and malignancy while it was used to exhibit iron load (> 100mg/ml) which should be taken into concern. Other tools were also used to measure iron load is magnetic resonance imaging (MRI), bio-magnetic liver suscepto-metry and super-conducting quantum interference device (SQUID)[3,5].

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Nevertheless, serum ferritin is still used as the generally suitable and adequate chemical variable to find out iron load. Raised serum ferritin level in subjects with MDS is probable due to recurrent PCV transfusions and might present even throughout analysis, earlier to RBS transfusion.[2,4] Unproductive Erythropoiesis and raised intestinal absorption of iron might be the causative factor. Elevation of serum ferritin levels have also been shown to decrease in survival rate. The predictive value of ferritin might contentious within different researches carry out in stem cell transplant of hematopoietic origin in MDS subjects[1,3].

The intend of this research is to estimate the outcome in five years, of serum ferritin level in prediction and endurance in subjects of MDS devoid of a record of PCV transfusions[2,6].

MATERIAL AND METHODS

Methods: These cases (MDS) were alienated into two groups, according to their serum ferritin levels.
Study design: Retrospective.
Sample size: Fifty eight cases of MDS, sample size calculated according to online service "Select Statistical Services Ltd" comparing two means. The diagnosed patient's data with MDS at different hospitals of entire Pakistan among 2016 and 2021 were retrospectively examined.
Inclusion criteria:

1. Laboratory values of serum ferritin measured and biopsies of bone marrow execute all through analysis were evaluated.
2. Male and female
3. Primary MDS and
4. MDS Transformed from AML or vice versa

Exclusion criteria:

1. Secondary MDS due to genotoxic drugs or radiation therapy
2. Patients who already diagnosed to have Ring sideroblast due to chronic Alcoholism, Tuberculosis (those who receive Isoniazid), Autoimmune diseases (those who receive Penicillamine)

Statistical analysis: For statistical analysis SPSS version 21.0 were used. Student's T-test and Chi-squire tests be applied while suitable in adding together to expressive data. For the independent variables Cox proportional hazards model was used and affecting over-all endurance categorical values comprises of two simple ordinal numbers. The P value of > 0.05 were measured statistically considerable.

Ethical permission: This study was approved by the Institutional Ethical Committee.

RESULTS

The total of 58 MDS subjects having mean age of 66.2±13.3, among them 22 were female (37.9%) and 36 are male (62.1%) be incorporated in this study. In attendance 33(56.8%), subjects more than age of 70 year. 5.09 years ± 4.8 months is the mean continued existence of these cases. The median Hb levels were 7.2G/dL, median platelet count was 117 × 10^9/L, and median leukocyte count was 2550/L during of diagnosis. (Table 2) blast ratio: of bone marrow was < 4.5% in 33(56.9%), 6–10% in 14(24.1%), and 9–20% in 11(19.0%) patients. Ring sidero-blast in bone marrow found in 11(18.9%) subjects. In this 15(25.8%) subjects having dysplasia in three-lineages, 17(29.3%) had dysplasia in two-lineages, and 26(44.9%) have dysplasia in single-lineage found in the bone marrow. In this 21(36.2%) cases were devoid of fibrosis, 23(39.7%), cases by grade I fibrosis, 9(17.2%) cases through grade II fibrosis and 4(6.9%) cases among grade III fibrosis (Table 1). During the period of follow-up, 31(53.4%) subjects were died. AML transformation is observed in 8(13.7%) patients. Median serum ferritin levels were 717ng/ml (minimum: 29.8ng/ml maximum: 4000ng/mL). Subjects with ferritin level of ≥ 500 ng/ml having reduced endurance (P=0.001). With ferritin values of ≥500ng/mL the mean endurance time for patients were 3.5 years ±5.6 months, and patients having ferritin <500ng/ml endurance is 6.2 years ±6.9 months. There was a considerable association among ferritin ≥500ng/mL and percentage of blast ≥ 5% (P=0.008).

Table 1: Myelodysplastic syndrome diagnostic laboratory parameters

Parameters		N	%
Bone marrow blast	< 5%	33	56.9%
	5–10%	14	24.1%
	10–20%	11	19.0%
Ring sideroblast		11	18.9%
Marrow dysplasia	Three-lineage dysplasia	15	25.8%
	Two-lineage dysplasia	17	29.3%
	Single-lineage dysplasia	26	44.9%
Fibrosis	No fibrosis	21	36.2%
	Grade I fibrosis	23	39.7%
	Grade II fibrosis	9	17.2%
	Grade III fibrosis	4	6.9%

Table 2: Blood cell counts at diagnosis

Cell counts	Median
Hemoglobin	7.2 G/dl
Platelet count	117x10^9/L
Leukocyte count	2550/L

Table 3: Comparison of the cases with ferritin levels ≥ 500 ng/mL and ferritin levels < 500 ng/mL.

Parameters	ferritin levels ≥ 500 ng/mL	ferritin levels <500 ng/mL	P value
Survival Time	3.5 years±5.6 months	6.2 years±6.9 months	0.001
blast percentage	≥ 5%	< 5%	0.009

In attendance were no statistically significant correlation between single lineage dysplasia, presence of ring sideroblast, fibrosis level of bone marrow, transformation in AML, thrombocytopenia leucopenia, and sometimes bi-cytopenia in subjects with ferritin values of ≥500ng/mL (P= 0.0001), age 70 years and elder (P = 0.004.5), AML alteration (P =0.045), blast ratio of bone marrow >5%, and bone marrow dysplasia in multiple lineages (P = 0.001) extensively reduced total rate of endurance. Ferritin ≥500ng/mL augment the death rate by six folds (95% CI 2–15.5), P = 0.001). The incidence of lineage dysplasia bone marrow stage II and III increases the rate of death by twelve folds (95% CI 0.33–0.45), P = 0.002). The 70 years of age and elder subjects showed elevated rate of death by seventeen times (95% CI (0.07–0.46) P = 0.001) (Table 3).

DISCUSSION

In this research study that resolute the total life expectancy in MDS subjects is low level of serum ferritin. Patients having considerably short life expectancy had > 500 ng/mL of serum ferritin[7]. The probable sign of overloaded iron is serum ferritin level. Subjects presented with AML-transformation in this study showed reduced entire endurance throughout period of follow up[3,5].

Nevertheless, in this study we could not uncover a relationship among raised serum ferritin and leukemic alteration. As stated by this study, the cutoff value of serum ferritin is 500ng/ml which is connecting to decreased life expectancy rate[8]. At the time of diagnosis when serum ferritin was >1000ng/ml in a research study of MDS 190 subjects, was linked with condensed total endurance. In this available information, no association found among raised serum iron, production of free radicals, and sharp leukemic alteration[7,8].

During this study period, the fraction of blast cells was considerably elevated in serum ferritin ≥ 500ng/mL group subjects, however there were no association with acute leukemic alteration. An additional study of different 47 MDS subjects information that the higher SF levels in subjects having diagnosed abnormal chromosomes in comparison to subjects with karyotyping in normal range[4,9].

Subjects of MDS was separated in two different groups in which one had low levels of SF < 500 ng/ml and other had elevated SF> 500ng/ml, among those the subjects of lower SF were appreciably long time survival in months (108.7 versus 11.1 months, P = 0.002).[10] In adding together, free of leukemia life expectancy in subjects of having lower levels of SF were considerably lengthy in comparison with subjects of higher SF levels (P = 0.010). Consequently, standard SF values have been recommended as a predictive feature for taken as a whole survival rate and free of leukemia in MDS subjects[8,10].

In this study period, we did not found any relationship among the incidence of ring sidero-blasts and in ferritin level of ≥ 500ng/ml. The ratio of blast ≥ 5% in a bone marrow and as judgment was connected with decreased in total life expectancy.[7,9] In accumulation, the level of serum ferritin was ≥ 500ng/ml in multiple numbers of presenting cases. The negative prognostic rate of blast figure for overall endurance of MDS subjects is identified[5,7,8]. At age of 70 years the overall life expectancy was reduced in MDS subjects. With Increase in age the frequency of MDS plus its complications of old ages' effects on MDS prediction.[6] during this study we were finding that the incidence of multiple lineages of dysplasia's two or three, in bone marrow can cause decreased in entire survival rate. Occurrence of multiple lineage dysplasia is an unfortunate predictive feature, particularly in subjects of having lower or transitional hazard of Myelodysplastic.[9,10] According to the WPSS scoring system, the incidence of manifold lineage dysplasia donate to the personalization in cases of MDS prognosis[7,10].

CONCLUSIONS

Recurrent blood transfusions in subjects with MDS causes excess serum iron levels. The conventional levels of serum ferritin is 1000ng/mL for iron chelation, while 500 ng/mL is the lower most required serum ferritin boundary level for overall endurance. In addition, near the beginning stages of MDS iron chelation is not well-known, for that reason the overall survival is likely to be extended, yet to some extent, by means of new management strategies. These recommend that early on commencement of iron

chelation might encompass a favorable outcome on endurance of MDS.

Conflict of interest: Nil

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