1 GENETIC DISORDERS

1.1 Prevalence of haemoglobinopathies among the Scheduled Tribes and Scheduled Castes of Nimar area of Madhya Pradesh

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Status: Completed (August 2004 - July 2005)

Rationale

Haemoglobinopathies in the form of sickle haemoglobin, β-thalasaemia, G-6-PD deficiency and unstable haemoglobin are commonly prevalent in the tribal and Scheduled Caste population of the central India. However there is a large variation in terms of prevalence rate of these disorders among various population groups. Micro level knowledge of prevalence of these disorders is needed to judge the disease load and to plan the prevention/ control strategies.

Objective

To find out the prevalence of haemoglobinopathies and G-6-PD deficiency among the Scheduled Tribes and Scheduled Caste population of Nimar area of Western M.P.

Methodology

About 3 ml of blood sample was drawn in EDTA vial from apparently healthy individuals of various castes/ tribes after obtaining consent. Family was taken as a sampling unit. Automatic blood cell counter was used for complete blood cell count (CBC). Sickle haemoglobin was identified by solubility test as well as electrophoresis at alkaline and acidic pH. Iron deficiency was judged by estimating the free erythrocyte protoporphyrin level. G-6-PD deficiency was done by DCIP decolourlizing test, β-thalassaemia trait was identified by determining the raised level of HbA_2 by micro column chromatography. Foetal haemoglobin was estimated by alkali denaturation test.

The study was carried out in Nimar area comprising the districts of East Nimar, West Nimar and Badwani (Fig. 1.1.1). As per 2001 census, total population of the area is about 43 million and the Scheduled Tribe (ST) and Scheduled Caste (SC) population was 41% and 10% respectively. The main tribal groups of the district are Korku, Bhil, Barela, and Bhilala. The main Scheduled Caste group in the district is Balai. In the present study, 1595 persons were screened for haemoglobinopathies and G-6-PD deficiency, which belong to various tribes/caste as follows: Korku-301, Bhil-316, Barela-316, Bhilala-370 and Balai-313.

Results

Sickle haemoglobin is most common haemoglobinopathy in both the tribal and Scheduled Caste groups ranging from moderate (13%) to high prevalence (27%) and with an overall prevalence of 18% (Fig. 1.1.2). The lowest prevalence was observed in Balai Scheduled Caste group (13.4%) and the highest was in Barela tribe (27.2%). In comparison to other tribal populations of M.P., the prevalence of sickle haemoglobin is high in these three study districts. The overall prevalence of β-thalasaemia trait in the five population groups under study are 1.6%, which varied from 1 to 2.3%. There were six persons with sickle cell disease (homozygous) in apparently normal condition; two patients each from Korku and Balai group and one each from Bhilala and Barela tribe. The age group of these patients varies from 6 to 35 years (Table 1.1.1). Only one sickle cell disease patient, a female aged 6 years, was severely anaemic i.e. Hb- 6.0 g/dl and four patients were moderately anaemic. Foetal haemoglobin level in these patients ranged from 10 to 18%. Four of these patients were having iron deficiency including the severely anaemic patient. The prevalence of G-6-PD deficiency in all the five groups ranges from 1 to 5.7% with an overall rate of 3.2% (Fig 1.1.2). Unstable haemoglobin was prevalent commonly in all the five population ranging from 3.5 to 8.1% with an overall rate of 5.8%. All the populations except Barela were in equilibrium state for sickle haemoglobin gene as per Hardy- Weinberg Law ($p<0.05$) whereas Barela showed significantly lower number of sickle cell disease patients than expected ($p<0.05$). The findings suggest that about 5 to 19 per thousand of newborn babies of SC and ST communities are expected to suffer from sickle cell disease. This proportion was highest for Barela tribe i.e. (19/1000) and lowest for Balai Scheduled Caste community i.e. (5/1000).

Anaemia (as per WHO) was common (62 to 90%) in the study area. It was more prevalent in the four tribes (76 to 90%) than the SC group (62%). Most of the anaemic persons (about 80%) fall under mild category. Prevalence of anaemia was many fold higher among children and particularly among female (above 12 years) in all the five populations. This depicts that practice of male preferential treatment is widely prevalent in the study area in all the age groups. A sizeable proportion, ranging from 10 to 30% of tribal population was moderately anaemic. The samples showed high variation in mean cell volume (MCV) and mean cell Haemoglobin (MCH) values but overall most of the anaemic population was microcytic and hypochromic. Prevalence of Iron deficiency (as measured by free FEP level) was much less, i.e. ranging from 9.6% to 21%, as compared to anaemia, i.e. ranging from 61.7% to 90%. It suggests that mild form of anemia may be due to other factors. Anaemia control programme needs to be strengthened especially in the tribal areas with a focus on children and women.

Fig. 1.1.1: Map of Madhya Pradesh showing the study area

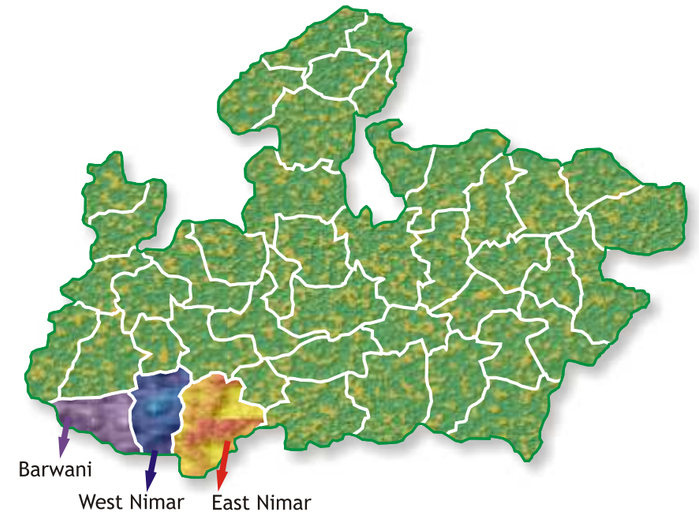

Fig. 1.1.2: Prevalence of haemoglobinopathies and G-6-PD deficiency in Nimar area

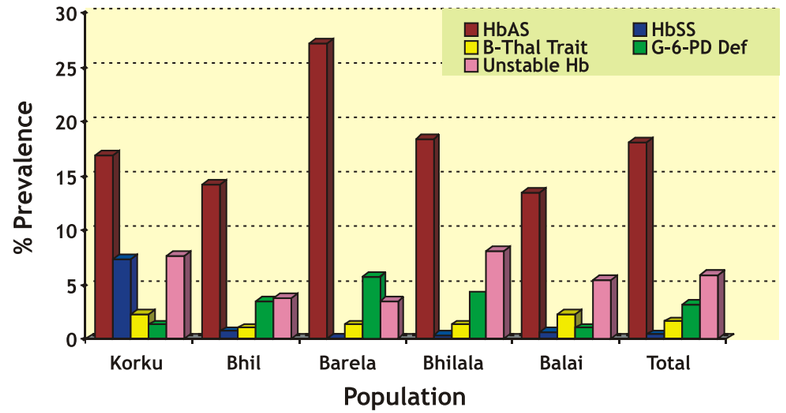

Table 1.1.1: Haematological parameters in sickle cell disease patients of Nimar Area

Tribe	Age/Sex	Hb(g/dl)	PCV(%)	TRBC ($x10^{12}$/L)	MCV (fl)	MCH(pg)	MCHC (l/l)	WBC ($x10^{6}$/l)	PLT	HbF (%)	HbA_2 (%)
Korku	8/M	9.3	21.6	2.1	104.6	44.9	43.0	8.6	-	11.8	2.6
Korku	15/M	12.2	33.9	4.7	71	25.7	35.9	6.3	-	12.6	2.9
Barela	6/F	6.0	14.1	2.5	56.0	23.6	42.3	8.5	183	14.6	3.1
Bhilala	28/M	7.3	18.9	3.0	63.0	24.2	38.3	5.6	165	1.1	3.3
Balai	35/F	7.6	20.3	3.3	62.0	23.4	37.5	8.9	172	18.3	2.4
Balai	34/M	8.8	21.1	2.3	93.0	38.8	41.7	11.7	285	11.2	1.6

Hb - Haemoglobin; PCV - Packed Cell Volume; TRBC-Total Red Blood Cell Count; MCV- Mean Cell Volume; MCH- Mean Cell Haemoglobin; MCHC- Mean Cell Haemoglobin Concentration; WBC- White Blood Cell Count; PLT- Platelet Count; HbF- Foetal Haemoglobin; HbA_2- Haemoglobin A_2.

Hereditary anaemia in the form of sickle haemoglobin, β-thalasaemia, G-6-PD deficiency and unstable haemoglobin in the study area were very high and require adequate inputs for its control/ prevention programme. Further anaemia was very common among women and children below 12 years of age.

1.2 Morbidity profile of sickle cell disease in Central India

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Status: Ongoing (October 2001 - September 2005)

Rationale

Sickle cell disease prevalent in India is caused by a mutation which belongs to different haplotype than the gene prevalent in other parts of the world. The disease profile in context to central India is not known. It is stated that the disease prevalent in India is of milder type. In this context the study was undertaken to understand the clinical profile of Sickle cell disease.

Objectives

1. To study the clinical and haematological profile of sickle cell disease.
2. To develop strategies for prevention and management of sickle cell disease.

Methodology

Sickle cell disease was identified from the suspected patients attending various clinics of NSCB Medical College, Jabalpur. The patients were enrolled in the Sickle Cell Clinic after obtaining written consent. The patients were evaluated clinically as per structured performa. All the patients were given folic acid to be taken daily. Patients/ and their parents were advised to avoid disease precipitating/ or aggravating factors like exposure to extreme climate, excessive exercise, dehydration etc. They were also told to seek appropriate medical intervention quickly upon any minor ailment. Patients were advised to take enough water/fluids. They were asked to present for clinical examination after every three months. Patients were given symptomatic treatment as outdoor patients and were referred to respective clinic of NSCB Medical Collge Hospital, Jabalpur, in case of emergency.

Results

In the sickle cell clinic, 62 additional patients were identified during this period (January 2004-December 2005) and 40 were registered making a total of 350 patients. Out of these 40 patients, 17 were enrolled for registration and 17 attended the clinic regularly. Among the new enrolled patients about 84% were below the age of 15 years. About 50% of these patients belong to SC (Jharia, Mehara, Deharia, etc.) community, 9% to ST and another 20 % to OBCs (Kurmi, Lodhi, Yadav, Sahu) group. Among the main clinical complications for which patient sought medical

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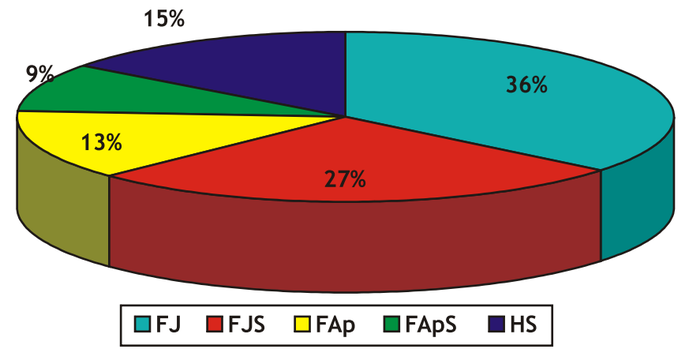
intervention are painful crisis of bone and joints with fever (85%), abdominal pain/splenic pain (30%). Splenomegaly is the most common clinical sign reported among 66% of the patients of all the age groups. Many of these clinical signs and symptoms occurs in combination more frequently. The most frequent was fever with joint pain (36%) followed by fever, joint pain and splenomegaly (27%) and hepatosplenomegaly(15%) (Fig.1.2.1). Nonpalpable spleen was reported from 24% patients. About 3.2% of the patients had massive spleen. About 3.2% of the patients had history of multiple blood transfusion i.e. more than 3 units of transfusion till date. The patients were followed up at fourth month in steady state and were requested to attend the clinic in between also if they fall sick. The patients were given folic acid, B-complex and antipyretic/anti-inflammatory tablets. Patients were also given treatment when reported sick. The patients and their guardians were educated about some preventive measure, to avoid the disease precipitating factors and complication of the disease.

Among the patients registered this year, there was reduction in the clinical severity of the disease, in most of the patients (81%) after intervention. Generally, the patient had higher level of foetal haemoglobin above 10% with mild to moderate level of anaemia (Table 1.2.1). There are wide variations in all the haematological parameters especially in Hb, MCV, MCH and MCHC.

The severity of the disease was accessed through converting the clinical observations into the numerical score. The major clinical signs and symptoms during the follow up period as well as the past history of patients were noted down. The frequencies of such episode in a year were converted into numerical score. The average score for each patient for the past history was computed as for the follow up period for each year. A total of 125 patients participated in the study but only 77 could be followed up for 2 or more years. A reduction in the severity of the disease was observed in majority (about 80%) of the patients after the intervention in a period of 2 to 3 years.

The disease is common in scheduled castes, Scheduled tribes and OBCs group of Jabalpur area. The minor intervention i.e. Supplementation with folic acid and quick administration of anti-pyretic /anti-inflamatory drugs as and when needed along with health education, reduced the severity of the disease considerably.

Fig. 1.2.1: Common combination of clinical signs and symptoms in Sickle Cell Disease Patients



INDEX: **FJ-** Fever+ Joint pain, **FJS-** Fever+Joint pain+ Splenomegaly, **FAp-** Fever+Abdominal Pain, **FApS-** Fever+Abdominal pain +Splenomegaly, **HS-**Hepatomegaly+Splenomegaly

Table 1.2.1: Haematological parameters in sickle cell disease patients

Group	N	Hb (g/dl)	PCV (l/l)	TRBC $x10^{12}/L$	MCV (fl)	MCH (pg)	MCHC g/dl	HbF (%)	HbA_2 (%)
Male	12	7.7 ± 1.5	0.225 ± 0.06	3.4 ± 1.1	69.2 ± 12.7	24.3 ± 6.0	34.8 ± 4.4	12.6 ± 7.0	2.5 ± 1.1
Female	5	7.0 ± 1.7	0.203 ± 0.047	2.5 ± 0.6	81.6 ± 5.8	28.4 ± 6.3	34.6 ± 5.6	13.5 ± 7.4	2.1 ± 0.8
Children	38	6.2 ± 1.9	0.183 ± 0.056	2.6 ± 0.8	70.6 ± 9.9	24.1 ± 4.4	34.1 ± 3.8	14.3 ± 6.0	2.5 ± 1.2

Hb-Haemoglobin; PCV-Packed Cell Volume; TRBC-Total Red Blood Cell Count; MCV- Mean Cell Volume; MCH- Mean Cell Haemoglobin; MCHC- Mean Cell Haemoglobin Concentration; WBC-White Blood Cell Count; PLT- Platelet Count; HbF- Foetal Haemoglobin; HbA_2 - Haemoglobin A_2.