Original Article

Steroid Response in Autoimmune Hemolytic Anemia

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Conflict of Interest: None
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Abstract:

Background: *Auto-immune hemolytic anemia is an uncommon but not rare disorder. Steroid is the best and commonly used drug for this disorder because it is cheap, easily available and less toxic. But there are a few studies on evaluation of response of steroids in auto-immune hemolytic anemia in our country.*

Objectives: *The purpose of the study was to find out the mean duration for attaining response with prednisolone at the dose of 1 mg/kg body weight, to categorize the patients according to response criteria and to find out the adverse effects due to prednisolone.*

Methodology: *This was a longitudinal and prospective study done in Hematology department of Dhaka Medical College Hospital, Dhaka over a period of one and half year from January 2011 to July 2012. All diagnosed cases of auto-immune hemolytic anemia attending in the hematology department full filling the inclusion and exclusion criteria were included in the study. Data were collected by using a structured questionnaire after taking written consent and history and doing physical examination and relevant baseline investigations. Patients were followed up for two weeks and further physical examination and investigations were done during this time.*

Result: *Mean age of the patient was 33.08 year. Most of the patients (33.33%) belonged to <20 year age group. Progressive pallor, weakness and anemia were the most prominent clinical features (100%), followed by jaundice (50%), splenomegaly (50%), dyspnea (45.8%), hepatosplenomegaly (33.33%), palpable lymph nodes (8.33%) purpuric spot (2%), bleeding manifestation (2%) and bloody diarrhea (2%). No cause of autoimmune hemolytic anemia was found in 43 (89.5%) patients. Among 5 patients with autoimmune hemolytic anemia 3 (6.25%) had non-Hodgkin's lymphoma, 1 (2.08%) had chronic lymphocytic leukemia and 1 (2.08%) had ulcerative colitis. DAT (Direct antiglobulin test) was found positive in 36 patients (75%) and both DAT and indirect antiglobulin test were found positive in 12 patients (25%). Out of 48 patients 32 patients (66.66%) responded within one week and the rest 16 patients (33.34%) responded within two weeks of starting treatment. 43 patients (89.58%) showed complete response and the rest 5 patients (10.42%) showed partial response.*

Conclusion: *Most of the patients responded completely within one week and no patients were found without response. So, Steroid (prednisolone) is very cheap and effective drug for the vast poor people of Bangladesh.*

Key Words:
Autoimmune hemolytic anemia (AIHA), Steroid

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Introduction:

The term auto-immune haemolytic anaemia is used to describe a group of haemolytic anaemias which result from the development of antibodies directed against the antigens on the surface of patient's own red cells i.e act as autoantibody. The antibodies are usually IgG or IgM and or rarely IgA and some of them bind compliments. In a recent population-based study[1] the incidence was 0.8/ 100 000/year, but the prevalence is 17/100 000.[2] Primary (idiopathic) AIHA is less frequent than secondary AIHA. Secondary cases are often challenging because not only AIHA but also the underlying disease(s) must be diagnosed and treated. AIHA is essentially diagnosed in the laboratory, and considerable improvement has been made in this field. However, progress in treatment has been much slower.[3-8] Therapy has been reviewed by several investigators, [8-15] but no treatment guidelines have yet been published.

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Primary warm antibody autoimmune hemolytic anemias respond well to steroids, but most patients remain steroid-dependent, and many require second-line treatment. Currently, splenectomy can be regarded as the most effective and best-evaluated second-line therapy, but there are still only limited data on long-term efficacy and adverse effects. The monoclonal anti-CD20 antibody rituximab is another second-line therapy with documented short-term efficacy, but there is limited information on long-term efficacy and side effects.

Methodology:

This was a longitudinal and prospective study done in Hematology department of Dhaka Medical College Hospital, Dhaka over a period of one and half year from January 2011 to July 2012. All diagnosed cases of auto-immune hemolytic anemia attending in the hematology department full filling the inclusion and exclusion criteria were included in the study. Data were collected by using a structured questionnaire after taking written consent and history and doing physical examination and relevant baseline investigations. Patients were followed up for two weeks and further physical examination and investigations were done during this time. According to accepted recommendations we started treatment immediately with an initial dose of 1 mg/kg/d prednisone (PDN) orally. This initial dose was administered until a hematocrit of greater than 30% or a hemoglobin level greater than 10 g/dL (thus, not necessarily a complete normalization of hemoglobin) is reached. If this goal was not achieved within 3 weeks, then the patient will be considered as a partial response or no response according to the response criteria.[16] Once the treatment goal is achieved, the dose of PDN is reduced to 20 to 30 mg/d within a few weeks. Thereafter, the PDN dose is tapered slowly (by 2.5-5 mg/d per month) under careful monitoring of hemoglobin and reticulocyte counts. An alternate-day regimen (reducing the dose gradually to nil on alternate days) may reduce the side effects of steroids. If the patient is still in remission after 3 to 4 months at a dose of 5 mg of PDN/day, an attempt to withdraw steroids is made. Blood glucose will be monitored carefully and diabetes will be treated aggressively because diabetes is a major risk factor for treatment-related deaths from infections.

Results:

Mean age of the patient was 33.08 (SD±15.68). Age ranged from 18-61 years. As figure I shows 16 patients (33.33%) belonged to the age group <20 years, 12 patients (25%) belonged to 21-30 year group, 4 patients (8.33%) belonged to 31-40 year group, 4 patients (8.33%) belonged to 41-50 year group, 8(16.66%) belonged to 51-60 year group and 4 (8.33%) belonged to age group above 60 year. Most of the patients (33.33%) belonged to <20 year age group.

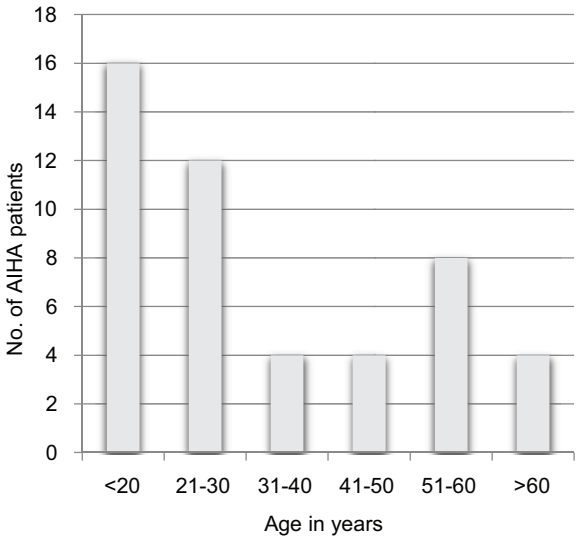

Fig. I *Age distribution of AIHA patients*

Among the patients 32(66.66%) were male and 16(33.34%) were female. Male: Female ratio was 2:1. Progressive pallor, weakness and anemia were the most prominent clinical features (100%), followed by jaundice (50%), splenomegaly (50%), dyspnea (45.8%), hepatosplenomegaly (33.33%), palpable lymph nodes (8.33%) purpuric spot (2%), bleeding manifestation (2%) and bloody diarrhea (2%) as shown in table I.

Table:I

Prominent symptoms and signs of patients

Symptoms/signs	No. of total cases (n=48)	Percentage
Progressive pallor	48	100
Weakness	48	100
Dyspnea	22	45.8
Bleeding manifestation	1	2
Bloody diarrhea	1	2
Anemia	48	100
Jaundice	24	50
Splenomegaly	24	50
Hepatosplenomegaly	16	33.3
Purpuric spot	1	2
Palpable lymph node	4	8.33

Figure II shows that no cause of autoimmune hemolytic anemia was found in 43 (89.5%) patients. Among 5 patients with autoimmune hemolytic anemia 3 (6.25%) had non-Hodgkin's lymphoma, 1 (2.08%) had chronic lymphocytic leukemia and 1 (2.08%) had ulcerative colitis.

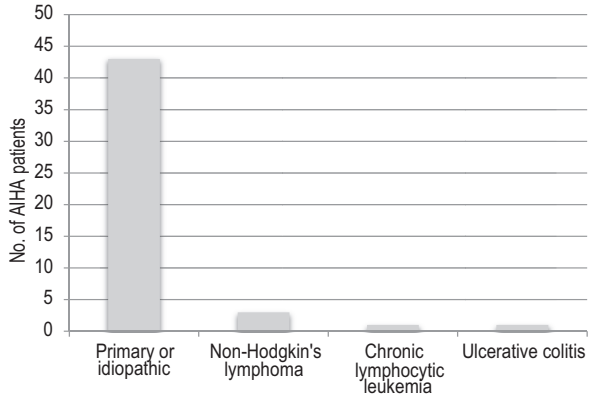

Fig.-2: *Categorization of patients according to causes*

Among the total number of patients 16 patients' (33.33%) hemoglobin level were within 1-3.9 gm/dl, 24 patients' (50%) were within 4-7.9 gm/dl and 8 patients' (16.66%) were 8-11.9 gm/dl at presentation (table II)

Table II

Hemoglobin level at initial presentation

Hemoglobin (gm/dl)	No. of cases	Percentage
1-3.9	16	33.33
4-7.9	24	50
8-11.9	8	16.66

Figure III shows 8 patients' (16.66%) reticulocyte count were 1-7.9%, 20 patients' (41.66%) were 8-15.9%, 8 patients 16-23.9%, 4 patients' 24-31.9% and 8 patients' were 32-39.9%.

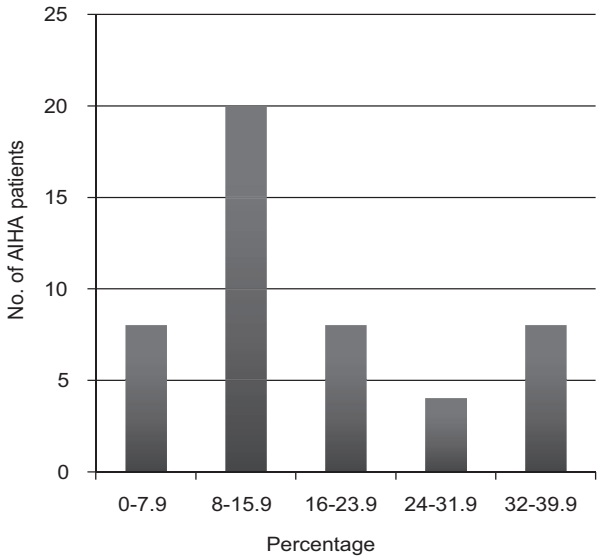

Fig.-3: *Reticulocyte count at initial presentation*

Table III shows 24 patients' (50%) PBF report showed RBC: normochromic, normocytic, plenty of polychromatic cells with few spherocytes and nucleated RBC. 4 patients' PBF report showed RBC: Macrocytic. 8 patients' (16.66%) PBF report showed RBC: normochromic, normocytic, plenty of polychromatic cells with few spherocytes and nucleated RBC. Platelets: reduced in number, 4 patients' report showed pancytopenia and 8 patients' (16.66%) PBF report showed RBC: normocytic and macrocytic.

Table III

PBF report at initial presentation

PBF report	No. of cases	Percentage
RBC: normochromic, normocytic, plenty of polychromatic cells with few spherocytes and nucleated RBC	24	50
RBC: Macrocytic	4	8.33
RBC: normochromic, normocytic, plenty of polychromatic cells with few spherocytes and nucleated RBC. Platelets: reduced in number	8	16.66
Pancytopenia	4	8.33
RBC:normocytic and macrocytic	8	16.66

DAT (Direct antiglobulin test) was found positive in 36 patients (75%) and both DAT and indirect antiglobulin test was found positive in 12 patients (25%) (Table IV)

Table IV

Coomb's test report at initial presentation

Coomb's test	No. of cases	Percentage
DAT positive	36	75
Both direct and indirect antiglobulin test positive	12	25

S. bilirubin was raised upto 2 mg/dl in 8 patients (16.66%), 2.1-5 mg/dl in 32 patients (66.66%) and 5.1-8 mg/dl in 8 patients (16.66%) (Table V)

Table V

Serum bilirubin (total) level at initial presentation

S. bilirubin (total) mg/dl	No. of cases	Percentage
Upto 2	8	16.66
2.1 to 5	32	6.66
5.1 to 8	8	16.66

Table VI shows no hepatosplenomegaly was found in 4 patients (8.33%) and splenomegaly was found 44 patients (91.66%).

Table-VI

USG of whole abdomen (W/A) report

USG of W/A	No. of cases	Percentage
No hepatoslenomegaly	4	8.33
Splenomegaly		
10.1-12 cm	8	16.66
12.1-14 cm	16	33.33
14.1-16 cm	20	41.66

Out of 48 patients 32 patients (66.66%) responded within one week and the rest 16 patients (33.34%) responded within two weeks of starting treatment (Table VII).

Table VII

Duration for attaining response

Duration	No. of cases	Percentage
Within one week	32	66.66
Within two weeks	16	33.34

Out of 48 patients 43 patients (89.58%) showed complete response and the rest 5 patients (10.42%) showed partial response (Table VIII).

Table VIII

Categorization of patients according to response criteria

Response	No. of cases	Percentage
Complete response	43	89.5
Partial response	5	10.5

Weight gain occurred in all 48 patients (100%) which was the most common side effects. Among the other side effects moon face was found in 46 patients (95.83%), acne in 40 patients (83.33%), increase blood glucose in 40 patients (83.33%), herpes zoster infection in 2 patients, fungal infection in 19 patients, striae in 16 patients, bruising in 1 patient and hair thinning in 1 patient (Table IX).

Table IX

Side effects of steroid

Side effects of steroid	No. of cases	Percentage
Weight gain	48	100
Moon face	46	95.83
Acne	40	83.33
Increased blood glucose	40	83.33
Fungal infection	19	39.58
Striae	16	33.33
Herpes zoster infection	2	4.16
Bruising	1	2.08
Hair thinning	1	2.08

Discussion:

Total number of cases were 48. Of them 32(66.66%) were male and 16(33.34%) were female. Male: Female ratio was 2:1 (Fig. 1). Less percentage of female in this study may be due to several reasons. One important is that the hospital provides very few beds for females in contrast to males. Health seeking behavior in female is not developed in our country for several reasons.

Mean age was 33.08 (SD±15.68). Age ranged from 18-61 years. 16 patients (33.33%) belonged to the age group <20 years, 12 patients (25%) belonged to 21-30 year group, 4 patients (8.33%) belonged to 31-40 year group, 4 patients (8.33%) belonged to 41-50 year group, 8(16.66%) belonged to 51-60 year group and 4 (8.33%) belonged to age group above 60 year. Most of the patients (33.33%) belonged to <20 year age group.

http://www.clinicalkey.com/topics/hematology/autoimmune-hemolytic-anemia.html showed Warm AIHA affects people of all ages, but its incidence increases with age and peaks in midlife. Chronic cold agglutinin disease predominates among patients in their 50s and 60s and Paroxysmal cold hemoglobinuria is usually a disorder of children or young adults.

Among 48 patients student were (n=20) 41.66%, housewife (n=12) 25%, service holder (n=12) 25% and day laborer (n=4) 8.33%.

Distribution of patients from various division shows maximum number of cases were from Dhaka division (66.66%) followed by Chittagong division (16.66%), Khulna division (8.33%), Sylhet division (8.33%).

Regarding prominent symptoms and signs of the patients progressive pallor, weakness and anemia was the most prominent clinical feature (100%), followed by jaundice (50%), splenomegaly (50%), dyspnea (45.8%), hepatosplenomegaly (33.33%), palpable lymph nodes

(8.33%) purpuric spot (2%), bleeding manifestation (2%) and bloody diarrhea (2%).

Out of 48 patients 16 patients' (33.33%) hemoglobin level were within 1-3.9 gm/dl, 24 patients' (50%) were within 4-7.9 gm/dl and 8 patients' (16.66%) were 8-11.9 gm/dl at presentation.

Among 48 patients 8 patients' (16.66%) reticulocyte count were 1-7.9%, 20 patients' (41.66%) were 8-15.9%, 8 patients 16-23.9%, 4 patients' 24-31.9% and 8 patients' were 32-39.9%.

Twenty four patients' (50%) PBF report showed RBC: normochromic, normocytic, plenty of polychromatic cells with few spherocytes and nucleated RBC. 4 patients' PBF report showed RBC: Macrocytic. 8 patients' (16.66%) PBF report showed RBC: normochromic, normocytic, plenty of polychromatic cells with few spherocytes and nucleated RBC. Platelets: reduced in number, 4 patients' report showed pancytopenia and 8 patients' (16.66%) PBF report showed RBC: normocytic and macrocytic.

DAT (Direct antiglobulin test) was found positive in 36 patients (75%) and both DAT and indirect antiglobulin test was found positive in 12 patients (25%).

S. bilirubin was raised upto 2 mg/dl in 8 patients (16.66%), 2.1-5 mg/dl in 32 patients (66.66%) and 5.1-8 mg/dl in 8 patients (16.66%).

No hepatosplenomegaly was found in 4 patients (8.33%), splenomegaly was found 44 patients (91.66%).

Erythroid hyperplasia was found in 46 patients (95.83%), erythroid hyperplasia with megaloblastic changes were found in 2 patients (4.17%).

No cause of autoimmune hemolytic anemia was found in 43 (89.5%) patients. Among 5 patients with autoimmune hemolytic anemia 3 (6.25%) had non-Hodgkin's lymphoma, 1 (2.08%) had chronic lymphocytic leukemia and 1 (2.08%) had ulcerative colitis.

Out of 48 patients 32 patients (66.66%) responded within one week and the rest 16 patients (33.34%) responded within two weeks of starting treatment. But Bradley C. Gehrs and Richard C. Friedberg et al. found that 70-80% patients improved within 3 weeks[16].

Out of 48 patients 43 patients (89.58%) showed complete response and the rest 5 patients (10.42%) showed partial response. The cause of this partial response may be delay in diagnosis and starting of specific treatment of primary disorder. . But Bradley C. Gehrs and Richard C. Friedberg et al. found that among new cases 15-20% achieved complete remission[16].

Weight gain occurred in all 48 patients (100%) which was the most common side effects. Among the other side effects moon face was found in 46 patients (95.83%), acne in 40 patients (83.33%), increased blood glucose in 40 patients (83.33%), opportunistic infection in 21 patients, striae in 16 patients, bruising in 1 patient and hair thinning in 1 patient.

Conclusion

Prednisolone is very effective in treating autoimmune hemolytic anemia as 66.66% patient responded within one week. The rest 33.34% patient responded at two weeks. Only 5 patients(10.5%) responded partially. No patient was found without any response. Though the complications like weight gain, acne, moon face, opportunistic infection were common they were reversible and easily manageable. Steroid (prednisolone) is very cheap and effective drug for the vast poor people of Bangladesh.

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