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WILSON'S DISEASE IN CHILDREN, REPORT OF 25 CASES.

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Abstract:

We conducted a retrospective study of 25 cases (15 boys and 12 girls) of Wilson's disease(Hepatolenticular degeneration)spanning a period of 8 years. Age at the time of diagnosis ranged between 3-17 years.
The following clinical forms were observed:
Hepatic-13, neurologic-4, mixed(hepatic & neurologic)-5, asymptomatic-3, Kayser-Fleischer corneal rings were observed in 12 patients.

Diagnosis was confirmed by low serum ceruloplasmin, low serum copper, Increased urinary copper and abnormal aminoaciduria. Of different treatment schedules(low copper diets, D. Penicillamine, metronidazole, K sulfide, T.E.T., 2Cl. and BAL) the diatary management plus D.Penicillamine was the most effective.Mortality was 8(32%)due to either fulminent hemorrhage or hepatic failure.

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Wilson's disease is an autosomal recessive disorder of copper metabolism and may be misdiagnosed or be unrecognized during childhood and adolescence because of atypical presentation. The classic triad of a Kayser-Fleischer rings, liver cirrhosis and neurologic dysfunction may bot be fully manifest and even the serum ceruloplasmin level may be normal.

Thus the main problem is the recognition of this disorder in the young and the selection of clinical or laboratory criteria that will clearly distinguish Wilson's disease from other hepatic disorders.

Methods:

We have reviewed the charts of 25 consecutive patients under 18 years diagnosed as having Wilson's disease between 1969-1977. See Fig. 1

Twenty two patients were symptomatic at the time of diagnosis, there were three asymptomatic siblings. All laboratory determination reported in this paper were performed at the time of diagnosis before Therapy was instituated.

Liver function test, CBC, serum ceruloplasmin level were performed at the laboratory of children hospital medical centre and at Hasarak Research Institute.

Slit lamp examination was performed on all patients by an experienced ophthalmologist.

Results:

Mode of presentation in symptomatic patients.

In 22 symptomatic patients, the primary mode of presentation was acute hemolytic anemia in 2, liver disease in 13, mixed form (hepatic & neurologic) in 5, CNS form in 2, Psychoneurotic form in 2, and Kayser-Fleischer rings

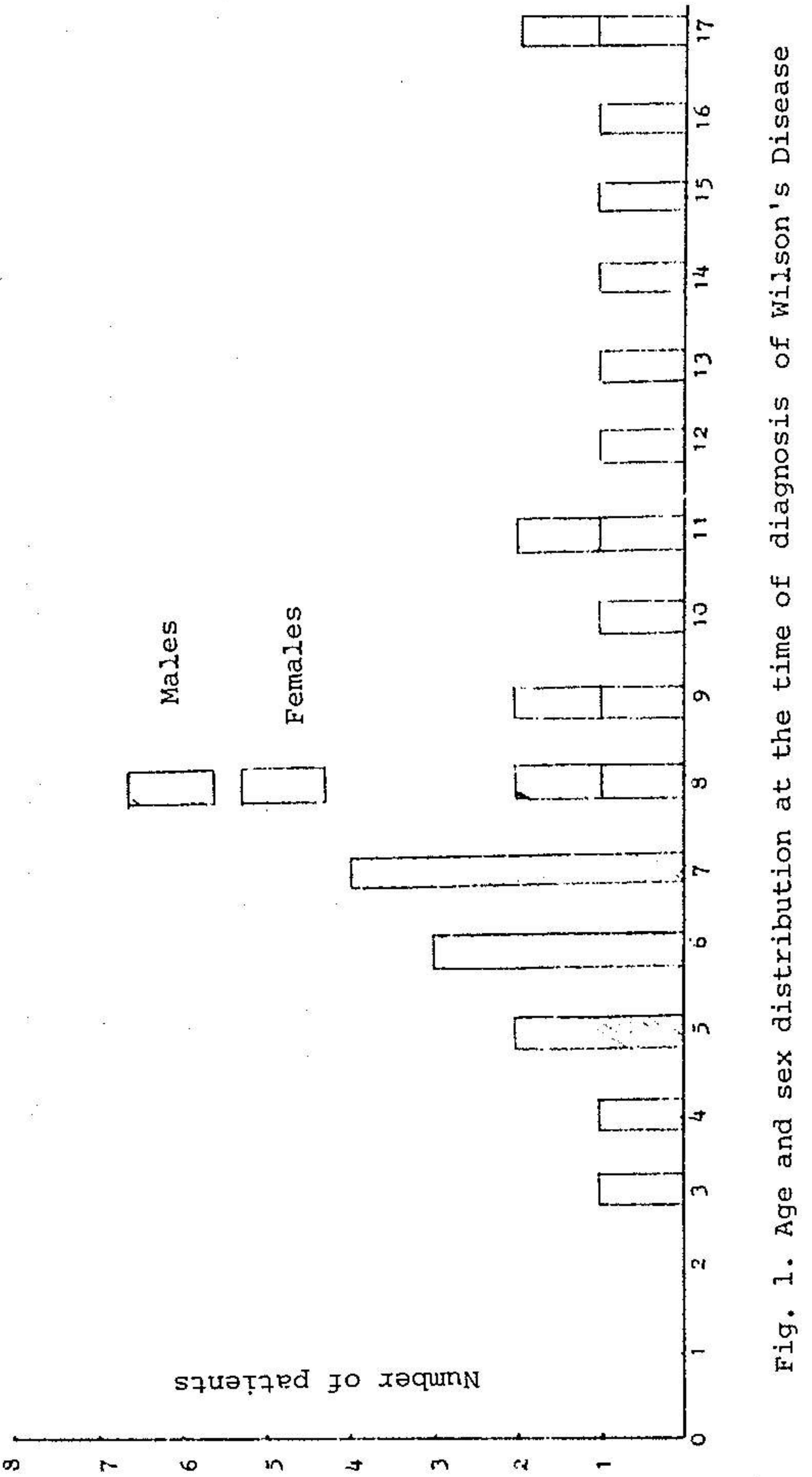

Fig. 1. Age and sex distribution at the time of diagnosis

Eight were dead because of liver failure or hemorrhage, and overwhelming in-fection.

Patients			Presentation	Duration of disorder	Duration of treatment	Cause of death
Case	Sex	Age				
1	Male	12	Rickets & CNS form	3 years	3 years	Infection
2	Female	10	Mixed form	30 months	2 years	Liver failure
3	Male	8	" "	3 months	Few days	Sudden death
4	Male	10	Hepatic form	1 month	2 weeks	Liver failure
5	Male	10	Hematuria+Hepatosplenomegaly	7 years	7 years	G.V.hemorrhage
6	Male	11	Hepatic form	2 months	1 month	Liver failure
7	Female	2	Mixed form	20 days	7 days	" "
8	Female	8	Hepatic form	6 months	2 months	" "

Tab. 3. Causes of death in 8 patients with hepatolenticular degeneration

were found in twelve cases.

See Fig. 2

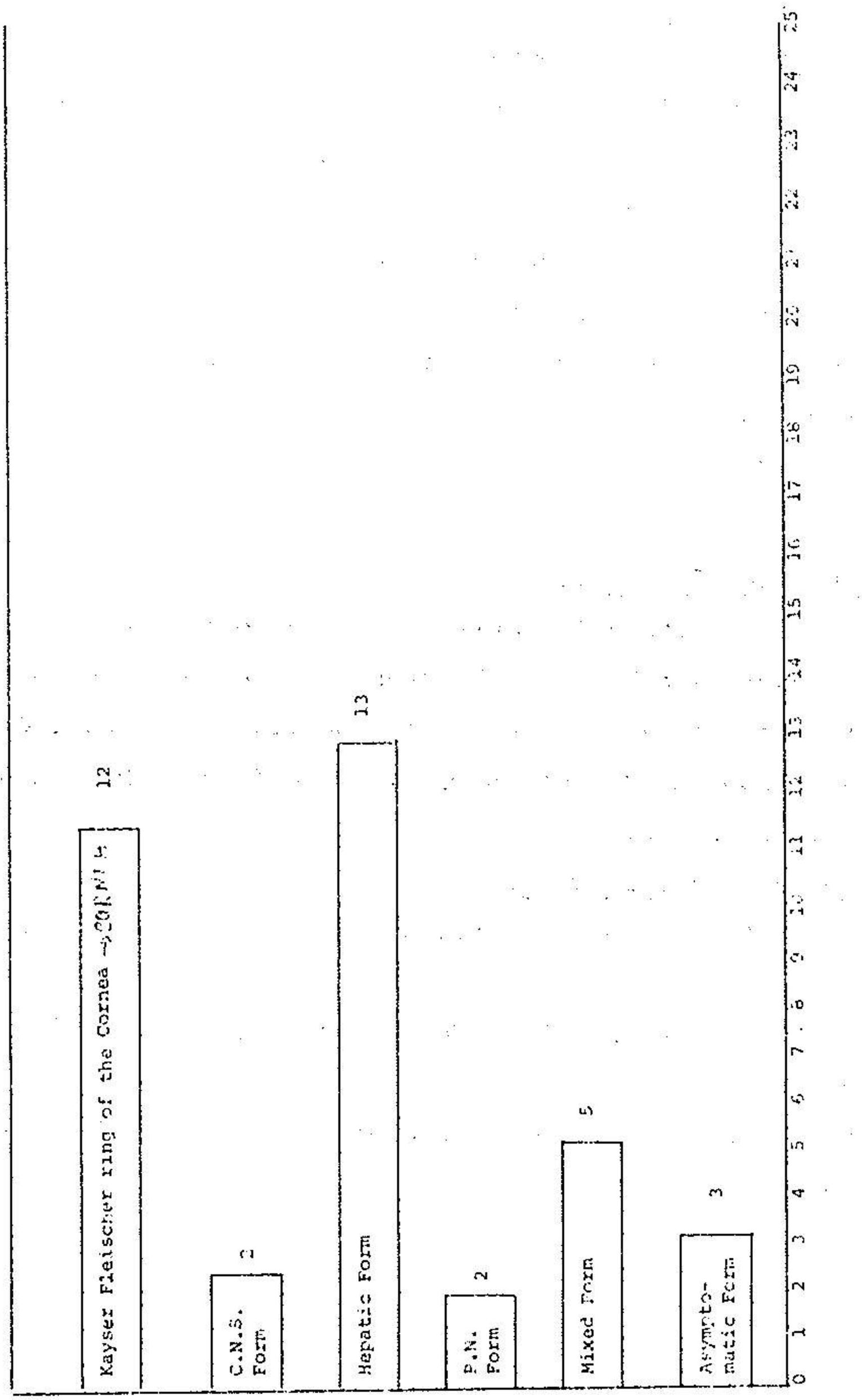

Fig. 2. Complaints and physical symptoms present at the time of diagnosis of Wilson's Disease

Abnormal Laboratory Tests Results:

Liver function tests were performed on all, with abnormal findings in 58% of cases.

Studies of copper metabolism:

Twelve of 25 cases (48%) had Kayser-Fleischer rings at the time of diagnosis and 100% had depressed serum ceruloplasmin levels.

Serum copper was low and urinary copper excretion was abnormal in all cases.

Hepatic copper concentration was elevated in two cases who had liver biopsy.

See Table 1

Studies of hemolysis:

In the symptomatic patients two had evidence of hemolysis as expressed by reticulocytosis, described previously reference No.(7) by Aghighi and Dahifar, the Ahari Children's Hospital Medical center, proceeding's, both had gallstones at autopsy.

Course and following:

All patients were treated with one of the following regimen:

D. Penicillamine, BAL, Metronidazole, plus low in copper diets.

The symptomatic and asymptomatic cases have done well.

See Table 2.

Tab. 2. Mortality and Morbidity of 25 Cases of Wilson's Disease according to therapeutic modalities

Medication	A D. Penicillamine	B BAL	C Metronidazole
No. of patients	18	6	1
Mortality	3	5	

Tab. 1. Laboratory results at the time of diagnosis of Wilson's Disease

	Cases	%
Abnormal liver function tests	13	52
Rheumatoid arthritis factor	1	4
Thrombocytopenia	1	4
Special tests for Wilson's Disease:		
a) Ceruloplasmin enzyme activity reduction	25	100
b) Total serum copper "	25	100
c) Urinary copper excretion > 50 µg/24 Hr urine	25	100
d) Abnormal excretion of more than 7 amino-acids	23	92
e) " " " 5 to 7 amino-acids	2	8
Liver & Kidney biopsy	2	8
Autopsy findings	2	8
Gall-stones	2	8

Discussion:

In this report we have tried to demonstrate the challenge in making a diagnosis of Wilson's disease in children may lack many of the expected typical features for example Kayser-Fleischer rings were not detected in 52% of cases, some may not have decreased serum ceruloplasmin level. On the other hands no patient had a normal 24-hour urine copper level excretion.

Hepatic copper concentration was abormal only on two of the performed biopsies.

Differential diagnosis:

Wilson's disease must be suspected in any child or adolescent after the age of three years, presenting with liver failure, atypical hepatitis, chronic active hepatitis, portal, hypertension, cirrhosis, rickets, unexplained hemolytic anemia and psychoneurosis.

In such a patient, Kayser-Fleischer corneal rings must be looked for by an experienced ophthalmologist and may by detected only by slit-lamp examination.

Although the presence of Kayser-Fleischer ring is pathognomic for Wilson's disease, in pediatric patients, their absence does not rule-out this disorder.

Patients presenting with CNS signs will have Kayser-Fleischer ring so slit lamp examination should be sufficient to establish or rule-out the diagnosis of Wilson's disease in such patients.

Treatment:

Treatment with D. Penicillamine gave the best and BAL or metronidazole produced the poorest therapeutic results.

D. Penicillamine was given in a dosage 20-25 mg/kg/day in two or three divided doses rarely exceeding 1 Gm/day continued indefinitely.

Prognosis:

The prognosis of Wilson's Disease primarily on the time of starting the therapy, the sooner it is started the better the prognosis.

If treated, in time asymptomatic patients do not develop symptoms and Kayser-Fleischer Ring if present fades.

The majority of symptomatic pediatric patients respond to therapy with normalization of liver hematologic and neurologic abnormalities.

At present the prognosis of Wilson's disease has improved, excellent results may be expected if the diagnosis can be made in time and treatment started as soon as possible.

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