D E C L A R A T I O N.

This work is original and has not been presented for a degree in any other University.

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This dissertation has been submitted for examination with my approval and supervision.

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CONTENTS

INTRODUCTION

Erlich in 1888 described the first cases of aplastic anaemia when he described a rapidly progressive fatal syndrome occurring chiefly in young adults (1). In his cases all the three formed elements of the blood were significantly depressed, and the bone marrow was accellular. In the last 87 years the concept of aplastic anaemia has broadened to include patients suffering from a congenital form with or without malformations (familial hypoplastic anaemia), congenital and acquired pure red cell aplasia (2) affecting all age groups (3).

There are many aetiological factors for aplastic anaemia. Some are constitutional, and others have acquired factors. The constitutional factors include the Blackfan Diamond syndrome, and the Fanconi anaemia. The acquired factors are many and no particular cause of these can be identified. Between 49 - 58% of all cases of aplastic anaemia fall into this group (4). The acquired factors comprise a host of drugs. Since 1955 more than 411 drugs and chemicals have been reported to be responsible for aplastic anaemia (5). Top of the list of these drugs is chloramphenicol (6). Others include phenylbutazone (7) while anticonvulsants like epanutin, cytotoxic drugs and heavy metals used in industries, and other agriculturally used chemicals like DDT have been implicated. Benzenes used in the dry cleaning industry and organophosphates have been implicated in the causation of aplastic anaemia. Some of the above drugs have direct effect on bone marrow (8), (9).

Infections too, play a role in the aetiology of aplastic anaemia, namely; bacterial infections, such as miliary tuberculosis, typhoid fever, diphtheria, bacterial endocarditis and brucellosis; all of which have been associated with pancytopenia. In children such infections are likely to cause aplastic anaemia (10). Viral infections have long been associated with granulocytopenia, but not pancytopenia (11). Hepatitis in humans has however been associated with hypoplastic bone marrow (12).

Radiation whether diagnostic or therapeutic may cause bone marrow aplasia in toxic doses.

It is not know how these agents operate to cause aplastic anaemia. The effects of various agents are variable (13). Studies of patients receiving chloramphenicol have revealed erythroid hypoplasia with abnormal vacuolation of cytoplasm of erythroblasts. These changes are reversible once the drug is withdrawn. The severer haematologic response to chloramphenicol is severe pancytopenia associated with hypocellular marrow. It is insidious and often regretably irreversible (14).

In one form of aplastic anaemia, the pure red cell aplasia, antibodies to the marrow erythroblasts either prevents their development, or destroys them as they are formed (15). Patients with pure red cell aplasia are not prone to infections and haemorrhage. Their white cells and platelets are normal in peripheral blood. Defective erythropoiesis is responsible for their anaemia. The disorder is regarded as familial (16).

The incidence of aplastic anaemia varies according to the aetiological factors mentioned. Incidence due to chloramphenicol is reported to be 1:6,000 - 1:9,000 (8).

Various diagnostic features are used. These are mainly clinical and haematological. The main clinical features of aplastic anaemia have been described (1). Onset is variable with majority occurring insiduously and with a few fulminating cases. First symptoms are generally due to anaemia, due to failure of erythropoiesis. These include weakness, lassitude, shortness of breath, palpitations and increasing pallor. Spontaneous haemorrhages due to thrombocytopenia occur from orifices, into skin, gastrointestinal tract and intracranial. Coma and stupor occur later in disease due to cerebral haemorrhages and infections. The haematological characteristics which are diagnostic of the condition are reduction in the peripheral blood to less than ½ million. Haemoglobin declines in parallel with the red cells (17). In particular the reticulocytes range from 0-4% (17). The leucocytes are usually markedly reduced, and number from 3,000-1,500 per cmm., of which polymorphs form about 20%. Lymphocytes remain within normal limits except terminally when they also decrease. In chronic types of marrow hypoplasia, lymphocytes are relatively increased. This is because the liver, spleen, and lymph glands are unaltered. Platelet counts are almost invariably reduced. Terminal figures of 10,000 are common and account for the spontaneous haemorrhage occurring in the patients (10)

The condition carries poor prognosis without treatment. The main treatment is blood transfusions and corticosteroids (18). The use of corticosteroids alone in aplastic anaemia has in general been disappointing. Splenectomy and bone marrow transplants are tried (19, 20). Immunosuppressive therapy is also under trial (21).

OBJECTIVES

(1) To establish the prevalence and types of aplastic anaemia at Kenyatta National Hospital by retrospective study.

(2) To study age, sex, and tribal distribution

(3) To assess methods used for management and their outcome.

(4) To determine possible aetiological factors in the cases.

MATERIALS AND METHODS

All the records of patients who had been diagnosed as cases of aplastic anaemia at the Kenyatta National Hospital (KNH) between mid. 1973 to December, 1978 were scrutinised. The period starting in mid. 1973 was the time the records office at the KNH started keeping patients records, according to the internationally accepted criterion depending on diagnosis. The following information was extracted and transferred on to a proforma and the date analysed as follows:-

The clinical presentation and duration of the illness plus any past medical history. This included signs and symptoms of the presenting illness.

- The age, sex and tribal distribution
- Associated disease and infections
- History of ingestion of drugs and herbs, exposure to chemicals and irradiation.
- Laboratory investigations - The peripheral blood film investigations were scrutinised for:-

(a) Levels of haemoglobin on admission and subsequent to treatment
(b) Platelets
(c) Leucocytes, total and differential
(d) Bone marrow
(e) Liver function tests
(f) Urine - microscopy
(g) Blood cultures if any

- Radiologic investigations

- Type of treatment given to the patient and its duration and his response to it.
- Ultimate fate of the patient - that is
  (a) Whether any response was noted
  (b) Defaulters
  (c) deaths

  Plus the duration each occurred
- Any relevant family and social history

TABLE I

RESULTS

AGE & SEX DISTRIBUTION

AGE IN YEARS	M	F	TOTAL
0-4 yrs	2	4	6
5-9 yrs	4	3	7
10-14 yrs	8	1	9
15-19 yrs	1	4	5
20-24 yrs	6	4	10
25-29 yrs	0	0	0
30-35 yrs	4	7	11
35-39 yrs	0	0	0
40 yrs	4	2	6
Total	29	25	54

Table I shows the age and sex distribution of the cases. A total of 54 patients were diagnosed and confirmed to have aplastic anaemia. Of these 54 cases, there were 29 males and 25 females with a M: F ratio of 1:1. The youngest case was 1½ years and the oldest was 65 years. 31 (50%) of the patients were in the age range 5-25 years.

Using 15 years as the arbitrary upper limit for childhood at the Kenyatta National Hospital, the number of patients in the age group 0-15 years were 21 (41%) of the total patients confirmed to have aplastic anaemia.

TABLE II

TRIBAL DISTRIBUTION

TRIBE	NUMBER	% OF CASES
KIKUYU	33	63%
KAMBA	7	13
LUO	3	6
LUHYA	2	4
KALENJIN	3	6
MERU	2	4
MASAI	2	4
KISII	1	2
TAITA	1	2

Table II shows the tribal distribution. The majority of the patients 33 (63%) were Kikuyu followed by 7 (13%) Kamba.

TABLE III

VARIOUS TYPES OF APLASTIC ANAEMIA

TYPES	NUMBER	% OF CASES
ACQUIRED APLASTIC ANAEMIA	48	88.9
CONGENITAL PURE RED CELL APLASIA	4	7.3
APLASIA FOLLOWING LEUKAEMIA	1	1.9
FANCONI APLASTIC ANAEMIA	1	1.9

Table III shows the distribution of the types of aplastic anaemia. 48 (89%) were of acquired type, while 4 (7%) were of the congenital pure red cell aplasia. One case belonged to the Fanconi aplasia anaemia. The four cases of congenital pure red cell aplasia together with the one case of Fanconi aplastic anaemia were below 15 years of age.

TABLE IV

PRESENTING CLINICAL FEATURES

TYPES	NUMBER	%
PALLOR	54	100
DIZZINESS	52	96
HAEMORRHAGE	42	78
HEADACHE	23	43
GENERAL WEAKNESS	23	43
PNEUMONIA	8	15
PALPITATIONS	7	13
OEDEMA	7	13
JOINT PAINS	7	13
EPIGASTRIC PAINS	6	11
DYSURIA	6	11
HEPATOMEGALY	3	6
JAUNDICE	2	4
SPLENOMEGALY	1	2
COMA	1	2

Table IV shows the presenting clinical features Pallor occurred in all patients, while dizziness occurred in 52 (89%) of the total cases. Haemorrhage was a common finding occurring in 42 cases (78%). Organomegaly occurred in very few patients. Hepatomegaly occurred in only 3 patients. One of these patients had hepatitis. 2 patients had clinical and radiologically proven pulmonary tuberculosis, while two more had viral hepatitis, and one adult was suspected to have a thymoma which was never confirmed. Most children under 15 years presented with the above features of anaemia, indicated in table IV.

HAEMOGLOBIN LEVELS IN DECILITRES

TABLE V

DEGREE OF ANAEMIA	HB in gms/100 cc Blood	NUMBER	% OF CASES
SEVERE	LESS THAN 5	47	87.0
MODERATE	6 - 8	6	11.1
MILD	9 - 12	1	1.9
NORMAL	ABOVE 12	0	0

Table V shows distribution of HB levels. 87% of the patients presented with markedly reduced haemoglobin, less than 5 gm %. In keeping with the number of patients who presented with pallor 6 patients (11%) had moderate anaemia while only one patient had mild anaemia with haemoglobin of 9.3 gm % which later fell to 3.5 gm %.

The range of haemoglobin values was 1.4 - 10.3 gm % with a mean haemoglobin of 4.6 gm %. No patient was noted to have haemoglobin above 12 gm %. 20 patients (37%) below 15 years had severe anaemia with haemoglobin less than 5 gm %. One patient, a 7 year old, had moderate anaemia with haemoglobin of 6.4 gm %, while one child aged 3 years old had mild anaemia, with haemoglobin of 10.3 gm %.

TABLE VI WHITE BLOOD CELLS PER MICRO LITRE UNITS

		%
Less than 3,000	23	42
3,000-10,000	26	48
10,000-20,000	4	8
Over 20,000	1	2

Table VI indicates that the WBC ranged from 780/mm^3 - 19,300/mm^3 with a mean of 1,140/mm^3. Leucopenia occurred in 42% of the patients. These patients had leucocyte counts of less than 3,000 WBC/mm^3 and this was mainly due to neutropenia. Lymphocytes in all the patients remained within normal limits, with differential counts of more than 70%.

Of the 23 patients with white blood cell count of less than 3,000, six were below 15 years of age and they were all aged 14 years. The patient with the lowest count was 8 years old.

Of the 26 patients with WBC between 3,000--10,000, eleven were below 15 years. The only patient with WBC of more than 20,000 was a child aged three years.

TABLE VII

PLATELET COUNTS

	NO	%
Less than 20,000	22	41
20,000-50,000	25	46
50,000-100,000	3	6
Above 100,000	4	7

Table VII shows that platelet counts ranged from 1,000/mm^3 - 280,000/mm^3 with a mean of 36,000/mm^3. A total of 48 patients (98%) of the total studied had platelet counts of less than 50,000/mm^3. All the 22 patients (41%) with platelet counts of less than 20,000/mm^3 had spontaneous haemorrhages, while a further 20 patients (39%) with slightly higher platelet counts, with levels of 20,000 - 50,000/mm^3 also had spontaneous haemorrhages. All the cases of pure red cell aplasia had platelet counts of more than 100,000/mm^3.

Of the 25 patients with platelet counts less than 20,000, five were below 15 years of age, and the lowest count occurred in a child of 2 years and 4 months of age. 6 of the 25 patients with platelet counts between 20,000 - 50,000 were under 15 years while only two of the four with counts of more than 100,000 were under 15 years.

PACKED CELL VOLUME

TABLE VIII

	NO	%
Less than 10%	13	24.2
10 - 20%	40	74
20 - 30%	1	1.9
30 - 40%	0	0
40 - 50%	0	0

Packed cell volume reduction was in keeping with the reduction in haemoglobin levels. 98% of the total patients had packed cell volume less than 20% (table VIII). This was consistent with the clinical finding of pallor at the time of admission (table IV).

BONE MARROW CELLULARITY

TABLE IX

TYPES	NUMBER	%
HYPOPLASTIC	54	100
NORMOCELLULAR	0	0

A total of 54 cases (100%) had hypoplastic marrow (table IX). 4 of these patients (6%) had depression of their erythropoiesis with absolutely no depression of their myeloid activity. These were patients confirmed to have pure red cell aplasia. It was observed that of the 54 bone marrows performed the iron load was raised in all. The 4 patients observed to have normal myelopoiesis were children below 15 years.

NUMBER OF PATIENTS TREATED WITH STEROIDS

TABLE X

DRUG	NO	%
PREDNISONE ALONE	3	5.6
PREDNISONE & OXYMETHOLONE	16	29.6
PREDNISONE & DECADURABOLIN	6	11.1
PREDNISONE & METHYLTESTOSTERONE	6	11.1
PREDNISONE & FLUOROMETHOLONE	1	1.9
TOTAL TREATED	32	59.3
NO STEROID THERAPY	22	40.7

Table X shows the number of patients on therapy. 32 patients (59.3%) were on prednisone and/or an androgenic steroid. These patients were treated with either prednisone alone 3 cases, prednisone and oxymetholone 16 cases, prednisone and decadurabolin 6 cases, prednisone and methyltestosterone 6 cases, and prednisone and flurometholone 1 case (table X).

All the patients had been put on folic acid and multivitamins while 26 patients were on various antibiotics, mainly crystalline penicillin or ampicillin for secondary chest and urinary infections respectively. 20 of these patients had pneumonia with 14 of them complicated by septicaemia. These 14 were variously on a combination of gentamycin with crystalline penicillin or Kanamycin with crystalline penicillin. Of the 32 patients on prednisone and/or an androgenic steroid, 22(40.7%) were below 15 years of age.

6 patients were on treatment for urinary tract infection while 2 were on anti TB therapy mainly streptomycin and thiazina.

RESPONSE TO TREATMENT

TABLE XI

RESPONSE	NUMBER	%
COMPLETE RESPONSE	0	0
PARTIAL REMISSION	16	30
NO RESPONSE	38	70

A patient was regarded to have complete response if clinically he was well and the following haematologic indices were found. A haemoglobin of more than 11.5 gm per decilitre, neutrophils 2500/mm^3, platelet counts of 150,000/mm^3, white blood cell count or 3,000/mm^3 with differential polymorph count of 50% and bone marrow with all cellular elements present in appreciable amounts (3). None of the patients qualified for this criterion.

Remission was regarded present if clinically the patient was better than on admission and if the reticulocyte count had risen to 0.5% and above and lymphocyte count fell to less than 70% reflecting inversely the population of haemopoietic cells.

Of the 16 patients showing partial response, 10 of them were children below 15 years. Most of them, though got lost to follow up subsequently and their fate could not be determined.

15 of the 54 patients died despite any form of therapy. Four of these patients had lived for periods ranging from 1 year to 4 years and had shown some remission before they succumbed to severe pneumonia and septicaemia, and died. Of the living patients partial remission occurred in 16 patients (30% of the total) (table VI). Most of these patients were later lost to follow up and their fates are unknown. 38 patients (70%) showed no response at all, (table XI). Two patients developed diabetes mellitus after 4 weeks and 6 weeks respectively of steroid therapy. These drugs had to be withdrawn. Again these patients were later lost to follow up and their fates unknown. All the 4 patients with pure red cell aplasia are still alive.

CAUSES OF DEATH

TABLE XII

	NO	%
Intercurrent Infections	5	33
Haemorrhages	6	40
Congestive cardiac failure due to anaemia	4	27

Out of the 15 patients in whom cause of death was ascertained, 5 died of infections (table XII). Of these, 4 had septicaemia one of which on postmortem had haemorrhages in the lungs and one had severe hepatitis.

Of the total 6 deaths due to haemorrhages, 4 were children under 15 years, while all the 4 children who died of congestive cardiac failure were under 15 years of age.

6 died of severe haemorrhages, 2 of these had severe gastrointestinal haemorrhage, one bled from a small pox vaccination site and one from an ordinary intramuscular injection site. One had severe intracranial haemorrhage and this was a patient who presented in coma, and never recovered from it. 4 deaths were due to congestive cardiac failure following severe anaemia. There was no particular age group with higher mortality than another.

Of the total patients who died, 8 (53%) of the total dead were in the age group 0-14 years. No deaths occurred between the age 15 years to 29 years, the period of highest default rate. The rest of the patients who died were more than 30 years.

FOLLOW UP IN MONTHS

TIME IN MONTHS	0-4	5-12	Over 12
ALIVE	0	1	8
LOST TO FOLLOW UP	19	-	4
DEAD	11	-	4

Of the total 9 live cases of aplastic anaemia, 4 of these (44%) are of the pure red cell aplastic type. The longest living is a female and has been followed up for more than six years. These 4 are children below 15 years of age and are being followed in the haematology clinic.

23 (81%) of the patients were lost to follow up before one year ended from the time of diagnosis (table XIII). 11 (73%) of the total 15 dead, died within the first 4 months of diagnosis, 4 died after one year of diagnosis as mentioned earlier. Bye and large the duration of follow up from the time of diagnosis to the time of loss to follow up or death averaged 9.6 months with a range of follow up of 5 days to more than 6 years.

D I S C U S S I O N

Invariably, all the patients satisfied the criterion for diagnosis of aplastic anaemia. Besides the other parameters all the bone marrows on aspiration or on trephine biobsy where dry aspirates were obtained, revealed hypoplastic marrow (3).

From the study of patients with aplastic anaemia diagnosed and treated at the Kenyatta National Hospital (KNH), it was found that the male to female ratio was equal, that is M:F ratio of 1.1:1. This is in keeping with work done elsewhere(3).

The finding that most cases of aplastic anaemia seen at the KNH occurred before the age of 35 years, there were 44 patients (89%), compares well with the findings of other workers (10) who report that aplastic anaemia occurs most commonly in the young age group, and that 75% occur before the thirty fifth year of life.

As was found, there were more males than females in the 0-10 years of age a ratio of males to female of 1.7:1. This is in keeping with the overall admission at Kenyatta National Hospital,where the ratio of males to females is 1.2:1. (22). 22 patients (42%) of the total were below the age of 15 years. This is in keeping with the childhood population in the country which is about 48% of the total Kenyan population (23). There is no particular explanation for notable absence of patients in the 25-29 and 35-39 age groups.

However, the sample is small for any conclusion to be made, to explain the irregular distribution. It is hence difficult to give the peak occurrence of aplastic anaemia at the Kenyatta National Hospital.

It has been a common practice to transfuse anaemic patients and discharge them home without further investigations in the paediatric observation ward and the adult observation ward, and this may partially explain why no cases were detected in the above age groups.

TRIBAL DISTRIBUTION

The tribes with the most cases of aplastic anaemia are the Kikuyus and to a certain extent the Kambas. It can be postulated that the Kikuyu and to a certain extend the Kambas live in a vicinity near the Kenyatta National Hospital, where they are likely to benefit from the specialised services. This will result in detection of aplastic anaemia early. The other postulates include the fact that the Kikuyus living in and around Nairobi are exposed to alot of noxious materials from the farming industry; the area where they live is a fertile farmland and lots of cash crops including coffee, tea, pyrethrum are grown, while animal ranching is carried out in a big scale. Lots of chemicals are used to spray the crops and the animals and this could contribute to exposure of the people, some of whom later acquire aplastic anaemia. This is more an occupational hazard of the farmers, rather than of ethnic origin.

As stated above, this is just a postulate and work is required to find out the role of these farm chemicals in causation of aplastic anaemia.

The Kikuyus also form the majority of the work force in the industrial sector of the city, where again they are likely to be exposed to noxious industrial chemicals. Most of the other ethnic groups in the country are represented and this would show that the disease occurs in all the tribes of Kenya.

TYPES OF APLASTIC ANAEMIA

The various types of aplastic anaemia were found with acquired aplastic anaemia forming the majority (95%). Although in half of the cases of acquired aplastic anaemia the aetiology is not known (24) effort was not made in all the cases diagnosed to find out whatever agents may have been responsible. For example, very few people were specifically asked whether they had been taking any medication or herbal preparation.

THE ROLE OF DRUGS & OTHER AGENTS IN THE AETIOLOGY OF APLASTIC ANAEMIA

The syndrome of aplastic anaemia assumes special significance today. Its association with certain drugs, chemical, irradiation has become well documented (25).

New compounds from the pharmaceutical industry appear with increasing frequency. Some of these are not properly tested and find a dumping area in developing countries, where facilities to test them are often lacking. Chemicals eg. insecticides are often released, and without much testing find their way into homes, where children especially may be exposed to them.

The hazards of the contamination of the atmosphere by atomic explosions and with expanding use of diagnostic xray cannot be underestimated. The role of the herbs in causation of aplastic anaemia is unknown and this is a virgin land requiring a lot of exploration.

Specific drugs like chloramphenicol and phenylbutazone have been associated with aplastic anaemia (6). Both of these drugs are very commonly used in Kenya, chloramphenicol being the mainstay of treatment of meningitis and some of the complications of measles. Forbes et al (26) claimed that chloramphenicol used in the paediatric observation ward had probably no effect on marrows of children.

Even if some of the agents used were identified, it would still be difficult to incriminate that agent as responsible for aplastic anaemia for some of the diseases are associated with red cell aplasia eg. rheumatoid arthritis (27), TB (38) and hepatitis (25). Some of the patients under study were on treatment for some of these diseases as mentioned earlier.

CLINICAL FEATURES NOTED

The presenting clinical features in the cases of aplastic anaemia were those due to anaemia mainly pallor, dizziness headache and general malaise.

A few cases were said to have dizziness, despite their very young ages, when they could not possibly have complained of dizziness, an error in history taking. The absence of organomegaly in most of the patients, namely hepatosplenomegaly, is a finding that has been reported by other workers (17) and was conspicuous in the patients studied. Haemorrhages that occurred were mainly due to thrombocytopenia, while the infections noted on admission that is pneumonia and urinary tract infection were mainly due to severe leucopenia which was noted in 42% of the patients.

Anaemia was very severe in most cases with a mean haemoglobin of 4.7 gm/%. All the patients except one were given blood transfusions and this was done after estimation of haemoglobin and packed cell volume. Later a peripheral film was made. Only three patients received platelet infusions.

It is not always easy to get platelet concentrate for fresh blood is not always available. Anaemia may be treated with infusions of packed cells. Nevertheless in acute case thrombocytopenic haemorrhages should be treated with fresh blood which is more effective. The frequency of blood transfusions should otherwise be dictated entirely by the need to control symptoms, and not aimed at maintaining the haemoglobin at any arbitrary figure. In the patients studied the criterion for transfusion in most patients was mainly clinical symptoms and quite a few patients were discharged home with haemoglobin levels of lett than 5 gm/%.

53 of the 54 patients (89%) were given blood transfusions.

In all a total of 600 pints of blood were given to all the patients at an average of about 12 pints. There was no particular lower value for which transfusion was given, but generally patients were transfused if their haemoglobin values fell below 5 gm per decilitre. Together with the blood transfusions, three patients were given platelet concentrates, each on one occasion. The one patient not transfused was a 2½ year old patient who died before transfusion could be given.

A conservative transfusion regimen reduces the incidence of isoimmunisation and haemosiderosis. Moreover, red cell from which the "buffy coat" has been removed help to reduce the incidence of reactions due to HL-A antibodies. In women the contraceptive pill and antifibrinolytic drugs are useful in controlling menorrhagia.

LABORATORY FINDINGS

Definite leucopenia occurred in a big proportion of the patients. Infections in aplastic anaemia are closely related with severity of the granulocytopenia, A neutrophil count of $250/mm^3$ is an ominous sign, and patients with this low count succumb very easily to fulminating fatal infections. The only patients without neutropenia were the 4 cases of pure red cell aplasia. It should be noted that none of them was found to have severe life threatening infections. Gram positive coccal infections particularly in the skin, bacterial pneumonia and Gram - negative septicaemia are particular risks (17). This was evident from patients studied. It is not known what organisms were responsible.

for the fatal infections however, the incidence of fungal infections is also increased, but this was never found in the patients studied. It was not looked for.

In patients with profound neutropenia, Gram - negative septicaemia is probably best treated with a combination of intravenous carbenicillin and cephaloridine. Gentamycin is probably less effective in the absence of functioning granulocytes (17). Most of the patients with septicaemia were treated with gentamycin and crystalline penicillin, after other antibiotics like ampicillin had been tried without much success.

SPECIFIC DRUG THERAPY

As noted earlier the treatment was not standardised and some patients received either no steroids, a combination of prednisone and an androgenic steroid, or prednisone alone. In short, steroid therapy was erratic. The results were generally disappointing although patients receiving androngens are said to have a better survival (3). Androgens have strong erythropoetic action (29). In the past survival rate was 10% without androgens and it has been shown that survival rate of patients on corticosterone alone is very low (30). Response is usually slow and reticulocytes do not reach peak until 2-9 months. Haemoglobin and granulocyte response occurs at 2-15 months while platelet level of 30,000 to 70,000/mm^3 occurs about the same period. Those of the patients studied who had slight remission had remission varying from a few months to a year.

OTHER DRUG THERAPY

It has been observed that there is nothing gained by giving the vitamin B factors, folic acid or riboflavin in aplastic anaemia (1).

In fact, iron therapy is not only ineffective in the refractory anaemia, but also is actually contraindicated. It is absorbed in increased amounts from the gastrointestinal tract to further overload these patients (3). All the patients seen were on iron and folic acid for variable periods.

Constitutional aplastic anaemia (Fanconi) are dependant on hormones and their withdrawal is followed by relapses (31). The fate of the only case of Fanconi in the study is unknown for he defaulted. The importance of using both androgens and corticosteroid simultaneously has been stressed by Shahidi et al (29). The catabolic effect of corticosteroid is opposed by the anabolic action of testosterone.

PROGNOSIS

Aplastic anaemia is a serious disorder and except in the reversible type due to cytotoxic drugs, complete clinical and haematological recovery may occur in as few as 10% of cases (32). None of the patients in the study recovered completely.

Mortality was high during the first four months, (table XIII). This compares well with the findings of other workers. G.C. Geary reports death rate of more than 50% during the first year (33). While Rubin et al found that 75% of patients died within 6 months (34).

Default rate and loss to follow up was very high with 81% of the patients involved. This is accounted for ignorance by the patients, of the gravity of the illness, and by hasty discharges from the wards.

C O N C L U S I O N

From the study, it was found that aplastic anaemia does occur in Kenya and affects all age and sex groups. However, the incidence and prevalence of aplastic anaemia in Kenya cannot be accurately assessed. A pilot study I did at the paediatric observation ward (35) under the guidance of Prof. Walton revealed that anaemia is grossly underdiagnosed. The practice of transfusing anaemic patients without finding the cause of the anaemia results in underdiagnosis of aplastic anaemia.

All the different types of aplastic anaemia namely: constitutional and acquired, were found to exist, with predominance of acquired anaemia. Morbidity and mortality was highest in the young age group, that is below 25 years.

The laboratory finding confirmed the diagnosis, and it was found that except for pure red aplasia, all the blood elements were diminished. In pure red cell aplasia,only the red cells were diminished. Prognosis is bad except for patients with red pure cell anaemia and death due to the disease was commonest before the fifteenth year of life and occurred a few months after the diagnosis was made.

No particular agent or disease was incriminated in the aetiology; however a few patients had taken chloramphenicol prior to admission, while others had pulmonary tuberculosis, and hepatitis, all of which have been incriminated in the causation of aplastic anaemia. No causal relationship was however established. Treatment was very randomised with some patients receiving steroids and others no steroids at all. However, most were transfused. Hospital stay was also very short and default rate with poor patient follow up very high.

RECOMMENDATIONS

(1) All patients who present with anaemia and/or haemorrhages should be screened for aplastic anaemia.

(2) Proper and adequate histories by admitting physicians is paramount to establish whether any causal relationship does occur.

(3) More work to find out why more Kikuyu and not the other tribes are affected by aplastic anaemia should be done. The role of farm chemicals and agents in its causation should be established.

(4) The treatment given should be standardised, with androgenic steroids being combined with corticosteroids.

(5) Fresh blood transfusion should be used since it is more effective in reducing haemorrhages.

(6) Marrow transfusion facilities should be introduced at KNH.

(7) All known agents responsible for aplastic anaemia should be used with caution.

(8) Follow up of patients is very vital.

SUMMARY

A total of 54 patients were diagnosed and treated for aplastic anaemia between July, 1973 to December, 1978 at the Kenyatta National Hospital. The sex distribution was equal. Most of the age groups were affected with the majority of cases occurring in the young age groups.

Most tribes in Kenya were found not to be free from aplastic anaemia and there was a predominance of the disease amongst the Kikuyu tribe, who lived in and around Nairobi.

Very few factors associated with aetiology could be elicited, and this was partially due to inadequate histories taken at the time of admission by the various physicians. Even though, great difficulties are encountered in establishing an aetiologic role for a given agent, so that in large proportion of patients disease remains unexplained.

The presenting clinical features were those of anaemia, haemorrhages due to thrombocytopenia and infections resulting from leucopenia, all of which were observed in all the patients reviewed except for the 4 patients with pure red cell aplasia. The other 50 patients had hypoplastic marrows. Confirmation of diagnosis was delayed due to initial blood transfusions given before peripheral blood film examination in most patients.

Massive blood transfusions were given to patients on admission. Although platelet concentrates are available and obviate the massive blood transfusions, only very few patients received platelet infusions.

Corticosteroid and androgenic steroids were administered but there was no laid down policy as to the protocol to be followed. Hence administration of these drugs was done in a haphazard manner with a big proportion of patients going without any steroid therapy. This may have accounted to a great extend, for the very poor remission rate noted.

Since it has been observed that pure red cell aplasia remits spontaneously, prolonged therapy of these patients should be pursued vigorously.

Most of the deaths encountered occurred during the first 4 months of admission and they were mainly due to complications of the disease process mainly infections, congestive cardiac failure and excessive haemorrhages.

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P R O F O R M A

Vital statistics
- Age
- Sex
- Tribe
- Race

Clinical features
- Haemorrhage
- Pallor
- Dizziness
- Organomegaly
- Infections
  - Types
    - Viral
    - Bacterial
    - Parasitic
- Associated illness
  - Type
    - Leukemia
    - Hodgkins disease etc.
    - Paroxysmal
    - Nocturnal haemoglobinuria
- Presence of tumour
  - Thymoma
  - Hodgkins disease
- Drugs
  - Ingested before
- Chemicals
- Herbs

Laboratory Findings
- Haemogram (Hb)
  - Platelets, Reticulocytes
  - WBC
    - Total
    - Neutrophils
    - Eosinophils
    - Monocytes

- Bone Marrow
- LFT

URINE - Microscopy
- Culture and sensitivity

Radiologic Investigations

Xray - Chest
- Bones

ULTIMATE FATE

- Death - Cause
- Duration from time of diagnosis

Response to treatment

- Type of treatment
- Duration - From time of diagnosis

Treatment

- Drugs
- Transfusions
- Others

Family/Social History