Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(7B):2436-2446 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i07.028

Original Research Article

A Clinical and Therapeutic Appraisal in Hemophilia-A

Dhermendra Pratap Singh[1], V P Singh[2]
[1]Assistant Professor, Department of Medicine, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India
[2]Professor ,Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi ,Uttar Pradesh, India

***Corresponding author**
Dhermendra Pratap Singh
Email: dpsingh87@yahoo.com

Abstract: The hemorrhagic diseases present a complex problem in medicine, for they are often difficult to diagnose and troublesome to manage. Understanding of structure of various coagulation factors and its genetic control, biological and immunological properties has revolutionized the management of coagulation disorders. Hemophilia A occupies a unique position among the hemorrhagic diseases. The present study centers on the critical evaluation of Hemophilia A patients. Attempt was also made to follow the cases carefully in order to study the natural history of disorder and to assess the response on treatment. The major clinical presentation of our patients was due to bleeding into Joints. Knee joint was the most common site of involvement, a major source of distress, incapacitation, and was showing gross deformity in 25% of cases. Recurrent gum bleeding, was a universal complaint and responsible for a sizeable number of hospital visits by hemophiliacs, surpassed only by joint problems in total burden on hemophilic patients. All the hemophiliacs had prolonged KCCT. WBCT was normal in 35% of cases. Thromboplastin generation test confirmed the type of Hemophilia. Factor VIII is expansive and financial constrain was the main limiting factor in treatment of Hemophiliacs. Inj. Factor VIII was given for episodes of bleeding into joints, bleeding into muscle, traumatic bleeding and intracranial bleeding. Acute hemarthroses was treated with factor transfusion and immobilization. For chronic hemophilic arthropathy emphasis was focused on physiotherapy specially in form of active exercises. Difficulty was experienced in continuing the programme because of super imposed episodes of acute bleeding into joint.
Keywords: hemorrhagic diseases, Hemophilia A, Thromboplastin generation test

INTRODUCTION

The hemorrhagic diseases present a complex and trying problems in medicine, for they are often difficult to diagnose, troublesome to manage, and sometimes frustrating to treat. Recent development in the understanding of structure of various coagulation factors and its genetic control, its biological and immunological properties has revolutionized the management and outlook of coagulation disorders. Hemophilia A occupies a unique position among the hemorrhagic diseases. Isolation and purification of factor VIII preparations, all most totally free of infective rises has ushered a new era in the management of hemophilia A patients. Preparation of these factors by molecular cloning has resulted in the availabilities of these materials totally free from other proteins. If there were no financial constrains Indian hemophiliacs could also enjoy the normal quality of life as is being done by similar patients in affluent countries.

Particularly in this country problems of Hemophilia and its allied disorders have been very infrequently studied. The literature on the incidence of different hereditary coagulation disorder, on the laboratory investigations and treatment in this country is remarkable scarce. The present study centers on the critical evaluation of Hemophilia A patients. Attempt was also made to follow the cases carefully in order to study the natural history of disorder and to assess the response on treatment.

MATERIAL AND METHODS

A Total of Thirty four patients were studied during the period of March 1995 to March 1997, who attended the different OPDs and wards of University Hospital, B.H.U.

The detailed clinical history end physical examination was recorded as outlined in proforma (Appendix-) Patients were questioned for enumeration

of major sites of bleeding in past, number of bleeds during last month, and treatments under taken and family history of the some kind of illness.

Appendix

Performa for evaluation of hemophilic patients

- Name, Age, Sex, Address
- History of present illness, Past history, Family history, Tt history
- General examination
- Systemic examination
- Joint examination- Swelling. Tenderness. Loss of range of movement. Deformity Hematological investigations
- Radiological investigations
- Tt.
- Follow **Up.**

Patients having involvement of joints were also examined radiologically with x-ray of respective Joint.

HEMATOLOGICAL INVESTIGATIONS

Blood samples were collected as follows:

(1) Nine ml. of blood was collected in a special polythene tubes (4" X 1/2") containing 1 ml of 3.8 percent sodium citrate solution and was kepi in melting ice after mixing the citrate solution with the blood. The above sample was centrifuged at high speed (3000 r.p.m.) for 15 minutes and the platelet poor plasma was transferred to another plastic lube, which was kept in ice bath during coagulation study.

(2) One ml. of blood was collected in each of the two plain glass tubes (Corning, 75 mm x 10mm). The two tubes were used initially for whole blood clotting lime and later on for assessing clot retraction. The serum separated was used for thromboplastin generation tests.

Two ml. of blood was collected in E D.T.A. This was used for platelet count and other routine hematological examination.

Blood films were prepared from fresh blood and stained by Leishman's stain. Coagulation studies were done mostly as described by Loeliger [1].

MANAGEMENT

Patients with major bleeding were treated by factor VIII infusion patients with minor bleeding were administered either Desmopressin nasal spray or factor VIII infusion. Other required treatment measures like blood transfusion, dressings etc were under taken. Patients were instructed regarding passive and active physiotherapy. A permanent record of these assessments were kept and revised with each time patients presented with some complaint.

OBSERVATIONS

A total of Thirty four cases were studied during the period of March-1995 to March 1997, who attended the different OPDs and wards of S.S. Hospital, B.H.U.

Age at which cases of hemophilia A presented for investigations is shown in Table 1.

Description of family history in cases of Hemophilia A is shown in Table No 2.

Death of sibling due to similar illness, i.e. due to excessive bleeding, signifying mortality due to disease in family, is shown In Table No. 3.

Common sites of bleeding (extra articular) in past as evaluated by history is shown in Table No. 4.

All patients gave history of recurrent superficial bruising on minor injuries and small hematoma formation. Also recurrent bleeding from gums, recurrent was complained by from all Next common sites were bleeding from nose and bleeding into muscle. None of them gave history suggestive of bleeding into central nervous system. Sites of bleeding (extra articular) as observed during follow up period is shown in Table No. 5.

Table 1: Age at which patients came for investigation

Age group (yrs)	No of cases %	of total cases
0-10	07	20.58
11-20	15	44.11
21-30	06	23.52
31-40	02	05.88
41-50	02	05.88
Total	**34**	**100.00**

Table 2: Family history in Hemophilia-A

Family history	No of cases	% of total cases
No family history	13	38.23
In present generation only	18	52.94
In more than one generation	03	08.92
Total No. of Cases	**34**	**100. 00**

Table 3: Mortality due to disease

Death of sibling due to similar illness	No of cases	% of total cases
1. History present	12	35.29
2 History abscent	22	64.70
Total No. of cases	**34**	**100.00**

Table 4: Sites of Bleeding (Extra articular)In Hemophilia A

Site of bleeding	No of Cases	% of Total Cases
1. Superficial bruising	34	100.00
2. Minor superficial hematoma	34	100.00
3. Muscles	25	73 52
4. Gastrointestinal tract	09	26 47
5. Urinary tract	07	20 58
6 Central nervous system	00	00 .00
7. Nasal	25	73 52
8. Oral	34	100 00

Table 5: Sites of Bleeding (Extra articular) during follow up period

Site of Bleeding	No of Cases	% of Total Cases
Superficial bruising	21	61.76
Minor superficial hematoma	20	58.82
Muscles	12	35.29
Gastrointestinal tract	01	02 94
Urinary tract	02	05 88
Central nervous system	01	02.94
Nasal	07	20.58
Oral	30	88 23

Most common site of bleeding during follow up period was from gums. Case No. 14 presented to us with a hematoma on left thigh (Fig.1). *X*- ray was taken which did not reveal any involvement of periosteum. He was diagnosed as a case of Hemophilia A. As patient was unable to afford Inj. AHF, he was treated conservatively in form of bed rest, Desmopressin nasal spray and local ice application. There has occurred no recurrence of bleeding into same site.

Case No. 20. A 48 yr male presented to us with a hematoma in lower part of abdominal wall Patient was given four Blood transfusions and a total of Inj. Factor VIII1100 IU over seven days. He was put on bed rest and stool softeners. He improved with this management.

Case No. 8 presented with complains of headache, vomiting and drowsiness on examination neck rigidity and kernig's sign were present. On CT scan he was diagnosed as a case of sub arachnoid haemrrhage. He was put to complete bed rest and was given Inj. Factor VIII1500 IU over seven days along with other supportive measures.

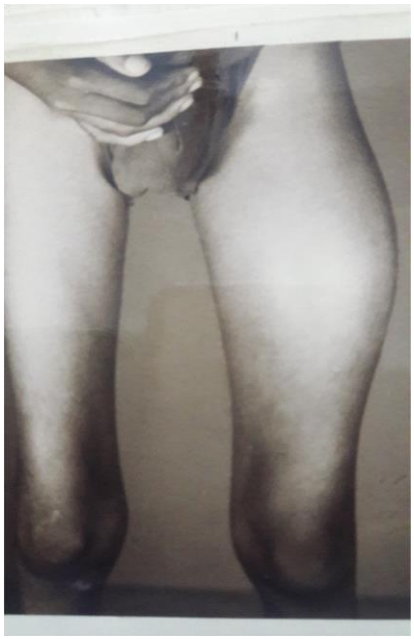

Fig-1: Patient with Hematoma left thigh

Total No. of Bleeding episodes observed at various sites were 440, out of them total bleeds at extra articular sites were 244. Site wise distribution of bleeding episodes is shown in Table No 6.

Table 6: Bleeding episodes during follow up period

Site of Blooding	No of Cases	No of Bleeding episodes Bleeds	% of Total (440)
Superficial bruising	21	54	12.29
Minor superficial hematoma	20	31	07.04
3. Muscles	12	21	04.77
Gastrointestinal tract	01	01	00.22
Urinary tract	02	02	00.45
6. Central nervous system	01	01	00.22
7. Nasal	07	16	03.63
8. Oral	30	98	22.27

Maximum no of bleeding episodes observed was from gums. Case No 18 was having 10 episodes with in a period of Ten months. He was advised for extraction of one tooth also.

Gastro intestinal tract and central Nervous system was the least common sites of Bleeding .Only one episode of each was observed in two different patients.

Case No 4 a 6 yr old male presented to us with a swelling over temple region. He was having history of recurrent swelling of Left knee joint. He was diagnosed as a case of hemophilia A and was given Inj. Factor VIII300 IU

Case No 33 Presented to us with excessive bleeding from a Traumatic wound over hip. There was no history of excessive bleeding from any site in past. He was diagnosed as a case of hemophilia A and was given two blood transfusions and Inj.

Factor VI 1100 IU spreaded over duration of four days. Case No 6 a 14 Yr old male presented to us with Bleeding from a traumatic wound over the face. Patient was given Inj. Factor VIII1000 IU spreaded over 7 days and local dressing was done.

Sites of bleeding into joints in past as evaluated by history is depicted in Table No 7.

Table 7: Sites of Bleeding into Joints in Hemophilia A

Joints	No. of cases	% Of Total Cases
1. Hip Joint	03	08.62
2. Knee Joint	26	78.47
3. Ankle Joint	23	67.64
4. Shoulder Joint	04	11.76
5. Elbow Joint	19	55 .88
6. Wrist Joint	07	20. 56
7. Other Joints	03	08.82

Commonest site of bleeding site was knee Joint. It was closely followed by two other hinge articulations Ankle Joint and Elbow Joint.

Other Joints included MP Joints, IP Joints and sternoclavicular Joints. Case No. 15. had recurrent bleeding episodes in past in I MP Joint. Case No. 18 gave history of Bleeding into right sternoclavicular joint and right I MP Joint.

Sites of Bleeding into Joints as observed during follow up period is depicted in Table No. 8.

Table 8: Bleeding into Joints during follow up period in Hemophilia A

Joints	No. of Cases	% of Total Cases
Hip Joint	03	08.82
Knee Joint	19	55 88
Ankle Joint	03	08 82
Shoulder Joint	01	02.90
Elbow Joint	02	05.80
8. Wrist Joint	03	08.82
7. Other Joints	02	05.80

Knee joint was the most common site of Bleeds in Maximum no of patients and it was far more commonly involved than any other Joint. At the second number Joints involved frequently were Hip. Ankle and elbow Joints, each one of them was involved in 3

patients. Least common site was shoulder, only one patient had bleeding into shoulder Joint.

Number of Bleeding episodes into Joints as observed during the follow up period is shown In Table No. 9.

Table 9: Bleeding Episodes in hemophilia A during follow up period

Joints	No. of Cases	No of Bleeds	% of Bleeding
1. Hip Joint	03	04	00.90
2. Knee Joint	19	142	32.27
3. Ankle Joint	03	12	02.72
4. Shoulder Joint	01	04	DO. 90
5. Elbow Joint	02	09	02.04
6. Wrist Joint	03	11	02.50
7. Other Joints	02	04	00.90

Total no of Bleeding episodes m Joints were 196 (44.54% of total bleeds). Maximum no. observed were in knee Joints (32.27 of Total no of Bleeding episodes into Joints). It was followed by Ankle Joint (02.72 of total no of bleeding episodes) and Elbow Joint (02.04 % of Total no of Bleeding episodes). Minimum no were seen in hip and shoulder Joints, only four episodes in each Joint.

Clinical examination of the major Joints at the time of presentation is summarized as follows.

Commonest finding was loss of range of movement signifying the bleeds which has occurred in past.

Only one patient, case No 11 presented to us with swelling and tenderness of hip Joint (Right). Pain was present. Roentgenogram was done which revealed presence of osteoporosis, soft tissue swelling and decrease Joint space, which was correlated to bleeds occurred previously into same joint. Patient was put to bed rest and was given Inj. factor VIII 500 IU.

Examination of Knee Joints in Hemophilia A - Scoring was varying from 00 to 10. Highest seen was in a 14 yr male (Fig. 3) having bilateral involvement of knee Joints, score was 10 and 09 on right and left side respectively.

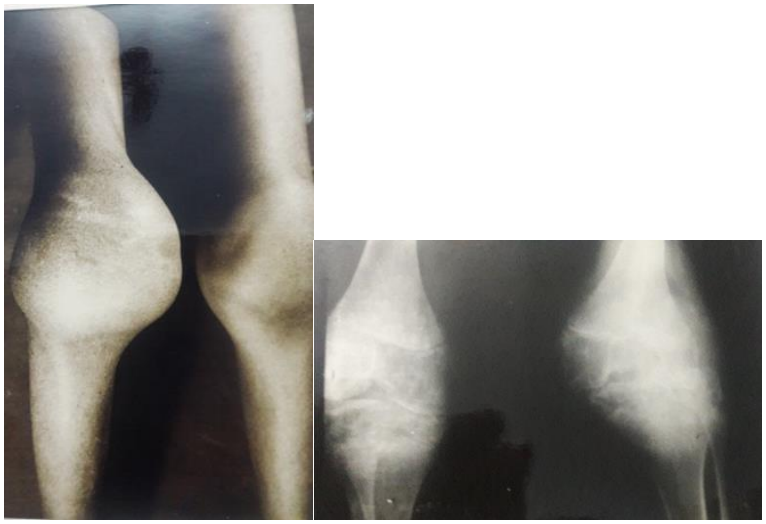

Fig-2: Patient, 14 year male, with severe knee hemophilic arthropathy with X-Ray

Examination of Ankle Joints- Many patients had a single finding that is loss range of movement in comparison to swelling and tenderness, which was present only in a single patient.

Examination of shoulder Joint- Shoulder Joints was involved uncommonly but who so ever had loss of range of movement was also having Deformity.

Examination of elbow joint- Elbow joint was a common site of loss of range of movement and Deformity.

Roentgenograms of two elbow joints, belonging to two different patients were also taken. Radiological findings are depicted in Table No. 10.

Table 10: Radiological findings in Elbow Joints in Hemophilia A

Finding	**Case No. 4**	Case No. 10
1. Osteoporosis	+	+
2. Enlarged epiphysis	-	-
3. Irregular subchondral surface	+	++
4. Narrowing of joint space	-	++
5. Subchondral cyst formation	-	++
6. Erosion at joint margins	-	+
7. Incongruence of joint surface	-	++
8. Joint deformity	-	++
9. Soft tissue swelling	+	-
10. Subluxation of radius	-	+
11. Overgrowth of radius	-	+

Elbow Joint of case No. 10 was having all the features of chronic hemophilic arthropathy (Fig 3.). Case no. 4 was presented as acute hemarthrosis. Case no. 4 was given Inj. factor VIII.

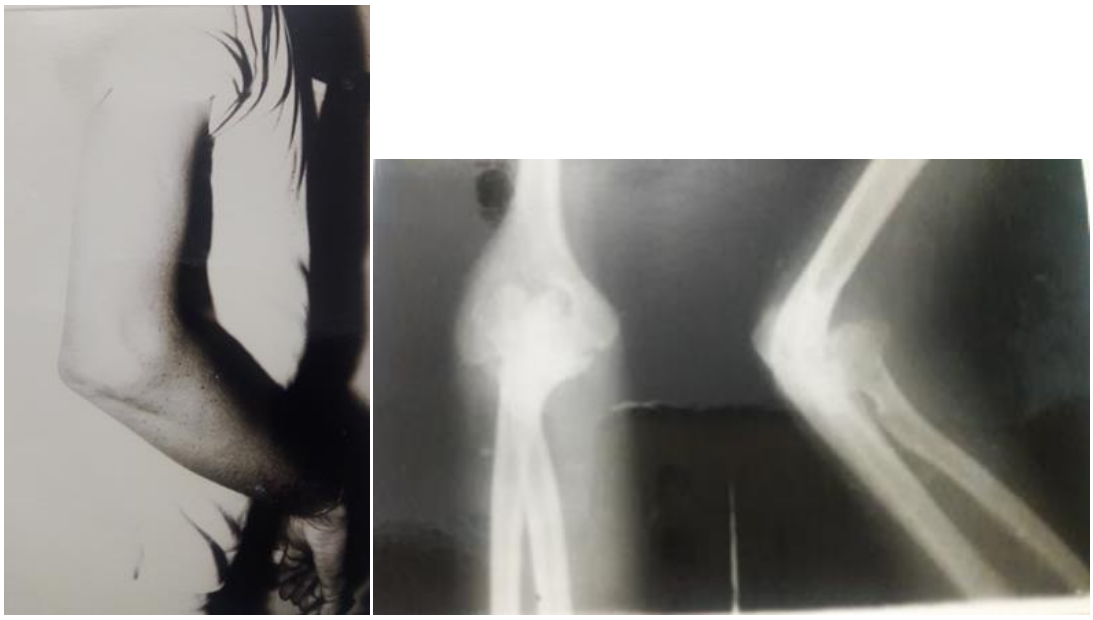

Fig-3: Patient with involvement of elbow joint with X –ray

Examination of Wrist Joint-As is other joints, commonest finding observed was the loss of range Movement Muscle atrophy was distinctly uncommon.

Examination of other Joints- One patient, case no 15 had recurrent swelling of IMP Joint. Also in case no 18 recurrent swelling was a complaint in pest history

The investigations performed on these cases is given in Table No 20.

Table 11: Coagulation studies in Hemophilia A

	Normal	**Abnormal**
1. Bleeding time	All	None
2. WBCT	12	22
3. KCCT	None	All
4. Clot retraction	All	None
5. Prothrombin time	All	None
6. Platelet Count	All	None
7. T.G.T.	None	All

The data in Table No 20 suggest that WBCT is not a sensitive test as it was normal in 35% of cases (12 Patients) However strong possibility can be kept if KCCT is abnormal; this test was abnormal in all the cases. The Diagnosis of these patients was confirmed by T G T Whose abnormality was corrected by

aluminium hydroxide adsorbed normal plasma 'Bleeding time was done only in five cases and it was normal in all of them.

DISCUSSION

We studied thirty four patients of Hemophilia A. Though exact incidence of Hemophilia is not known in this country but the discovery of large no. of these patients at our center during last 30 years indicate that these are not infrequent disorders. Incidence of Hemophilia in England has been estimated to be about 1 per 30.000 [2], In U.S.A. 1 per 27,000 [3]. So estimates from Developed world indicate that there will be one new case of Hemophilia in 1: 10,000 live male births.

Prevalence of Hemophilia in Developed world is around 6 per 10,000 populations; India should therefore have about 50,000 patients with Hemophilia A: However, over a three year period (1985-1986) three major referral central in our country (Delhi, Bombay, Vellore registered only 315 new patients with hemophilia A therefore, in India, many patients with disease are not even identified [4].

In Hemophilia A. family history was present m 21 cases (68%). 18 had the bleeders in present generation only The mutational earner state of the mother, or neonatal deaths or the passage of the trait through a succession of female carriers may explain negative family histroy, Basu and Roychowdhry also found family history locking in 30% of 86 patients analyzed by them [5]. Teatia also found negative family history in 42% of 113 patients analyzed by him **[6].** So negative family history is of little value in excluding the possibility of Hemophilia A.

We also analyzed the history of Death of sibling due to similar illness reflecting severity of diseases in family, lack of awareness and inadequacy of existing health services for management of Hemophilia. History was present in 12 cases of hemophilia A (35%).

Excessive superficial bruising, minor superficial hematoma formation and gum bleeding were common complaints of our patients.

Superficial bruising also occurred commonly during follow up period (81% of cases), and comprised of a quite high proportion of total no. of bleeds (12%). Although most of the patients did not required any specific treatment and bruises subsided on its own. Excessive bruising has also been noticed commonly by other workers at Varanasi [6-8], and at other centres in India [4]. Stuart *et al* in study of 21 patients also noticed superficial bruising very frequently but it did not result in any loss of schooling or working days [9]. So excessive superficial bruising can be considered as an important clue to diagnosis and further evaluation of patients even though may not be a source of much incapacitation.

Small superficial hematomas were also seen very frequently in our patients (06% of cases) and consisted of a quite no. of bleeding episodes (7% of episodes). It was major clinical manifestation (49% of 113 cases) in analysis of Teotia and was occurring due to mild trauma [6]. Aronstarm *et al*. did not notice a significant relationship of trauma to occurrence of minor superficial hematoma. [10]. Stuart *et al* also felt that superficial hematoma formation is related more to severity of disease then trauma [9]. So putting severe restrains on activities of a child may not be of a great help in reducing frequencies of superficial hematoma formation.

Bleeding from nose was a very common complaint in past history (73%). But it was seen only in 21% of patients during follow up period. It was commonly related to habit of nose picking but none of our patient required Antihemophilic factors for control of epistaxis. Only one patient of Chawla had complaint of epistaxis but Dube and Teotia noticed it more frequently [6-8]. Stuart *et al* noticed nasal bleeding in 25% of his patients and in one patient it was due to obvious trauma and required blood transfusion. [6] So bleeding from nose may commonly see in Hemophilia patients but it does not constitute a Major burden and can be controlled easily by local measures in form of pinching the nose for 15 minutes and applying zinc sol and main preventive measure is to teach the child regarding avoidance of nose picking.

Bleeding from gums, recurrent, lasting hours to days was a problem of almost every patient of our study, at some or other time. It was observed in 86% of patients during follow up period. It constituted a major portion of total bleeding episodes (22 %). It was particularly related to use of self-made tooth brush so called DATUN and poor oral hygiene .Two of our patients went through root canal fillings. Two were advised tooth extraction also.

In previous studies at varanasi Teotia reported it in 25% of his analysis of 113 patients [6]. Stuart *et al* found it only in 2 of his 21 patient over a follow up of five years [9]; Aronstorm *et al* in his study of 82 patients did not mention about gum bleeding although in his study group of other bleeding sites comprised of 11% bleeding episodes [10].

Situation is really grave in this aspect in our patients. All most all patients were in need of specialized dental care. Because of improper way of brushing, brushing leading to bleeding, followed by stoppage of brushing due to fear by patient leading to

more destruction of teeth, and this resulting in to more bleeding was a vicious circle seen in our patients.

History of bleeding from gastrointestinal tract was elicited only in 26% of patients. During follow up period only one of our patient developed malena. None of the patient of Chawla and Teotia had bleeding from gastrointestinal tract [7, 6]. Dube noticed bleeding per rectum in one patient out of 8 Hemophilia A patients studied by them [8]. In series of stuart *et al.* Bleeding from gastrointestinal tract comprised of 14 Bleeding episodes and it was more common in older group of patients; and it ranked second in frequency to urinary tract, among extra articular bleeds [9]. Aronstarm *et al*. included such bleeds into group of other bleeds and reported in 11% of patients [10]. So it can be said that bleeding from gastrointestinal tract is not a major problem in Hemophilia and it is even less common in our patients then the western counterparts.

Hematuria was noticed by 20% of Hemophilia A patients in their life at some or other time. During follow up period two patients (5%) reported hematuria and it comprised of only 0.45% of total bleeds in patients. There was no history suggestive of any pathology in urinary tract and examination was also unremarkable in both patients. Chandy also found bleeding from urinary tract an uncommon complaint in Hemophilia cases and none of their patient found to be suffering from a disease of urinary system to account for hematuria [6]. Stuart *et al.* in his prospective study of 21 patients over a period of five year noticed hematuria a total of 20 times in his patients. It accounted for most common cause of loss of schooling or work apart from hemarthroses and it occurred in 32% of his patients. It was never traumatic nor secondary to demonstrable urinary tract disease [9]. So it can be concluded that bleeding from urinary tract is a less common but significant problem in our patients.

Bleeding into central nervous system, past history was given by none, but was seen during follow up period. One patient of Hemophilia A developed subarachnoid haemorhage fortunately patient survived the crisis with the help of AHF and other supportive measures.

Other workers at varanasi did not reported any case of central nervous system bleed in Hemophilia patients. Chaudhary has mentioned central nervous system bleeds as the most common cause of death in Hemophilics [5]. Chandy *et al* noticed it in thirty of total 315 patients of Hemophilia analysed by him retrospectively (9.5%) [3]. Mehta also observed that with proper management untoward outcome can be averted in Hemophilia in cases of central nervous system bleeds [11]. Silverstein studied the instances of Hemophilia and intracranial haemorrhage presented in the literature since 1840. He reached the conclusion that 31 such patients had been described up to 1960 [12]. He attached great importance to preventive measures for hemophilic patients to avoid intracranial bleed and its consequences. Even in the presence of only a trivial head injury it is important to ensure an optimal factor concentration during 5-7 days.

Bleeding into muscles affected 73% of patients in past. During follow up period it occurred in 12 patients (35%) and constituted 4% of total bleeds . Aronstarm *et al* noticed bleeding into muscles in 75% of their patients [10]. Teotia found bleeding affecting muscles in 60% of 113 patients analysed by them [6], Stuart et al in 1966 counted the No. of bleeds occurring in 21 patients of Hemophilia over a 5 year period and reported it as making 5% of total bleeds, which is almost similar to our observation and some others [9, 18]. Four of our patients required factor transfusion for the control of bleeding into muscles. In two of them history of obvious trauma was also there. In study of stuart *et al.* only one instance of bleeding into muscles occurred following obvious trauma So bleeding into muscles in hemophilia is a common and important manifestation and in most case history of obvious trauma may not be available.

In our study 27 patients (86% of total cases) had history of bleeding into joints .During follow up period itself. 21 patients (61% of total cases) suffered acute hemarthroses. Chawla reported hemarthroses in 8 of his cases (52%) **[7].** Dube also noticed hemarthroses in 50% of hemophilia cases [8]. Teotia *et al* in his analysis of 113 cases found hemarthroses in 53 patients (47%) [6]. Chandy in his report on ICMR collaborative study on hemophilia, found that joint bleeding was the major problem in hemophiliacs, occurring in 60% of cases [3]. R Madhok reported hemarthrosis in 80% of cases in concordance with some others [13, 19, 20].

Hemerthroses of hip joint was seen in 8% of cases in our study, but gross deformity was seen in only two of hip joints, and roentgenogram revealed presence of osteoporosis, soft tissue swelling and decrease in joint space. In Ahlberg series hip arthropathy occurred m 11% of his cases and osteoporosis was universal finding [14]. Aronstam *et al* found hip arthropathy to be a rare feature [10].

Bleeding into knee joints was the most common site of articular bleeding in our patients during follow up period (55 %). There was presence of gross deformity in 27% of total knee joints examined in Hemophilia A. Teolia observed involvement of knee joint in 35% of Hemophilia [6]. Chandy *et al* reported knee hemarthrosis in 47% of cases of Hemophilia [3]. Ahlberg and Stuart *et al* also noticed knee joint as the most common site of involvement in Hemophilia [14, 9]. But Aronstam**,** *et al* in their study of 82 patients found elbow joint as the most common site of

arthropathy in hemophilia in contrast to others [10, 16, 17].

All the deformed knee joints were also examined radiologically. Osteoporosis was seen in 70% of cases. Ahlberg also found Osteoporosis in 80% of knee joints showing clinical deformity. Widening of inter condylor notch was seen in 65% of deformed joints. Although Ahlberg noticed it less frequently [14]. Squaring of femoral condyles was observed in 55% of joints examined radiologically. This finding was not noticed by Ahlberg but R Madhok reported it in some of their cases. Squaring of patella was seen in 50% of cases. Enlarged epiphysis was distinctly uncommon in our study, probably because younger patient constituted a small percentage of our study.

During follow up period acute hemarthroses involving ankle joint occurred only in 3 of our patients (8%), constituting 2% of total bleeds. One of our patients had bony ankylosis of Ankle.In Ahlberg's material, 25% of Ankles showed evidence of arthropathy [14]. R Madhok**,** reported Ankle joint involvement in 13% of cases, similar to some other authors [13, 22]. Teotia found Ankle arthropathy in 5% of cases only [6]. So Ankle arthropathy is the third most common site of involvement following knee joint. But it definitely becomes less common with increase in age. There is some evidence from previous studies also that disease starts declining in severity, at least subjectively, after the age of 20.

As for as the joints of upper limb an concerned, shoulder joint was an uncommon site of involvement Only one patient (2%) suffered bleeding into shoulder joint and on examination only 7% (of total shoulder joint examined) were having evidence of some deformity. Ahlberg found involvement of shoulder in less than 10% of joints evaluated by him [14]. Stuart *et al* found bleeding into shoulder joint in less than 7% of cases followed by them [9]. But Aronsiarm *et al*. reported bleeding into shoulder joint in 57 of 82 cases evaluated by them (69%) [10]. They felt that their finding is differing considerably from all other studies conducted on Hemophilias, and it was probably because all of the their patients were adolescent and engaged in active work. Teotia and Chandy *et al* grouped the shoulder joint in 'other joints' group and considered it an uncommon site of bleeding [6, 3].

Elbow joint bleeding occurred in 2 cases (5%) in our series. It constituted 2% of total bleeds. 10 % of examined elbow joints had obvious deformity. In Ahlberg's series Elbow joint was the second most common site of bleeding among joint bleeds [14]. Stuart *et al* also noted that 24% of total bleeds, in their 21 patients, occurred in Elbow joints, Aronsiarm *et al.*, reported Elbow joint as the most common site of involvement in 82 adolescents studied by them [9,14]. Radiologically main findings were osteoporosis, irregular subchondral surface, overgrowth and subluxation of radius and subchondral cyst formation .So in the present series, Elbow joint was the second most common site of deformity .Its social impact was felt in Hemophiliacs and one of our patient lost his job because of recurrent bleeds into Elbow joints.

Bleeding into wrist joint occured in 8% of cases and it constituted 2% of total bleeds during follow up period. Ahlberg also noticed bleeding in wrist joint only in 6% of his 157 cases Stuart *et al* found wrist joint involvement only in 5% of cases. It was a more common site of involvement in study of adolosconls (50% of total cases) conducted by Aronstorm *et al* in 1979 [14, 9, 10]. In previous studies at varanasi no separate mention was made of wrist joint and Teotia included them under "other joints" group as chandy *et al.* [6, 3]. So wrist joint is an uncommon Site of bleeding and deformity in Hemophilics but in individual patient could be source of major incapacitation and distress.

Regarding the laboratory test for the diagnosis of Hemophilia, it is striking that WBCT was normal in 35% of cases . KCCT in contrast, was more sensitive and reliable test in all the cases and it was abnormal in all. There was also rough correlation of KCCT with the clinical seventy of the disease. Other workers have also found this test to be sensitive to factor VIII deficiency [6-8].

The management of Hemophilias is improving remarkably with time due to wider availability of factor VIII in this country. But these are expansive and financial constrain is main limiting factor in treatment of acute episodes of bleeding in Hemophilia, particularly in the eastern part of country. In our study the patients of Hemophilia required Inj. Factor VIII for management of episodes of bleeding into Joints, bleeding into muscle, traumatic bleeding and intracranial bleeding. Acute hemarthroses was treated with factor transfusion, immobilization of limb followed by gradual resumption of active exercises. For chronic hemophilic arthropathy emphasis was focused on physiotherapy especially in form of active exercises. Initially patients went through supervised, twice a week physiotherapy followed by instruction and education to continue exercise programme at home. Two of the patients were put on skin traction to improve flexion contracture. Difficulty was experienced in continuing the programme because of super imposed episodes of acute bleeding into joint.

Two of our patients experienced life threatening episodes of Intracranial bleeding, but could be managed successfully because of timely administration of factor transfusion and other supportive measures.

Desmopressin nasal spray was used by a total of five patients. Desmopressin nasal spray (STIMATE/MINIRIN) was administered by nasal Insufflations, one spray per nostril to provide a total dose of 300 µg. In patients weighing less than 50 kg, 150 µg was administered as a single spray' They were instructed to use two sprays just at the beginning of premonitory symptoms, tike tingling sensation or pain at some site. All of them reported arrest of hematoma formalin at the use of nasal spray. The repeat administration of nasal spray was done only after 48 hours to avoid tachyphylaxis. Except mild irritation m nose no other side effect was reported by our patients. Requirement of keeping drugs at 4°C was the main limiting factor m use of this nasal spray. Majority of our patients were from rural area and could not have access to refrigerator,

Synthetic 'Danazol is another agent reported to be useful for minor bleeding episodes [21]. It was used in 10 of our patients in dosage varying from 200mg to 800mg/day for 5-10 days and results were encouraging.

CONCLUSIONS

The major clinical presentation of our patients was due to bleeding into Joints. Knee joint was the most common site of involvement and was a major source of distress and incapacitation, and was showing gross deformity in 25% of cases. Recurrent gum bleeding, lasting for hours to days was a universal complaint from our patients, persistent distressing them and was responsible for a sizeable number of hospital visits by hemophiliacs, surpassed only by joint problems in total burden on hemophilic patients. Excessive superficial bruising and minor superficial hematoma also occurred commonly during follow up period but did not resulted into much disturbance to patients nor required factor replacement therapy. All the hemophilics had prolonged KCCT. WBCT was normal in 35% of cases Thromboplastin generation test confirmed the type of Hemophilia.

The management of Hemophilias has improved remarkably during present decade due to wider availability of factor VIII . But this is expansive and financial constrain is main limiting factor in treatment of acute episodes of bleeding in Hemophilia, particularly in this eastern part of country. In our study the patients of Hemophilia required Inj. Factor VIII for management of episodes of bleeding into joints, bleeding into muscle, traumatic bleeding and Intracranial bleeding. Acute hemarthroses was treated with factor transfusion, immobilization of limb followed by gradual resumption of active exercises For chronic hemophilic arthropathy emphasis was focused on physiotherapy specially in form of active exercises. Difficulty was experienced in continuing the programme because of super imposed episodes of acute bleeding into joint.

Desmopressin nasal spray was used by a total of five patients . All of them reported definite arrest of hematoma formation at the use of nasal spray. Synthetic 'Danazol' is another newer agent reported to be useful for minor bleeding episodes and results were encouraging.

REFRENCES

1. Loeliger EA; Bull World Health Organ, 1973; 48(6): 727–736.
2. Biggs R; Human Bllod Coagulation, Haemostasi and Thrombosis, OXford: Blackwell, 1976.
3. Quick AJ; Haemorrhegic diseases and thrombosis, lea 8 febiger. P. Philadelphia, 1966.
4. Chandy M; Collaborative study on Hemophilia. An ICMR task force project Report, 1990.
5. Choudhary VP; Advances in the management of hemophilia Curent problems in pediatric hematotogy-oncoiogy. Publication of WH O Chapter of IAP, 1988; 49-53.
6. Teotia YS; study of bleeding disorders with special reference to Hemophilia. Thesis submitted for M.D Pathology, Banaras Hindu University, 1984.
7. Subhash C; Some observation on bleeding disorders at Varanasi. Thesis submitted for M.D. pathology, Banaras Hindu University, 1969.
8. Dube SM; study of Bleeding Disorders. Thesis submitted for M D Pediatrics, Banaras Hindu University, 1972.
9. Stuart J, Davies SH, Cumming RA, Girdwood RH, Darg A; Haemorrhagic episodes in haemophilia: a 5-year prospective study. Br Med J., 1966; 2(5530):1624-6.
10. Aronstam A, Rainsford SG, Painter MJ; Patterns of bleeding in adolescents with severe haemophilia. Br Med J., 1979; 1(6161): 469–470.
11. Mehta BC; Recent advances in the management of bleeding disorders. Ped Clin Ind., 1989; 24 5-9.
12. Silverstein A; Management of neurologic complications of hemophilia. In The Hemophilias, ed KM Brinkhous. Chapel Hill: University of North Carolina Press, 1964.
13. Madhok R, York J, Sturrock RD; Hemophilic Arthritis. Ann Rheum Dis., 1991; 50(8): 588–591.
14. Ahlberg A; Hemophilia in Sweden: VII Incidence, treatment and prophylaxis of arthropathy and other musculoskeletal manifestations of haemophilia A and B. Acta Orhop Scand. (suppl.) 1965; 77: 5-132
15. Ishiguro N, Yasuo S, Takamatu S, Iwata H; Hemophilic arthropathy of the elbow. Journal of Pediatric Orthopaedics, 1995; 15(6):821-5.
16. Stein H, Duthie RB; The pathogenesis of chronic hemophilic arthropathy. J Bone Joint Surg., 1981; 63: 501.
17. Biggs R, MacForlane RG; Haemophilia and related conditions: 187 cases. Br JHaematol., 1958; 4:1.
18. Fernades PF; Hematomas within the iliopsoas muscles in hemophilic patients. clinc orthop., 1995;

19.
19. Ribbans WJ; Hemophilia ankle arthropathy. clin-orthop, 1995; 39.
20. Duthie RB, Rizza CR; Rheumatologlcal manifestations of the haemophilias. Clin Rheum Dis., 1975; 1:53-93
21. Gralnick H.R. and Rick, ME. Danazol in hemophilia. N Engl Med., 1983; 308-1393.
22. Fernadez PF; Radioactive synnoviorthesis in hemophilic hemoarhrosis. clin orthop, 1996; 14.