HANDIGODU SYNDROME

A MULTICENTRIC-MULTIDISCIPLINARY STUDY

HANDIGODU SYNDROME
AN ICMR MULTICENTRIC-MULTIDISCIPLINARY STUDY

CENTERS		PRINCIPAL INVESTIGATOR CO-INVESTIGATOR
1. ICMR Centre for Advanced Research in Genetics K.G. Medical College and Sanjay Gandhi Postgraduate Institute of Medical Sciences	LUCKNOW	Dr. S.S. Agarwal Dr. Siddhartha Das Dr. G.K. Singh
2. Postgraduate Department of Human Mebabolism and Endocrinology LLRM Medical College	MEERUT	Dr. S.P.S. Teotia Dr. M. Teotia
3. a) Geeta Nursing Home	BANGALORE	Dr. H.K. Srinivas Murthy
b) Department of Medicine St. John Medical College		Dr. C.B. Sridhar
4. National Institute of Nutrition	HYDERABAD	Dr. S. Bapu Rao
		CO-ORDINATORS
5. Directorate of Medical Health and Family Welfare Provincial Health Services	BANGALORE SHIMOGA SAGAR	Dr. Krishnamachari Dr. T. Ranganath Achar Dr.S.R. Biligi Dr. Halagi Dr. H. Sriniwas Dr. G. Meetya Naik
6. Indian Council of Medical Research, Division of Human Resource Development Research	NEW DELHI	Dr. B.N. Saxena Dr. S. Mayurnath Dr. Rakesh Mittal

CENTRE	RESEARCH AND TECHNICAL STAFF	
1. Lucknow	Dr. Anand Kumar Dr. R.B. Gupta (RMRC, Jabalpur) Dr. J.P. Sharma Dr. S. Phadke	Mr. S.K. Sharma
2. Meerut	Dr. M. Nath Dr. Raj Kumar Mr. Kanti Prasad Mr. N.P. Singh Mr. K.P. Verma	Ms. Alka Samalia Mr. Y. John Mr. Pritam Singh Mr. Vidya Ram Mr. Jitendra Singh
3. Hyderabad	P.K. Paranjape	
4. Bangalore	-	
5. Sagar	Dr. S. Krishnamurthy Dr. M.S. Jayashree Dr. Kashi Nath Petkar Mr. Chandra Shekhar Mr. B.S. Nagaraja Mr. Jaya Shankar Mr. Nunjundaswamy Mr. Pandurang Shetty Mr. G.N. Ranganath Rao NNMB, Karnataka State	

CONTENTS

EXECUTIVE SUMMARY

EXECUTIVE SUMMARY

HANDIGODU DISEASE is a peculiar disease of osteoarticular system which is geographically restricted to only a few villages in two districts of Karnataka, a state of South India. The disease was first identified in a patient from village Handigodu in Sagar Taluk of Shimoga District; hence the name of the disease. Besides the geographic localisation, the disease predominantly affects only the Chanangi & Chaluvadi communities of Harijans.

The disease was first identified by a team of doctors from Bangalore in 1974. They rightly described it as a disease of osteoarticular system but could not ascertain its aetiology. A subsequent epidemiological survey by a team from National Institute of Nutrition, Hyderabad ascribed it to eating of crabs poisoned with pesticides or insecticides (DDT, Folidol, Endrin).

They coined the term 'Endemic Arthritis of Malnad' for this disease, and inspite of identification of strong familial clustering, genetic nature of the disease escaped. However, new cases continued to occur, though at a slower rate, all along. In 1982 another focus of similar disease was spotted in

In some individuals, marked deformity in form of genu valgam and genu varum develops at knee joints. Some children in affected families, though clinically and radiologically normal, have knock knees. Likewise, the armspan in many healthy individuals is significantly larger than height. Future course in these patients needs to be studied.

There is also preponderance of dwarfs in affected families. This may represent homozygous manifestation of disease allele.

Besides strong evidence for genetic aetiology of the disease, the study has also identified the presence of marked deficiency of dietary calcium intake in the entire population. It is reflected by decreased excretion of urinary calcium, negative balance of calcium which is corrected by normal calcium diet, rise in serum HPTH levels and histomorphometric evidences of secondary hyperparathyroidism. Clinically and radiologically there was no evidence of rickets or osteomalacia. It appears that deficiency in vitamin D intake is compensated by sun exposure. It is proposed that dietary calcium deficiency may precipitate or aggravate the genetically determined dysplasia of epiphyses.

On basis of conclusions drawn above, appropriate therapeutic

1. INTRODUCTION

Handigodu Syndrome is a peculiar disease of bones & joints which is geographically & ethnically restricted to Chaluvadi & Channangi Harijan communities of Shimoga and Chickmagalore districts of Karnataka. It was first brought to medical attention in 1975 from the Handigodu village of Sagar Taluk, hence the name of the disease. Chief complaint of the patients first seen was difficulty in walking. Accordingly, the disease was ~~first~~ investigated by Dr. K.S. Mani (a Neurologist) & Dr. H.K. Srinivasa Murthy (an Orthopedic Surgeon) who reported on 45 patients and 13 controls. It was concluded by them that Handigodu syndrome is primarily an osteoarticular disease involving hip joints. A systematic clinical & epidemiologic study was carried out by these investigators, the report of which was submitted to Govt. of Karnataka. It was followed up by a comprehensive study from National Institute of Nutrition, Hyderabad. This led to identifying the disease as an `Endemic Familial Arthritis' precipitated

Prof. of Orthopedics; Dr. Krishna Murthy, Prof of Pathology; Dr. Parthasarathy, Prof of Radiology & Dr. Aswath, Professor of Preventive & Social Medicine). The team opined that the cases from Halandur village were quite similar to those reported from Handigodu village. Further, on basis of strong familial aggregation of the disease, the team recommended to conduct genetic studies. This prompted the Govt of Karnataka to request the ICMR to have a fresh look on the whole problem. As a result of this request the then Director-General of ICMR, Dr. V. Ramalingaswami himself surveyed the affected area alongwith a group of experts on July 17th, 1983. The group decided to launch a joint ICMR-Govt of Karanataka sponsored multidisciplinary study with expertise drawn from all over the country. A group of 4 centres from Bangalore, Hyderabad, Lucknow & Meerut was identified to formulate the project. Simultaneously, the Govt of Karnataka undertook to strengthen the Taluk Hospital of Sagar and ICMR established a field station at Sagar. From 1985 to 1988 each group made several field visits

dominant type of spondyloepiphyseal dysplasia); the studies have led to more questions than answers. Nevertheless, on basis of what is known, a strategy of intervention can be recommended. For more definitive answers further research is clearly warranted. It is an unique Indian problem which has the potential of making substantial basic contribubtions.

2. Historical & Geographic aspects

'Handigodu Disease' was first identified in patients from Handigodu village of Sagar Taluk, Shimoga District, Karnataka. South India in 1975.

Field surveys have shown that the disease is localised to 2 adjoining districts of the Karnataka State, viz Shimoga & Chikmagalore in South India (Fig.1). These two districts are separated by 150 kms by road and 50 kms by dense forest aerially. Even in these districts, only selected villages in few taluks are affected (Fig. 2). The list of hamlets/villages known to be affected in Sagar Taluk and adjoining areas is given in Table I.

The affected villages are situated in the Western Ghats in Malnad area between 13^{o} - 14^{o} latitude north, 75^{o} - 76^{o} longitude east & at an altitude of 700-1000 meters above sea level. The river Shravati flows in this region to the Arabian Sea on which Linkanmakki dam has been made at world famous Jog falls. The region is rich in thick tropical rain forest and gets an annual rainfall of 200-300 cms. The temperature varies from ^{o} ^{o}

The people

According to mythology and legend Sagar is named after the famous Emperor Sagara who performed the sacrifice (Yaga) in this area. The Emperor prayed the Goddess to provide water for the Yaga and since then Varada (Vara=Grace, da=give) river flows in this area.

The Sagar area was settled by King Sadahiva Naik of Keladi dynasty. Even today, the Keladi Samasthan is preserved as a historical monument, 5 miles from the Sagar town. Historical evidences suggest that Keladi kingdom was established in 1499 and ended in 1763. In between, during the period from 1583 to 1630, in the reign of King Venkatappa Naik, Sagara town was established as a base between Keladi and the capital Ikkeri.

The economy of Sagar Taluk mainly depends upon cultivation of arecanut, paddy, cardamom, banana, ragi, ginger, coconut, pepper, coffee and sugar cane.

The rural folks of Sagar Taluk are preserving their ancient and traditional values, both in cultural heritage and festivals. Each family of Hindu community

rituals. There are several small and big temples of great historical importance situated in the villages of Sagar Taluk. There exists cordial communal harmony between Hindus, Muslims and Christaians in this area, each following their religious, cultural and social traditions and worship in mosques, churches and temples.

The Sagar General Hosptial is the main medical and health care centre of the Taluk.

Population distribution

The disease has been found to be restricted predominantly to Chanangi & Chaluvadi communities of Harijans (a socio-economically backward class of Hindus). Only occasional families of other castes viz. Edigas, Vokkaligas, Uppars and Achars have been reported to be affected. None of the Brahmins & Lingayats living in the affected villages have been found to be suffering with Handigodu disease.

Both Chanangi & Chaluvadi belong to a community known as Adi-Karnataka. They are landless labourers

separate from non-Harijan communities living in the same village.

Census data (1981) of Sagar Taluk is shown in Table 2 . Out of a total population of 160,267 the Harijan population constituted 13,969 (8.7%). Largest community in rural areas is of Edigas. It is followed by Brahmins, Lingayats, & Vokkaligas. Other communities living in the area include Modiwalla, Mehtara, Uppara, Maghvira, Shetty, & Pujari's. At the time of first survey by Dr. K.S. Mani & Dr. H.K. Srinivasa Murthy in 1975-76 a total of 130 cases were recorded in Sagar Taluk. An additional 20 cases were reported from Tirthalli Taluk of Shimoga district and 60 from Chikmagalore. On the basis of clinocoepidemiological survey, Dr. Bhat & Dr. Krishnamachari identified ~~presence of~~ Handigodu disease as Endemic Arthritis of Malnad in 34 villages. Detailed survey in 18 villages detected 223 cases in 73 out of 206 familes. In 1981-82 the team from Bangalore Medical College identified a total of 290 affected cases in the two districts. The results of the survey carried out as a part of the present

3. REVIEW OF PREVIOUS STUDIES

Dr. Mani & Dr. Srinivas Murthy have studied 45 patients suffering with Handigodu disease & 13 controls who were admitted to Sagar Taluk Hospital. Among patients there were 18 males & 27 females. The age range varied from 5-45 years, about 25% being below 10 years. Seventy percent of the patients were Harijans from Handigodu village. There were 16% non-Harijans from Adderi village. The duration of symptoms varied from 3 weeks to 4 years. The disease had been of insiduous onset in majority of patients (except in one where peak disability was reached within 48 hours). In seven patients there was a history of fever, few days to a month prior to onset of the disease.

The main symptom was pain. The ~~areas~~ joints most commonly affected were knee joints (100%) & hip joints (82%) followed by ankles (33%) & shoulders (22%). Nine subjects presented with low back ache. History of swelling of joints was present in 13 individuals (20%).

Activities of daily living, defined as follows, were full in 5, mild in 11, moderate in seventeen,

can squat, get up or bend without help and freely. (N=11)

Moderate: Walking restricted and pace slower, but without support and/or can squat, get up and bend without support but with difficulty. (N=17)

Severe: Walking restricted and needs support for walking and/or needs help for squatting, getting up or bending. (N=7)

Gross: Cannot walk except a few paces, that too with support and/or cannot stand. (N=5)

On examination, age-sex adjusted heights & weights did not show any difference between cases & controls. Xerosis of conjunctiva was seen in 3 patients. Vitamin B complex deficiency clinically was suspected in one patient.

Detailed general & neurological assesment was within normal limits.

Objective evidence of joint involvement was seen in 32 of the 45 patients (71%). Hip joints were involved in 30, knees in 10, shoulders in 3 and

knee joints & in one each at ankle or wrist. Spasm of the flexors & adductors at hip and of flexors at knees was seen in a significant proportion of patients (57%,53% 33%, respectively).

Fixed deformities were noted in hip joints in 19 patients & in knee joints in 2 cases. It correlated with the duration of the disease.

Laboratory investigations did not reveal any significant difference between cases & controls. The values obtained are given in Table No 1.3

Aerobic & anaerobic cultures of CSF from 4 patients; synovial fluid from one knee joint; cartilage, synovial membrane & periosteum from hip joint, and gluteus medius & vastus medialis from one patient; were negative for microorganisms including fungi & mycobacterium tuberculosis.

Detailed radiological examination was done in 41 patients. This included PA view of chest, AP view of pelvis & hip joints, AP & lateral views of lumbar spine, AP & lateral views of knee joint & AP view of wrists. Shoulder joints were seen in 37 of the chest X-rays. X-rays of ankle joints were taken in 4

were categorised into mild, moderate, severe & gross on basis of following criteria:-

Normal: None of the below

Mild : Narrowing of joint spaces

Moderate : Narrowing of joint spaces and minimal bone changes- cystic areas, sclerosis,oseophytic lipping

Severe: Gross degree of diminution of joint space and/or irregular articular surfaces and marginal sclerosis.

Gross: Complete loss of joint space and/or destruction of the articular ends with or without displacement.

On the basis of above, the changes seen in various joints are given in Table No. 24

In addition to above, following changes were also seen in hip joints:-

i) Premature closure of the epiphyses of femoral head, greater trochanter & lesser trochanter, to varying extent, in patients below 16 years of age.

to Perthe's disease. Lumbar spine was found to show platyspondylia and mariginal lipping in nearly three quarters of the patients.

In 3 cases diaphyseal aclasis was seen involving femur/humerus, or both.

Incidientally 3 of the controls showed radiological changes in hip joints which were similar to those seen in patients. (In 7 of the control subjects, Handigodu syndrome was seen in family members).

The results of the study carried out by Mani & Srinivas Murthy were submitted to the Govt. of Karnataka in 1976.

One of the major deficiency of the above study was that controls were not appropriate. They were not matched for age & sex. Only 13 individuals were studied. Two of the controls had significant anemia, and 7 had positive family history of Handigodu disease.

Second investigation was carried out by Dr. Krishnamachari & Dr. Bhat from National Institutes of

1. The disease apparently appeared 6-8 years prior to investigation. There were very few new cases over previous 2 years. In some families 6-8 members were affected over a period of few months. Even where 3 generations were affected, all got the disease within five years. In many households children were affected before the parents. The onset was not seasonal. It was also not associated with any acute conditions like drought or flood. There was no sex prediliction. Infants & preschool children were spared.

2. Over 85% of the affected individuals belonged to Harijan community. Some Deevuru (Edigas) & Vokkaligas were also affected. In 18 villages, out of 206 families studied, 73 families were affected with the disease. In 40 of the 73 families, two or more members were affected. In some families even upto 6 to 8 members were affected. Besides the siblings, even parents & grand parents were affected. The affected families, even in different villages, were interrelated. In all 88 males & 135 females (total 223) were affected in 73

households. Some were affected themselves. One dwarf was related to at least 15 subjects who had arthritis.

The study was restricted to clinical observations. Radiographs of the patients were not taken. It was concluded by the investigators that exposure to newly introduced synthetic pesticides in a genetically succeptible population may have resulted in the `epidemic' of Handigodu syndrome.

The third study was carried out by a team of doctors from Bangalore Medical college because of the report of new cases from Halandur village of Sringeri Taluk in Chickmagalore district. This team visited 4 villages in Sagar taluk & 3 villages in Chickmagalore district. In all, a total of 95 patients were studied. Their salient observations were as follows:-

i) Maximum number of cases were seen in the age group of 5-15 years. The prevalence in two sexes was similar.

ii) All patients belonged to Harijans, Vokkaligas & Edigas (same as Deevaru).

remarkably normal in all the cases. There was no evidence of joint inflammation in any of the individuals examined. There was no neurological or other systemic defect seen in these patients.

v) Patients generally were of short stature. Lower segment was shorter than the upper segment. Span length was considered to be abnormal.

iv) A total of 80 affected individuals in 4 villages (2 in Sagar taluk & 2 in Chickamaglore) were found to be distributed in 26 families. History of consanguinity was found in 8 of these families. Number of affected individuals in a given family varied from one to seven (one affected in 7, two affected in 2, three affected in 6, four affected in 7, five affected in 2, six affected in 1 & seven affected in 1). In 19 of the 26 families, there was more than one case in each family.

Total number of individuals in each family and distribution of disease in different generations was not recorded.

heredofamilial disorder of endochondral ossification and had made several recommendations including further studies to be done.

4. Material and Methods

LLRM Medical College centre, Meerut

A comprehensive epidemiological, environmental, laboratory and genealogical study was designed to (1) discover and identify nature and aetiology of the Handigodu disease, (2) estimate severity and magnitude of the public health problem caused by the disease and (3) suggest appropriate therapeutic measures for affected individuals and strategies for control and prevention of the disease.

The epidemiological survey (from house to house) was carried out by SPST of 38 villages of Sagar Taluk during the period 1986-88. All the villages were geographically located within a distance of 2-40 KM from Sagar town. The residents of the villages were explained the aims and objectives of the project. A minimum of three contacts were attempted to reach each individual for examination, failing which he/she was left unexamined.

All the sources of drinking water were located and

to obtain comparable films. Two hundred and thirty two samples of water, one from each source, were collected in plastic bottles and chemically analysed.

Metabolic and endocrine investigations were performed on 52 samples of plasma and 63 specimens of 24 hour collection of urine. Blood was taken in heparinised polypropylene stopperd tubes and the 24 hour urine was collected in plastic jars containing toluene as preservative. These samples were brought to the department of Human Metabolism and Endocrinology for analysis and were air-lifted for reasons of quick and accurate analysis.

Five patients of Handigodu disease were brought from Sagar Taluk and admitted in metabolic and endocrine wards of the department of Human Metabolism and Endocrinology, Meerut for detailed investigations. In addition to the laboratory tests performed on other patients studied at Sagar Taluk itself, additional investigations in these five patients included

kitchen by a trained dietitian. First two periods were on a diet similar to their intake at home in Sagar and the last two on normal adult intake.

Bone histopathology and dynamic histomorphometric measurements were made on undecalcified double tetracycline labelled iliac crest biopsies. All the laboratory investigations were performed using standard published procedures established in the department and with appropriate quality control.

ICMR Centre for Advanced Research in Genetics, Lucknow

I. Evaluation of familial clustering and definition of heterogeneity in clinical presentation of patients with Handigodu disease.

First field visit was made in Feb. 1986. On the basis of proximity, road conditions, anticipated cooperation and identified number of cases of handigodu disease and dwarfs by the ICMR team at Sagar, 3

Amongst harijans all the households in all the 3 villages were examined in detail by the medical team as per proforma given in Appendix II. Besides clinical evaluation, antrhopometric measurements and radiological examination were also carried out. This was done to identify any heterogeneity in clinico-radiological presentation of the Handigodu disease and to identify families for detailed geneological evaluation.

Amongst non-harijans the team of medical doctors visited the houses of individuals with osteoarticular symptoms which were identified in the above survey and where necessary appropriate investigations were carried out

II. Anthpropometric measurements

Srecond field trip was made in the month of Feb. 1987. I.t was done primarily to carry out antrhopometric measurements on normal healthy individuals to establish norms for stature and body proportion since in first visit during the course of clinical examination variations in body proportions were

analysis. For this purpose clinical, antrhopometric and radiological evaluation of all Harijan households in 4 villages, namely Kugve Ambapura, Harokoppa, Bandgadde & Handigodu was done. In adition, all reported families from villages Chikbilgunji, Kolisalu, Maliliyooru & Baruve were also studied.

Simultaneously another study was carried out to determine marital pattern of affected & unaffected Chaluvadi & Chanangi villages to evaluate the role of genetic drift in determining the distribution of the disease.

Also, a field survey for identification of Dwarfs was carried out to cover the entire Sagar Taluk employing dwarfism as marker of Handigodu disease. The proforma used is given in Appendix IV.

Bangalore

The Bangalore centre had carried out the following studies:-

1) Estimation of 27 trace metals in water from a well

3) Estimation of fluoride content in nail clippings from affected & normal controls. It was done in collaboration wth Dr. A.K. Susheela of AIIMS, New Delhi.

4) Estimation of Pb,Mn & Cd in bone ash of patients with Handigodu disease. It was done in collaboration with Dr. Satya Chandra of ITRC, Lucknow.

5) Review of bone biopsy slides from patients with Handigodu disease.

In addition, estimation of serum & urinary calcium, serum alkaline phosphatase, urinary aminoacids & urinary glucose was lso carried out on samples from patients.

The team of Dr. Srinivas Murthy & Dr. Sridhar visited the field several times to provide consultative support for medical, surgical & rehabilitative measures to the local team of doctors posted at Sagar General Hospital. Dr. Srinivas Murthy was able to follow up 15 of the 40 patients whom he had operated 10 years earlier. During corrective surgical procedures

rice as a mashed preparation. These were compared with samples collected from Bangalore and other rural areas. The samples of air, water and diet, after duely processing, were analysed for Cd,Cu,Cr,Mn,Ni,Pb and Zn by standard methods. In addition to these, fluoride, iodine and magnesium were also analysed in water samples using standard methods. Metals were analysed after ashing the samples.

Fluoride in water samples was estimated by ion selective electrode (ISE) and iodine in water samples was estimated by standard method. For all the analysis carried out there have been recovery studies and internal and external quality control in addition to spiked samples.

5. Epidemiological studies

5.1 Village Scenario, Environment and Socio-Economic Status

All the affected as well as unaffected villages have similar geographical, agricultural, geochemical and meterological characteristics, socio-economic and occupational status and dietary habits.

Poor sections of the community have typical mud houses with thatched roof while houses belonging to the rich landlords are made of bricks, cement and wood. Almost all the Brahmin houses had wells/pumps to the poor communities have been provided by the Government of Karnataka. The houses of the Harijans are segregated in one part of the village. Almost all the villages lack in sanitation, toilet facilities, educational facilities, bank credit, health, family welfare, nurtition and supplementary feeding programmes.

The fuel used for household cooking is either dried wood or dried cowdung-cake. For cooking the traditional chulah is generally preferred. The rich landlords have all kinds of facilities in their houses

chicken and goats etc. The Brahmin community is mostly vegetarian while other communities have mixed dietary habits.

Breast feeding is universal; its duration varies for 1 to 3 years or longer. Cultural food fads, and taboos commonly affected the period of gestation and lactation and may exacerbate certain illnesses in infants. The need for increased intake of milk, food, nutrients and vitamins during the period of growth, pregnancy and lactation is not recognised in any community. Traditional beliefs usually determine the type of foods given to the infants. Cost and availability are also relevant factors. Due to food taboos during diarrhoea and febrile illness, foods and fluids are frequently withheld which aggravate starvation, dehydration and illness in the child. Milk and milk products, fruits, green vegetables and salad are rarely eaten in poor communities and not adequately eaten even in upper class communities. Habits of taking

the liquor quickly (within 12-15 days) and to make it more stronger, aluminium chloride (black powder contained in dry battery cell), urea, bark of guava or cashewnut tree and the bark of nausar are added to the jaggery syrup.

Three seasons of the year are generally recorded: the cold, the hot an the rainy season. The cropping seasons, kharif and rabi, are closely related to summer and winter monsoon seasons. The village economy is essentially agrarian with dominant cultivation of arecanut, cardamom and paddy. All agricultural products are stored within the household. More than 90 percent of the landholders have cows, buffaloes and bullocks while the landless labourers, usually Harijans, have poultry and very few have goats. The Harijan and lower classes are usually the agricultural landless labourers obtaining only cash wages around Rs. 1.50 per day or grain as wages. The dowry system has further burdened the landless population and the small farmers. The upper class community has a very comfortable family budget and have television and radio sets etc.

On interogation with local persons it was noted

the drinking habit has increased and nutrition has suffered.

About 75% of the families are nuclear, 11 percent joint families and remaining 14 perrcent are extended nuclear families. The average family size ranges from 4 to 6 members. All the communities are religious and god fearing, and decorate their houses with temples and pictures of Gods and Goddesses.

Chanangi & Chaluvadi sub-divisions of Harijans generally marry within thier sub-divisions and live in separate villages. Although, most hosueholds are interrelated to each other, yet consanguinity is not common. Detailed analysis of marital patterns is given under genetic studies.

The people continue to do much of their travelling on foot and the most common mode of transport within the village and to the fields is still the bullock cart. In some areas there is public transport in the form of buses between villages. The Government of Karnataka is providing appropriate allowances to the handicapped individuals and is also improving and providing other

5.2 Population survey of Handigodu syndrome (LLRM, Meerut)

The Handigodu disease has been reported to be restricted to Sagar Taluk of Shimoga district (Fig 2). Even within the Sagar Taluk the disease has been identified only in a limited number of villages/ hamlets (Fig 3). On the basis of information available 38 villages/hamlets were selected for detailed door to door survey. Names of villages/hamlets selected according to Hobli is given in Table No 5. The communitywise distribution of the population surveyed in these villages/hamlets is given in Table No. 6. Age & sexwise breakup of the population surveyed is given in Table No. 7. Under category of children, individuals between 0-18 years were included. Further distribution in different age groups is shown in Table No. 8. The marital & reproductive status of women included in the survey is given in Table No. 9.

Out of the total of 11158 individuals surveyed, 10370 volunteered for examination. A complete history & physical evaluation of all individuals who volunteered

affected individuals. The prevalence of Handigodu disease in different communities villageswise is given in Table No. 10. Summary of the findings for the entire surveyed population is given in Table No. 11.

Distribution of disease in different communities

Harijans

The disease was predominantly seen amongst Harijans. Amongst a total of 286 affected individuals 214 (74.8%) were Harijans. The prevalence of Handigodu disease in 2207 Harijans was 9.7%, compared to 1.2% in 5873 non-Harijan/non-Brahmins.

The distribution of Handigodu syndrome amongst Harijans in different villages is shown in Table No. 12.

Non-Harijan/Non-Brahmins

This is a heterogenous group and consituted 57.2 % of the total population surveyed in 38 villages/hamlets (see Table No. 6). Forty two communities were recorded in this group, many comprising of only few individuals each. Numerically significant groups comprised of Edigas (2738), Vokkaligas (1117), Lingayats (590), Mediwal (421), Poojars (293), Uppars (168), Achars (129)

542=2.2%). Achars (5/68=7.3%), Madiwal (3/397=0.75%), Poojars (1/262), & Uppars (1/113), were also seen. Remaining were isolated cases (Shetty 1, Magaveera 1, Channaya 2, Christian 1, & Jogi 2).

Age-Sex distribution

Amongst 286 affected individuals, 139 were males & 147 females; the male to female ratio being 0.94. The M:F ratio in the examined population was 1.04 for Harijans, 1.01 for non- Harijan/Non-Brahmins & 1.02 for Brahmins (see Table No. 7). This shows that prevalence of disease both amongst men & women was similar in all groups.

With reference to age, the disease appears to be more prevalent amongst adults. In Harijans, the prevalence in adults was 7.1% compared to 2.6% in children. In non-Harijan/non-Brahmins also, the disease was slightly more common in adults, 0.77% v/s 0.5%, but the difference was not significant statistically (see Table No. 11).

5.3 Marital Pattern

The geographical distribution of Handigodu disease is extremely patchy. Out of a total of 977 hamlets in the Sagar Taluk only 37 have seen reported to have cases of Handigodu disease. Even in adjoining villages with Chanangi & Chaluvadi Harijans some villages are affected while others are not. During discussions with families living in an unaffected village it was mentioned that as custom they do not bring brides from affected villages. This led us to survey the marital pattern amongst affected & unaffected Chaluvadi & Chanangi villages. Information about the place of birth of bride for each couple living in the village was collected by local field interviewer. The data is given in Table No. 14. Adjoining Sagar town, there were 13 villages with predominantly Chaluvadi Harijans. In 8 villages, the disease was present and in 5 no affected individual was seen. In affected villages, 80% of the brides of 145 couples have come from other affected villages compared to none amongst 90 couples in unaffected villages. Likewise, in villages with predominantly Chanangi population, 71.3% of the brides

role of gene flow in influencing the distribution of disease in different villages.

5.4 Dwarf survey, Sagar Taluk (SGPGI, Lucknow)

On basis of detailed pedigree studies it was observed that in large number of instances dwarfism was segregating alongwith classical Handigodu disease. It was, therefore, used as a readily identifiable marker for micro-mapping of the Handigodu disease in the entire Taluk. The proforma used for the purpose is given in Appendix IV.

The survey was carried out by a team of 2 persons, from Nov. '87 to Jan. 88.

Distribution of villages and hamlets in the 6 hoblis of Sagar Taluk is given in Table No. 15. The work area comprised of 242 villages including 974 hamlets. In addition, information was also collected on 12,300 children from 35 schools of Sagar Taluk (Appendix V). The survey identified 39 dwarfs. Their list is given in Appendix VI. This list does not include the dwarfs that were identified in the surveyed villages. School survey did not identify any additional dwarf which was not identified in village survey.

8, Chanangi 5, Chaluvadi 1, Adi Karnataka 1, Uppar 1, Achar 1, Muslim 5, Christian 3, Not known 2.

Twenty two of the 40 dwarfs were seen in those communities which are affected with Handigodu disease. These may represent additional pockets of the Handigodu disease.

Photographs were taken of all the patients. The features seen from these photographs suggest that the type of defect seen in communities other than those known to have Handigodu disease may be different. Families of fourteen of the 40 cases had orginally belonged to places outside Sagar Taluk, Shimoga District. They had moved in the Sagar area rather recently. It would be useful to examine these patients and their families radiologically to define these entities.

From the dwarf survey it appears that Handigodu disease may not extend beyond the identified villages & Chanangi & Chaluvadi communities to a large extent.

6. AETIOLOGY

6.1 Environmental factors

In order to evaluate the role of minerals & trace metals in the causation of Handigodu disease, drinking water was analysed for various constituents by the Meerut, Hyderabad & Bangalore centres. In addition, NIN had measured heavy metal content of air samples (19) & food samples (15), while Bangalore centre has carried out trace element analysis on hair clippings. The data is given below.

LLRM Medical College, Meerut

Water samples were collected from 232 sources from all the 38 villages surveyed by the Meerut centre. This included 175 samples from wells, (mean depth 40.0 + 6.9 ft), from Hand pumps, 24 from ponds, 3 from rivers & 2 from taps. The Hand pumps had a mean depth of 48.0 + 11.0 ft. The data for the chemical constituents (Ca,Mg,F,I,Cl,Na,K,Hardness, Total Acidity, Total Alkalinity, pH) and trace elements (Cd,Cu & Zn) for all the sources is given in Table No. 16.

The results show that water samples from all the villages and all the sources were quite comparable. On

difference in any of the chemical constituents & trace metals from any of the villages.

NIN HYDERABAD

The NIN centre had analysed 57 water samples from the Sagar area and compared them with 10 samples from Bangalore and 12-17 samples from a rural area in Andhra Pradesh. The analysis included measurement of F,I & Mg, besides 7 trace metals (Cd, Cr, Cu, Mn, Ni,Pb,Zn). The results are given in Table No. 17 & 18. In this study too, the values were generally on the lower side in water samples from Sagar area.

The results of heavy metal analysis in air & food samples from Sagar area are given in Table No. 18, 19 & 20. respectively. Again on comparison with samples from Bangalore and a rural area in Andhra Pradesh, no significant differences were seen.

BANGALORE

The results of water and hair clipping analysis for trace metals, carried out by the Bangalore Centre, are given in Table No. 21 & 22, respectively. Since only 1 sample each of water from the study (Sagar) & control

clippings did not show any significant difference between patients & controls (Table No. 23). Analysis of bone ash from patients with Handigodu disease also did not show any abnormality.

6.2 **Nutritional Assesment**

Diets in Harijan community were critically deficient in foods rich in calcium and vitamins A and D. The entire community is nonvegetarian and usually eats crabs and fishes collected from ponds and paddy fields and the meat of chicken and goats. The staple diet of Harijan community consisted of rice and sambar (prepared from plants and weeds growth on marginal lands) and lacked in milk, milk products, vegetables and fruits. The cooking salt used was coarse, unprocessed and of the sea variety. Chewing of betels and tobacco, smoking and drinking of liquor illicitly prepared is an established practice in this community. Smoking, excessive consumption of non-vegetarian food and liquor, and high phytate cereal diet practically in each household had further aggravated the nutrtional deficiencies particularly of calcium. The effects of dietary calcium deficiency were more severe in growing children and in

Deficiences in the intake of various nutrients as per ICMR standards of rcommended allowances (Gopalan C and Narshinga Rao B, NIN, ICMR, 1985) are shown in table No. 24. The Brahmins (Agricultural landords) were largely vegetarians and had adequate dietary intake.

Clinical examination revealed that nutritional disorders such as iodine deficiency disorders, rickets, osteomalacia and nutrition related renal stone disease were practically nonexistent. The very low intake of iodine obtained from the drinking water was adequately compensated through consumption of sea salt.

6.3 Biochemical, Metabolic and Endocrine Investigations

Plasma biochemical, metabolic and endocrine investigations were performed in 47 patients of Handigodu Disease. The results are given in Table Nos. 25 & 26. These investigations do not reveal any abnormalities specific for the diagnosis of Handigodu syndrome. Cicrulating thyroid hormones (T3,T4, TSH) were normal; alkaline phosphatase was raised in 40 percent; growth hormone levels were raised in 33 percent; 25(OH)D3 concentrations were normal, while 1,25 (OH)2D3 and 1-34 HPTH levels were elevated in 60 percent of the cases. Gonadal functions were normal.

Twenty four hour urinary excretions were studied on 58 patients. It revealed that mean 24-hour urinary excretion of calcium, phosphorus, magnesium, creatinine, 17-KS, 17-KGS and 17-OHCS were within the expected normal range. Normal excretion of calcium in presence of dietary calcium deficiency suggests the presence of secondary hyperparathyroidism in all the patients. Urinary excretion of aminoacids revealed a normal pattern with predominance of glycine.

6.3.1 Detailed clinical, laboratory, radiological and bone histomorophometric studies in 5 patients bone histomorphometric studies in 5 patients with Handigodu Disease

Five patients of Handigodu disease were brought from Sagar Taluk and admitted to Metabolic and Endocrine Wards at the Postgraduate Department of Human Metabolism and Endocrinology, LLRM Medical College, Meerut for detailed investigations. All the 5 patients studied were males in the age range of 18 to 25 years. The detailed clinical & radiological data and anthropometric measurements of these 5 patients are given in Table Nos 27 & 28, rspectively. Of the five individuals, two were of subnormal height (case Nos 1 & 2) while the other 3 were dwarfs (case No. 3,4,5). The radiological findings of these patients were similar to those found in other patients suffering from Handigodu disease.

Mean dietary content of calcium in home diets of these patients at Sagar Taluk was extremely low ranging from 80-120 mg/day only (Table No. 29). The diets lacked in foods rich in fats and vitamin D. Fat intake ranged from 6-9 g, and vitamin D of 5 to 8 units per day. Since none of the patients had any clinical deficiency of

raised in 2 patients (Table No. 30). All the 5 patients revealed a negative calcium balance (-26 to-70 mg/day) on a mean dietary intake of 98 mg of calcium per day (similar to their home diet). However, all the patients turned into positive calcium balance on diet served from the metabolic kitchen containing 850 mg of calcium per day.

Metabolic and endocrine investigations showed normal values of T3,T4, TSH growth hormone and 25(OH)D3 in all the five patients. The values of 1,25-(OH)2 D3 were in the higher range of normal (48-65 pg/ml) in 3 and above normal range in 2 patients (68 and 82 pg/ml).

The plasma circulating level of immunoreactive 1-34 HPTH was raised in 4 patients (77-275 pg/ml). Raised levels of 1,25-(OH)2 D3 and HPTH are indicative of secondary hyperparathyroidism in these patients which is secondary to dietary calcium deficiency.

Chromosomal analysis did not show any structural or numerical abnormality in any of the five cases.

24-hour urinary excretion of calcium, phosphorus, magnesium, creatinine, ammonia, aminoacids, 17-KS, 17-KGS, 17-OHCS was in the normal range (Table No. 31).

represent the compensatory mechanism to increase 1, 25-(OH)2 D3 dependent intestinal absorption of calcium in calcium deficient patients.

Bone histomorphometric studies on undecalcified sections of double tetracycline labelled iliac crest biopsies in 5 cases (Table Nos. 32 & 33) demonstrated characteristic findings of dietary calcium deficiency and osteopenia in 2 cases and of secondary hyperparathyroidism in 3 cases. In one case (No. 4, Table No. 33) findings indicative of osteogenesis imperfecta tarda were present, though clinically and radiologically this patient had dwarfism with spondyloephyseal dysplasia.

These observations suggest heterogeneity in the bone histopathology, and bone dynamic mechanisms underlying the Handigodu syndrome of genetic epiphyseal dysplasia. The bone disease was more severe and complex due to associated secondary hyperparathyroidism. It is proposed that secondary hyperparathyroidism develops as a compensatory mechanism to maintain the extracellular ionised calcium deficiency in these patients.

6.4 Genetic aspects

In order to analyse contribution of genetic factors in causation of a disease or trait, following evidences can be considered.:-

a) Geographic & ethnic distribution

b) Familial clustering

c) Clinical presentation

d) Pedigree analysis

a) Geographic & ethnic distribution

The peculiar geographic & ethnic distribution of Handigodu disease has been elaborated on pages 7 to 10 & 32 of this report. Some observations that support the hypothesis of genetic causation are as follows:-

i) At microgeographic level, the villages where Handigodu disease was prevalent were randomly distributed. Some afffected villages were close together while others were far apart. Several of the adjoining villages with similar community distribution were unaffected.

ii) Within the affected village only the Harijans were affected. The Brahmins were totally spared. Amongst non-

iii) The brides in the affected villages were largely drawn from affected villages & vice-versa. The community was aware that disease was present in some villages & not others. They have adopted the aforesaid marital preference to avoid bringing in of disease, if the village was spared from the disease so far. The affected villages perhaps had no choice. The data related to marital pattern is given on page no 35.

(v) A comprehensive Dwarf survey of the entire Taluk including 242 villages & 974 hamlets led to identification of 40 additional dwarfs. Seven of them were amongst Chanangi-Chaluvadi-Adi-karnataka community which may represent additional pockets of Handigodu disease. Another 15 were in Ediga, Vokkaliga, Uppar & Achar communities, which are also known to be affected. The remaining 18 were in communities which have hithertoo been not reported to be affected (Brahmin, Lingayat, Jain, Muslim, Christian & others). These cases remain to be examined in detail to evaluate the clinico-radiological presentation of these patients. Some of them, on the basis of photographs taken, appear to be distinct entitities.

b) Familial clustering

A comprehensive survey of 2 affected villages (Harekoppa & Bandagadde) revealed that out of 59 Harijan households, 31 were affected. In 21 of them only one person was affected, while in other 10 two or more individuals were affected. It has to be noted that there is strong tendency for married couples to move out into independent households. Most of the 21 affected households, with one affected individual only, were in fact related to each other, and at one point in time have lived together. The pedigree charts show that there is very strong familial clustering of the disease.

There was no significant migration, in or out, of the population to study its effect.

c) Clinical-radiological presentation

Every disease has a characteristic clinical presentation. This is particularly true for genetic syndromes where identification and delineation of phenotypic heterogenity is largely dependent on comparison with clinical descriptions, photographs and radiological appearances of known genetic disorders. On applying the same approach to Handigodu disease, the

bones of the apppendicular skeleton support this. In fact the histological studies of the growth plates by the Bangalore centre have indicated the presence of defects in enchondral ossification which is characteristic of osteochondrodysplasias.

Amongst skeletal dysplasias, the clinical picture very closely resembles the picture of spondyloepiphyseal dysplasia, tarda. Involvement of hip joints alone in some cases could raise the possibility of the diagnosis of multipleepiphyseal dysplasia. But in view of cosegregation of hip and spine involvement in the same family, (described later), the diagnosis of spondylo-epiphyseal dysplasia, tarda appears to be most plausible diagnosis for Handigodu syndrome which is a single gene determined disorder.

d)<u>Pedigree analysis</u>

The genetic aetiology of a disease, if it is determined by a single gene, is best supported by the evidence of mendelian pattern of inheritance on pedigree analysis. Pedigree analysis also helps to resolve heterogeneity. Accordingly, pedigree charts were

Mode of ascertainment:

For segregation analysis detailed pedigree charts were prepared for all the Harijan households (Chaluvadi & Chanangi communities) in the following 4 villages:-

1. Kugve-Ambapura
2. Harekoppa
3. Bandagadde
4. Handigodu

In addition affected families of other castes were also studied in the following villages:-

1. Kolisalu -Uppar & Vokkaliga
2. Chikabilgungi - Vokkaliga
3. Baruve - Achar
4. Malilyooru -Ediga

The third group comprised of isolated family studies from several other villages:-

1. Sagar
2. Sagar Armanakeri
3. Belleyooru
4. Kanlepura
5. Kaladipura
6. Hirle

orthopaedic examination. In symptomatic individuals the history was also recorded. The abreviated proforma used for clinical evaluation is given in Appendix I.

Anthropometry

Following measurements were initially planned to be taken on all individuals as far as possible:-

Wt,Ht, Sitting Ht, Span, Total upper limb, Total lower limb, Upper arm, Lower arm, Hand, Middle finger, Lower leg, & Foot lengths. Later, the measurements were restricted to first six parameters.

Measurements were taken on a total of 246 subjects.

Radiological

All individuals above 2 years of age were examined radiologically. Pregnant women were excluded.

An anterio-posterior view of pelvis, including both hip joints, and a lateral view of dorso-lumbar spine were taken for all the studied subjects. In persons with clinically detectable malformations additional X-rays were taken and in dwarfs total skeletal survey was carried out in most instances. All people were brought to the Sagar General Hospital for taking of X-rays.

pedigrees studied were classified into one of the following groups:-

a) Normal

b) Average height, adults with pain in hip joints & low back, flexion deformity at hips, lumbar lordosis, waddling gait and severe osteoarthritis on X-ray of the hip joints.

c) Subnormal stature, hands reaching upto middle 1/3 or lower of thigh, with variable symptoms & malformations & characteristic radiological changes of spine with or without osteoarthrosis of the hip joints.

d) Dwarfs with dyaplasia of femoral head & spine with or without arthritis. In most instances other joints were also involved.

Analysis

The pattern of inheritance was analysed by inspection of pedigrees. Some of the representative charts are shown Fig. Nos. 4 to 10 The salient observations are as follows:-

1. Both males & females are affected, almost equally.
2. Earliest disease is noted around 8-10 years of age.

observations suggest the possibility of disease being caused by a mutant antosomal dominant gene.

5. In most instances of dwarfs both parents are affected suggesting that the dwarfism could be homozygous state of the dominant gene.

6. Generally osteoarthritis type of presentation is more common in older individuals and dysplastic type in younger ones.

7. Although, families are closely interrelated but the prevalence of consanguinity is not very high in history elicited upto 3 generations.

8. We have come across one marriage between two dwarfs. All the 3 children of theirs died within few hours to 2 days.

10. New cases continue to occur. In several instances total duration of illness was less than 14 years, ie the time when the disease was first recorded.

11. The radiological picture is characteristic of spondyloepiphyseal dysplasia. But in patients presenting with arthritic type of disease, spine is spared. Hip joints are almost invariably affected.

13. The clinico-radiological presentation of 3 types is quite similar in different communities (Chaluvadi, Chanangi, Vokkaliga, Achar, Ediga & Uppar).

14. The earliest radiological change observed was fragmentation of epiphysis in a child around 10 years of age who was otherwise asymptomatic.

15. The adaptation to disability is remarkable. Most affected individuals have difficulty & limitation in walking, squatting & sitting cross legged but they carry on their usual routine with extraordinary ease.

16. The disease does not appear to have any effect on longevity or reproductive ability. However, in some instances high fetal wastage and child mortality was observed.

17. The clinical onset is of two kinds. In most instances the onset is gradual & the course is slowly progressive. But in some cases the onset is very acute & severe making the individual bed ridden for several days. Thereafter, most of these individuals gradually recover but residual disability persists. Both kind of presentations were seen in the same pedigree.

7. SYNDROME DELINEATION

7.1 Clinical features

In the Survey carried out by the Meerut team, 286 individuals were found to be affected. Among these 200 were adults (67 men & 133 women) and 86 were children (51 boys & 35 girls). In the later category no child was found to be affected below 5 years of age.

The onset of the disease is insiduous in most instances. It follows a slow, progressive course spread over several years. In few cases relatively acute onset was also noted. The presenting feature is pain in low back. It is mild to moderate in intensity & gets aggravated on exertion. It spreads over to buttocks & knees, but there is no definite radiation. Alongwith pain walking gets limited and gait becomes abnormal. One characteristic complaint of most patients was inability to run or walk long distances. In early stages the most important physical sign was inability of the patient to sit cross legged on floor. Later they also find difficulty in squatting. At this juncture one can elicit restriction of movements at the hip joints, particularly of abduction & external rotation. As the disease progresses, patients develop flexion deformity

are noted around hip & knee joints. This includes shortness of limbs and tilting of pelvis alongwith alteration of anatomical landmarks around hip joint.

The most common clinical presentation (26.8%) was found to be flexion deformity at hip & knee joints with lumbar lordosis and limping. Limping, waddling gait, stiffness & pain in the back were observed in another 9.0% of the affected individuals. In almost similar number of cases (26.7%) genu valgam & genu varum deformities were noted at knee joints. These were associated with wind shift & rotational deformities of legs. Spinal deformities were present in 7.8% cases. About 12% patients were dwarfs and in 8.2% patients various congenital defects of fingers, toes, ears, eyes, nose, palate, limbs, & heart etc. were found to be associated with major manifestations of Handigodu disease (see Fig. 11 to 16).

None of the patients had goitre, renal stone, rickets, osteomalacia or fractures. However, 2 cases were found to be suffering with skeletal fluorosis. These cases have originated from Sagar town which is known to be endemic for it.

Premature and secondary degenerative

During the course of evaluation of families, the Lucknow team observed that on basis of stature, body proportions and radiological changes 3 presentations of Handigodu disease could be delineated (see p 51). But they did not differ significantly in onset, course and major clinical manifestations.

Knock knee appeared to be a relatively common finding in many asymptomatic children in affected families. Its significance remains to be evaluated.

7.2 Radiological Features (SGPGI, Lucknow)

X-ray examination of pelvis, including both hips, and lumbar spine was carried out in 475 individuals. X-rays of other bones & joints were taken where indicated. Out of 475 individuals examined, there were 229 males & 246 females. This included both normal as well affected family members. Each X-ray was examined by two individuals according to a predesigned scoring sheet. The following criteria were used for different diagnoses:-

1. Hip joints & Pelvis

An AP view of pelvis was taken in neutral position of hip joint. One limiting factor was that many patients had associated deformities of hip & spine which affected positioning. However, to a large extent there was no problem in classifying the changes into major groups.

a) Osteoarthritis

Narrowing of the joint space, sclerosis/irregularity of the articular margins (excluding browing of the upper-outer margin of acetabulum) and presence of osteophytes, singly or jointly, were taken as criterion

b) Presence of above changes in association with dysplasia of femoral head/greater trochanter/acetabulum was labelled as osteoarthroses. In such cases subarticular bony changes in form of cystic degeneration were present.

c) Dysplasia of femoral head, neck, greater trochanter

A wide variety of radiological changes were included under this heading. These depended upon appearance & development of epiphyses, closure of epiphyseal growth plate and moulding of bones. Various changes seen are summarised as follows:-

i) Flattening & fragmentation of epiphyses of femoral head (rare)

ii)Slippage & abnormal angulation of epiphyses of femoral head (uncommon)

iii) Delay in closure of epiphysis (difficult to interpret because of inaccuracies in chronological age)

iv) Replacement of round femoral head by flat, irregular, squashed terminal end of femoral neck mushrooming. This was usually associated with abnormalities in the shape of acetabulum, wide joint space and loss of articular alignment between femoral

vi) Abnormalities of epiphysis & epiphyseal plate of greater trochanter.

vii) Associated dysplastic abnormalities of pubis, ischium & ileum.

viii) Associated changes indicative of osteoarthroes of the hip joint, as described above.

2. Spine

A lateral view of dorsolumbar spine was taken for study of changes in spine. Height of vertebrae, appearance of end plates, intervertebral disc space and presence/absence of osteophytes was noted. Following changes were observed:-

1. Irregularity of the end plates.
2. Anterior scalloping and posterior hump, singly or jointly, of the adjoining end plates.
3. Wedge shaped appearance of vertebral with widening of inter vertebral disc space anteriorly .
4. Classical platyspondyly with marked narrowing of vertebrae.

Presence of any of the above changes was taken as indicative of presence of dysplasia of spine.

individuals some dysplasia of hips (37) or spine (28) or both (113) was the major finding. In 42 subjects (22 males, 20 females) multiple bones, including hips, spine and others, were affected by the dysplastic process.

Among 220 individuals with dysplasia, secondary osteoarthrosis was seen in 113 (51.4%) individuals; the prevalence in females being 52% & males 41.4%.

All types of radiological changes were seen to be segregating together in different pedigrees. This suggests that radiological findings represent pleiotropic manifestations of a single gene. It is well known in skeletal dysplasias that modelling of the bone improves with age. It is possible that in the group where only osteorthritic changes were seen, dysplastic changes were of milder nature, and have disappeared by the time of radiological examination. It can be confirmed by serial radiological studies. Likewise, dysplastic changes in bones other than hips & spine, indicate more severer manifestation of the same disease.

Correlation betwen radiological changes & anthropometric measurements (SGPGI, Lucknow)

height. In a another 14 (22.2%) the height was between -2 to -3SD of mean. The armspan was also greater than height, exceeding even 10 cms in 51.2 % of 41 individuals with involvement of spine & spine & hips. But where other bones were showing dysplastic changes (which would have included the bones of upper extremities as well), in only 3 out of 22 individuals (13.6%) the difference was greater than 10 cms compared to 6.3% in individuals without any radiological abnormalities.

On the basis of above following conclusions can be drawn:-

1) Longer arm span appears to be the characteristic of Chanangi & Chaluwadi communities. This was observed in individuals even without radiological changes (the difference between arm span & height was between 5-10 cms in 22.1% & more than 10 cms in 6.3%). However, among individuals with radiological changes of Handigodu disease, a much greater percentage had larger arm spans, particularly more than 10 cms, (between 5-10cms in 28.7% and more than 10 cms in 32.7%)

2) The height in patients with Handigodu disease is shorter than in normal controls of the same community; particulalry in those where x-rays show dysplastic

Radiological changes seen in x-rays taken by the Meerut Centre

The team from Meerut centre had taken x-rays of 213 patients with Handigodu Disease. There were 15 common patients between the Lucknow centre & Meerut centre. The evaluation of radiological changes at the 2 centre for same patients was similar. In the remainder 198 cases, X-rays were taken only by the Meerut team to avoid repeated exposure of the same subjects. The data for the entire 213 cases is shown in Table No. 37.

In 60 patients (28.17%), predominant change was of osteoarthroses. The age group of these individuals was higher than those of others. In 118 patients (55.4%), predominantly dysplastic changes were seen. These included various combinations, both in terms of parts of bones involved (epiphysis, metaphysis, diaphysis) and parts of the skeleton system involved (hips, spine, others). In 18 individuals (men only) changes suggestive of secondary hyperparathyroidism were recorded. Twelve cases (men only) had generalised osteosclerosis. In 5 patients exostoses were seen as an isolated finding.

7.3 Anthropometry

One striking feature in patients suffering with Handigodu disease was short stature and apparently long arms. However, the variation was quite marked. In order to evaluate these parameters objectively, particularly in growing children, a need was felt for establishing the anthropometric norms for the non-affected amongst Harijan community. The study was carried out on two hundred ninty eight, 5-17 year old normal children (both sexes) of Chanangi & Chaluwadi communities. The landmarks used for anthropometric studies are given in Appendix III. For this purpose following institutions were visited:-

1. Girls Hostel, Sagar
2. Harijan Boys Hostel, Sagar
3. Boys Hostel, Sagar
4. Primary school, Bandgadde
5. Higher Secondary school near Masoor.
6. Local schools at Hiremane, Talguppa, Tyagrathi, Anandpura & Gautempura

In addition, children from villages with sizable

check the ages of the children, but there were no records to substantiate the exact age of the children. Nevertheless, the height & weight curves suggest that ages were probably reliable. An additional set of antrhopometric measurements on 288 normal healthy adult males & females of the two communities were also undertaken. The data is given in Table No.38 & Fig Nos.29 & 36.

Most of the anthropometric data in adults was found to be normally distributed. Mean + 2 SD has, therefore, been used as cut-off for defining abnormalities. On this basis males below 145.3 cms & females below 134.5 cms were labelled as short statured in this community. For diagnosis of dwarfs height less than 130 cm in adults was taken as the cut-off point.

During the course of earlier clinical observations it has been seen that in patients with Handigodu disease span exceeds height by several cms. We have also noticed that the arms of patients with Handigodu disease often reach upto lower 1/3 of thigh. We, therefore, examined several individuals with span exceeding 10 cms of their height radiologically. We did not find any radiological evidence of Handigodu disease in these individuals. Thus, the measurement of span-height

appears to be the population characteristic of Chanangi & Chaluvadi's (Fig 33). The difference between arm span and height exceeded 5 cms in 26 (22½%) of normal healthy individuls, in 6·3% being greater than 10 cms.

8. SURGICAL & REHABLITATIVE ASPECTS

Dr. Sriniwas Murthy has follwed-up 30 patients of Handigodu disease whom he has evaluated & managed in 1975, after a period of more than 10 years. At follow-up he has observed that in patients below 12 years of age, where epiphyses of femoral head has not closed, its contour was maintained and the joint space has either remained normal or increased. In some there was premature closure of epiphysis. In patients above 12 years of age, the joint space was reduced, there was sclerosis of articular margins and marked secondary osteoarthritic changes have appeared. This may explain two types of presentation described under 7.1.

The indication for surgery was marked deformity. It was mostly in the form of corrective osteotomy with or without tenotomy. The operated patients have shown an improvement of 60-80%.

The list of the operated patients is given in Appendix VII. The remainder were treated with physiotherapy. According to his assesment of Prof. Sriniwas Murthy, the cases which were mildly affected have significantly improved over time, whereas moderate

The Govt. of Karnataka has provided a disability allowance to handicapped patients of Handigodu disease. Also, an unit has been set up for vocational training of these patients.

During the period of 11 years 16 deaths were recorded among approximately 350 patients suffering with Handigodu disease.

9. DISCUSSION

The role of genetic factors in causation of Handigodu disease has been suspected from begining. But because of apparent absence of disease in population prior to 1974 and simultaneous involvement of several generations at around the same time it was considered that some environmental factor has been responsible for trigerring of the disease in genetically succeptible individuals. However, no such environmental agent has been identified so far. Even the most comprehensive nutritional, water & environmental survey carried out in the present study did not reveal any environmental factor which can be incriminated in the causation of the disease.

Our studies show that Handigodu disease may be totally genetically determined. A single dominant gene could explain the pattern of disease seen in families. Also, the clinical & epidemiological features of Handigodu disease fit with genetic aetiology. Lack of detection of Handigodu disease prior to 1974 could be another example of a similar experience in Amish population where high prevalence of Elis Van-Crevald Syndrome was detected fortuitiously. The high prevalence

dominant type. It remains to be examined whether Handigodu disease fits with one of the described entities of SED tarda or is a new one.

According to our observations the heterozygous form of Handigodu disease presents as one of two alternate phenotypes. In one, the arthritic type of presentation, individual is of average height, spine is spared and radiological changes at hip joints are predominantly of osteorarhtitic type. In the other form, the dysplastic type of presentation, head next of femur is greatly deformed which appears flattened and mushroom shaped, secondary osteoarthrotic changes if present are limited and spine frequently shows abnormalities. The spinal abnoramalities include platyspondyly as well as presence of exuberations in the posterior half of both superior and inferior surfaces of vertebrae. The later type of changes in spine are often associated with deficiency in ossification of anterior part of vertebral apophyseal plates presenting as anteriorly placed 'Schmorl' nodes. In the second phenotype, affected individuals are often short statured, arms appear longer reaching to lower third of thigh and various minor malformations such as short great toe (or other toes), varus deformity at

because both forms segregate together in the same families. The differences could be due to age of onset, severity of disease or pleiotropis of gene effect.

The third clinical entity is the dwarfs. It appears to represent homozygous state of the dominant SED gene. Dwarfs are usually seen where both parents are affected (or could have carried the gene). The major clinical & radiological findings in dwarfs are similar to second phenotype of heterozygous state i.e. of dysplastic variety except that the spinal changes are considerably more marked leading to truncal type of dwarfism. Also, in dwarfs other joints including knees, wrists, ankles, shoulder etc. are often involved.

On the basis of inspection of pedigrees it appears that the gene in question has variable penetrance. This could explain occurrence of the disease in families where both parents are normal but there is a positive family history of Handigodu disease.

The disease does not manifest clinically until the end of first decade. Earliest radiological changes are seen around 10 years of age. A suitable age related correction factor would have to be computed for proper evaluation of segregation ratios. Also, the segregation

Chikamagalore district. However, a close resemblence of radiological picture of the patients from two areas and earlier observations by Bhat & Krishnamachari that the two populations are related, suggests that the problem at Chikamagalore district may also be the same. It remains to be examined.

The fact that the Handigodu disease is single gene determined disease lends itself to the possibilities of appropriate genetic counselling. It could be possible to identify the affected individuals at around 10 years of age by a plain X-ray of pelvis in all children of affected families. Theoretically, elimination of weight bearing at this stage for several years may protect them from subsequent crippline & morbidity. This deserves to be tested.

Another major observation of the present study was the identification of marked deficiency in daily dietary intake of calcium. The nutritional survey data was supported by biochemical & histomorpho-metric evidences of compensatory increase in (OH)2 it D3 and secondary hyperparathyroidism in these patients. Although, calcium

10. CONCLUSIONS

On the basis of comprehensive multidisciplinary study carried out by the ICMR team from 1986-89, the following conclusions are drawn:-

a) Genetic studies

i) Handigodu disease is a genetically determined disease of bones, predominantly affecting the epiphyses of femoral heads & vertebral end plates. (spondylo-epiphyseal dysplasia tarda). Other bones may also be involved.

ii) The disease is inherited in an autosomal dominant pattern indicating a risk of 50% to siblings & off-springs of affected individuals.

iii) The heterozygotes may present in one of two forms; either Arthritic form or Dysplastic form. The major distinction between the two types is on basis of radiological examination of hip joints. Clinically, the affected individuals of the arthritic form are of normal height while of dysplastic form are short statured (mainly truncal).

iv) Dwarfs represent the homozygous state for the

vi) The earliest change is radiological. It appears around 8-10 years of age. This includes fragmentation & reduction in height of epiphyses of femoral head. Clinically, at this stage the only difficulty may be in form of inability to squat or sit cross-legged.

b) NUTRITIONAL, BIOCHEMICAL, METABOLIC STUDIES including histomorphometric studies of the bones.

i) The diet of Harijans was grossly deficient in calcium & vitamin D intake. The calcium intake was deficient by as much as 700-900 mg per day in all age groups & both sexes. The deficiency of vit D intake appears to be compensated by sun-light exposure.

ii) There was marked negative balance of calcium in 5 patients studied in detail (-26 to -70 mg/day). However, it could change to positive balance (+97to+215 mg/day) on diet containing 850 mg calcium per day. Negative calcium balance in population was reflected by low calcium excretion in urine.

iii) Deficiency of calcium intake could have aggravated the clinical presentation by inducing secondary hyperparathyroidism. The serum I-34 HPTH levels in 30 adult patients were 135.4 + 141.4 pg/ml compared to less

iv) There was no clinical or radiological evidence of rickets, or osteomalacia in the Harijan population. Also, the changes were not indicative of fluorosis.

v) All the other biochemical & metabolic studies did not reveal any abnormality. Urinary screening tests for mucopolysaccharides were negative.

c) **Environmental studies**

i) There was no evidence of any environmental or industrial pollution which could have selectively affected the Harijans in discrete villages.

ii) A comprehensive water analysis from a variety of sources did not reveal any abnormality. In fact the levels of all trace elements & heavy metals in water samples were on the lower side of normal. The water was stored in earthen wares in the Harijan households.

iii) The analysis of water, air, food samples & hair clipping for heavy metals also did not show any abnormality.

iv) Detailed interogation in all the surveyed villages did not provide any evidence for presence of toxins, excessive use of pesticides & crabs. The population needs to be reassured on this account.

and 71 amongst non-Harijan-Non-Brahmins.

iii) The prevalence of disease in Harijans was 9.7%; being 7.1% in adults & 2.6% in children upto 18 yrs of age.

iv) Dwarf survey of the entire taluk revealed some additional pockets of Handigodu disease, but still the microdistribution of disease was extremely patchy.

v) Marital survey revealed that the affected community is already practising genetic counselling instinctively.

vi) Anthropometric survey revealed that the average height of adult males & females in Harijans was 159.07+6.78 & 146.78+6.15 cms, respectively. Corresponding arm spans were 166.08+7.9 & 152.78+7.67 cms. 5 cms in 28.4% & The arm span exceeded the height by more than 5 cms in 28.4% & 10 cms in 6.3% of the normal healthy individuals. The ratio of sitting height to total height varied from 0.47 to 0.53. These norms could be of great relevance in identifying & classifying the affected individuals.

11. RECOMMENDATIONS

11.1 Therapeutic and Preventive Strategies

1. The therapy of the affected individuals should include improvement in nutritional status (particularly of calcium nutrition), correction of nutritional deficiencies, use of analgesics, physiotherapy, rehabilitation and surgical correction of the deformities including use of appropriate braces.

2. The preventive strategy on basis of results of the currer study could be as follows:-

(i) appropriate genetic counselling

(ii) improvement of calcium and Vitamin D nutrition status of the individuals at risk.

3. Ohter improvement strategies in the village scenario should be undertaken simultaneously to make the preventive measures more effective and to obtain the cooperation of all the villagers for the success of the programme. Long term strategies for prevention (genetic) and nutritional improvement should also be planned.

4. The improvement strategies should also include facilities for health and family welfare, education and total development of the village scenario, including:-

(iii) The Rural Landless Employment Guarantee Programme (RLEGP).

Such programmes should be aggressive and targeted to the most vulnerable, needy and the affected community of Harijans which also constitutes the rural poorest. This shall assist in their rising out of impoverishment, rehabilitation, resettlement, achievement of self sufficiency and change in life style. These all factors will be very rewarding in achieving the ultimate goal of prevention and eradication of the Handigodu syndrome.

11.2 Future research plans

Having found that the Handigodu disease is a single gene determined disease does not solve the problem entirely. As mentioned above one of the most important steps to follow is to detect the disease at asymptomatic stage and to evaluate various modalities for prevention of progression of the disease/disability. While this may serve as one of the most important immediate needs, it would not eliminate the genetic load of the disease in the population. The later calls for detailed biochemical and molecular studies for finding a lasting solution. It is recommended that informative pedigrees should be identified and linkage studies with collagen genes be done to identify the gene/genes responsible for Handigodu skeletal dysplasia, if possible. Knowing the location of the abnormal gene and precise mutation resulting in appearance of the Handigodu syndrome of spondylo-epiphyseal dysplasia, shall (a) give insight into pathophysiology of the disease, and b) useful for precise and early diagnosis which may forestall the onset of dysplasia and provide opportunities for preventive management.

1. Follow up of patients and families previously studied to evaluate the course of progression of the disease.

2. Short survey & detailed clinical evaluation of patients in Chickamagalore district for confirmation of the identity of the syndrome in two places (viz Shimoga and Chickamagalore district).

3. Education of public regarding genetic and nutritional aspects of the disease to prepare them for the intervention programme comprising of nutritional and genetic counselling.

4. To study the effectiveness of calcium and vitamin D supplemenation in the control and progression of Handigodu disease.

5. Detailed clinico-radiological evaluation of dwarfs in the Sagar Taluk to delineate genetic heterogeneity.

6. Detailed biochemical analysis of collagen metabolism and proteoglycans from cartilagenous tissue of patients with Handigodu disease to understand the pathophysiology of skeletal dysplasia.

7. DNA linkage studies to collagen genes to identify a possible genetic marker for premorbid diagnosis and

ACKNOWLEDGEMENTS

The generous support of ICMR for carrying out the study is gratefully acknowledged. The success of the project is largely due to dependent on the keeness & interest of Dr. B.N. Saxena, the Sr. Deputy Director General of ICMR. Equally important was the generous hospitality & support of Karnataka Govt.'s medical department. All the Directors & doctors in the Directorate (Dr T. Rangnath Achar Dr. Krishnamachari), and Shimoga District Hospital (Dr. Bilgi, Dr. Halgi & their staff) as well as at Sagar General Hospital (Dr. H. Sriniwas and Dr. G. Meetya Naik) were actively involved in the entire study. The assistance of local ICMR unit of the Handigodu project (Dr. Mayur Nath, Deputy Director ICMR, Dr. S.Krishnamurthy & Dr. Petkar) was invaluable. Dr. Rakesh Mittal, Sr Research officer, ICMR provided the needed cooperation at ICMR headquarters.

The technical staff of Sagar General Hospital deserves a word of special mention. The entire infrastructure of the hospital including the ANMS, and Technicians etc. wholeheartedly contributed towards the success of the study. The X-ray technicians and

our sincere appreciation for their cooperation.

The most important pillar of the entire field study was Mr. H.M. Chandrashekhar, the social messiah from the Handigodu village, whose selfless devotion could make it possible to mobilise the entire population. Without his active participation it would have been hard to carry out the large scale pedigree based radiological survey which was one of the key ingredients of the epidemiological genetic study. He with Mr. Nagraja conducted the village-wise survey of the entire Sagar Taluk for micro-mapping of Dwarfs and Handigodu disease besides evaluation of village marital relationships. Mr. Nagaraja also accompanied the patients to Meerut for detailed clinical & laboratory studies at the cost of his own occupation.

A word of acknowledgement for the research staff. for Lucknow centre Dr. Anand Kumar, Dr. J.P. Sharma (ROS), Mr. S.K. Sharma and Dr. R.B. Gupta of RMRC, Jabalpur deserve special mention. Without their leaving their homes the study would not have seen the light of the day. Dr. Shubha Phadke has actively participated in the analysis of radiological data. Also, our thanks

sunset with the investigator, is greatly appreciated. In addition, the hard work of Miss Alka Samalia in preparation of the report, technical assistance of Dr. M. Nath, Mr. R.B. Yadav, Mr, Vidya Ram & Mr. Jitendra Singh in the analysis of the samples, of Miss Swapna Chaturvedi, Mr. K. P. Varma & Mr. Pritam Singh in data analysis and of Mr. Y John in typing of the report is grateful acknowledged.

Last but not the least the unsung heroes are the patients and their relations who reposed their unabiding faith in us and wholeheartedly volunteered, themselves for the study. We owe them a debt of gratitude and our all the results are dedicated to them.

Finally, the credit for putting the report on record goes to Ms Seema Dixit who has carried out endless editings on the word processor & fought with printers to prepare this report.

List of Tables

List of Appendixes

Table No. 1

VILLAGES IN SAGAR TALUK & ADJOINING AREAS KNOWN TO BE AFFECTED WITH HANDIGODU DISEASE

Sr. No.	Name of Village/ Hamlet	Total No. of cases	Caste
	SAGAR TALUK		
1	Sagar Armanekeri	6	Chaluvadi
2	Balgodu	3	Channangi
3	Bandagadde	34	Channangi
4	Belur	6	Channangi
5	Beleyooru	7	Channangi
6	Bhemankone	1	Channangi
7	Bommathi	3	Channangi
8	B.Manchale	11	Channangi
9	Chikabilgunji	14	Vokkaliga
10	Ganganahonda	1	Chaluvadi
11	Gijagaru	1	Chaluvadi
12	Handigodu	50	Chaluvadi
13	Harokoppa	13	Chaluvadi
14	Hirethota	7	Ediga
15	Hosanthe	6	Vokkaliga
16	Kagodu Dimba	7	Channangi
17	Kalasipete	11	Channangi
18	Kanle	3	Channangi
19	Kanlepura	14	Channangi
20	Karehonda	8	Channangi
21	Keladipura	19	Chaluvadi
22	Kelagimane	2	Vokkaliga
23	Khandika	1	Channangi
24	Kolisalu	7	Vokkaliga/Uppara
25	Kudigere	7	Vokkaliga
26	Kugve-Ambapura	16	Channangi
27	Lingadahalli	11	Channangi
28	Maliliyooru	7	Ediga
29	Mandagalale	3	Chaluvadi
30	Maneghatta	2	Channangi
31	Mkangodu	9	Channangi

Table No. 2

CENSUS DATA OF SAGAR TALUK, 1981

1	Area	19384 Sq. Km.
2	Revenue Divisions	
	Hoblies	6
	Mandals	17
	Villages	269
	Hamlets	977
3	Population	
	(a) Male	82,282
	Female	77,985
	Total	160,267
	(b) Rural	108,343
	Urban	51,924
	(c) Scheduled Caste (Harijans)	13,969
	Sheduled Tribes	2,375

Table No.3

Laboratory investigations in Handigodu Syndrome.

	Cases (45)	Controls (13)
Hb below 13 gm%	27%	36%
Eosinophils above 1000/cumm.	73%	38%
Toxic granuls in neutrophils	12%	54%
ESR>20mm	52%	60%
Normal Serum protein electrophoresis	75%	85%
Alk Phos> 13KA.	100% (16-26 KA)	100% (16-25 KA)
LFT	N *	N
Albuminuria	3	0
VDRL postive at dilution of 1:8 or above	3**	0
CRP positive	21/41	Not tested
Rose Waaler test positive	14/41	Not tested
CSF***	N	Not tested
ECG	N+	N
EMG/Nerve Cond#	N	N

Mani & Srinivasamurthy 1975

*Indices in one patient indicated mild liver dysfunction

** Two were husband & wife.

***CSF examination was done in 10 patients. In one it was traumatic. CSF VDRL was negative in all.

+ In 6 individuals (4 below 10 years & 2 of 12 & 15 years age) there were inverted T waves in leads V1-3 associated with ST segment changes.

Table No. 4

Radiological findings in Handigodu Disease

	Hips	Knees	Ankles	Wrists	Shoulders
Normal	0	3	1	13	21
Mild	6	10	1	11	7
Moderate	5	18	1	14	7
Severe	21	9	1	2	2
Gross	9	1	0	0	0
Total	41	41	4	40	37

Mani & Srinivas Murthy 1975

Table No. 5

Hamlets selected for door to door survey in Sagar Taluk

Hobli	Village	Hamlet
Kasaba	Balgodu	
	Beluru	
	Brahman	Bomatthi
	Manchale	Karehonda
	Chikka-Nelluru	Beleyooru Maneghatta
	Eli	Handigodu
	Ganganhonda	
	Keladi	Keladipura
		Bandagadde
		Harokoppa
	Madasura	Lingadahalli
	Malla	Kagod-Dimba
	Malve	Kolisalu
	Nada Kalasi	Kalasipete
		Umbalibylu
	Nada Manchale	Kangodu
	Neechadi	

Anandapuram	Chikkabilagunji	
	Gantinkoppa	Karekoppa
	Kudigere	
	Yedehalli	Malaligadde
Avinahalli	Gensinakuni	Hirethota

Table No.6

Communitywise distribution of population in surveyed villages/hamlets

Community	Households No	%	Total population No.	%	No. of persons per household
Harijans	562	26.3	2469	22.1	4.39
Non-Harijan Non-Brahmin	1085	50.8	6376	57.2	5.88
Brahmin	405	19.0	2313	20.7	5.71
Total	2052*		11158		

* The total no. of households was 2134. Of these 82 were found locked.

Table No.7

age & sexwise distribution of population surveyed.

Community	Adults			Children			Adult: Children	M:F
	M	F	T	M	F	T		
Harijans	741	738	1479	518	472	990	1.46	1.04
Non-Harijan Non-Brahmin	1869	1773	3642	1321	1413	2734	1.33	1.01
Brahmin	847	872	1719	319	275	594	2.84	1.02
Total	3457	3383	6840	2158	2160	4318		

*0-18 years of age

Table No.8

Agewise distribution of Child population surveyed in different comunities

	0-5			5-10			10-18			Total
	M	F	T	M	F	T	M	F	T	
Harijans	126	150	276	198	146	344	194	176	370	990
Non-Harijan Non-Brahmin	322	365	687	373	409	782	626	639	1265	2734
Brahmin	76	69	145	69	76	145	174	130	304	594
	524	584	1108	640	631	1271	994	945	1939	4318

Table No.9

Distribution of Adult female population

	Unmarried	Non Pregnant	Pregnant	Lactating	Post menopausal	Total
Harijans	149	337	14	63	180	743
Non-Harijan Non-Brahmin	346	837	13	121	447	1764
Brahmin	167	417	1	24	267	876
	662	1591	28	208	894	3383

Table No. 10

Prevalence of Handigodu Disease communitywise & villagewise

SL NO.		SURVEYED				EXAMINED				AFFECTED			
		Hari-jans	Non-Hari-jans	Brah-mins	Total	Hari-jans	Non-Hari-jans	Brah-mins	Total	Hari-jans	Non-Hari-jans	Brah-mins	Total
1	Kudigere	113	210	-	323	101 (89.4)	177 (84.3)	-	278 (86.1)	10 (9.9)	8 (4.5)	-	18 (6.5)
2	Chikabilagunji	-	185	-	185	-	164 (86.1)	-	164 (86.1)	-	8 (4.9)	-	8 (4.9)
3	Kalasipete	70	79	-	149	70 (100.0)	79 (100.0)	-	149 (100.0)	11 (15.7)	-	-	18 (6.9)
4	Kanlepura	56	6	9	71	56 (100.0)	6 (100.0)	9 (100.0)	71 (100.0)	18 (32.1)	3 (50.0)	-	21 (29.6)
5	Kanle	154	746	135	1035	154 (100.0)	147 (100.0)	135 (100.0)	1035 (100.0)	3 (1.9)	6 (0.8)	-	9 (0.9)
6	Lingadahalli	61	221	104	386	48 (78.7)	193 (87.3)	104 (100.0)	345 (89.4)	15 (31.3)	18 (9.3)	-	33 (9.6)
7	Handigodu	92	26	153	271	92 (100.0)	26 (100.0)	153 (100.0)	271 (100.0)	43 (46.7)	-	-	43 (15.9)
8	Kolisalu	-	165	-	165	----------NOT EXAMINED----------							
9	Beleyooru	91	106	170	367	73 (80.2)	102 (96.2)	170 (100.0)	345 (94.0)	9 (12.3)	-	-	9 (2.9)
10	Bomathi	15	128	32	175	15 (100.0)	128 (100.0)	32	175 (100.0)	-	2 (1.6)	-	2 (1.1)
11	M. Manchale Kangod	25	13	80	118	19 (76)	10 (76.9)	80 (100.0)	109 (92.4)	5 (26.3)	-	-	5 (4.6)
12	B. Manchale	50	-	120	170	50 (100.0)	-	114 (95.0)	164 (96.5)	----------NONE----------			

SL NO.		SURVEYED				EXAMINED				AFFECTED			
		Hari-jans	Non-Hari-jans	Brah-mins	Total	Hari-jans	Non-Hari-jans	Brah-mins	Total	Hari-jans	Non-Hari-jans	Brah-mins	Total
21	Hirethota	-	37	34	71	-	37 (100.0)	34 (100.0)	71 (100.0)	----------NONE----------			
22	Appemane	-	46	106	152	-	46 (100.0)	106 (100.0)	152 (100.0)	2 (2.2)	-	2 (0.7)	
23	Pura	33	82	64	179	33 (100.0)	82 (100.0)	64 (100.0)	179 (100.0)	-	3 (3.1)	3 (1.7)	
24	Belooru	121	478	179	778	114 (94.2)	449 (93.9)	176 (98.3)	739 (95.0)	2 (1.8)	2 (0.5)	-	4 (0.5)
25	Manehatta	42	256	36	334	42 (100.0)	256 (100.0)	36 (100.0)	334 (100.0)	----------NONE----------			
26	Ganganhonda	8	-	-	8	8 (100.0)	-	-	8 (100.0)	3 (37.5)	-	-	3 (37.5)
27	Karehonda	335	-	-	335	328 (97.9)	-	-	328 (97.9)	8 (2.4)	-	-	8 (2.4)
28	Khandika	93	51	121	265	93 (100.0)	51 (100.0)	121 (100.0)	265 (100.0)	----------NONE----------			
29	Geejagaru	92	63	175	330	92 (100.0)	63 (100.0)	175 (100.0)	330 (100.0)	----------NONE----------			
30	Umbalibylu	-	133	-	133	-	125 (94.0)	-	125 (94.0)	-	4 (3.2)	-	4 (3.2)
31	Kagodudimba	71	152	-	223	71 (100.0)	133 (87.5)	-	204 (91.5)	2 (2.8)	1 (0.8)	-	3 (1.5)
32	Neechadi	67	10	236	313	45 (67.2)	10 (100.0)	232 (98.3)	287 (91.7)	3 (3.7)	-	1 (0.4)	4 (1.4)
33	Harokoppa	66	40	97	203	54 (81.8	35 (87.5)	97 (100.0)	186 (91.6)	14 (25.9)	-	-	14 (7.5
34	Bandagadde	175	78	111	364	73 (41.7)	46 (59.0)	105 (94.6)	224 (61.5)	8 (1.0)	-	-	8 (3.6)
35	Barauve	-	61	-	61	----------NOT EXAMINED----------							

Table No. 11

PREVALENCE OF HANDIGODU DISEASE COMMUNITYWISE

	All age groups			Adults			Children		
Harijans	T	M	F	T	M	F	T	M	F
Surveyed	2469	1259 (51)	1210 (49.0)	1479 (59.9)	741 (30.0)	738 (29.9)	990 (40.1)	518 (21.0)	472 (19.1)
Examined	2207 (89.4)	1128 (45.7)	1079 (43.7)	1331 (59.9)	670 (27.1)	661 (26.8)	876 (35.5)	458 (18.6)	418 (16.9)
Affected	214 (9.7)	92 (4.2)	122 (5.5)	157 (7.1)	52 (2.4)	105 (4.7)	57 (2.6)	40 (1.8)	17 (0.7)
Non-Brahmin Non-Harijan									
Surveyed	6376	3190 (50.0)	3186 (50.0)	3642 (57.1)	1869 (29.3)	1773 (27.8)	2734 (42.9)	1321 (20.7)	1413 (22.2)
Examined	5873 (92.1)	2973 (46.1)	2935 (46.0)	3369 (52.8)	1727 (27.1)	1642 (25.7)	2504 (39.3)	1211 (19.0)	1293 (20.3)
Affected	71 (1.2)	46 (0.8)	25 (0.4)	42 (0.7)	14 (0.2)	28 (0.5)	29 (0.5)	11 (0.2)	18 (0.3)
Brahmins									
Surveyed	2313	1166 (50.4)	1147 (49.6)	1719 (74.3)	847 (36.6)	872 (37.6)	594 (25.7)	319 (13.8)	275 (11.9)
Examined	2290 (99.0)	1154 (49.9)	1136 (49.1)	1705 (73.7)	840 (36.3)	865 (37.4)	585 (25.3)	314 (13.6)	271 (11.7)
Affected	1 (0.04)	1 (9.04)	None	1 (0.04)	1 (0.04)	None	None	None	None

Table No. 12

Prevalence of Handigodu Disease in Non Harijan/Non-Brahmines communitywise

	VILLAGES	SURVEYED									EXAMINED									AFFECTED								
		Total			Adults			Children			Total			Adults			Children			Total			Adults			Children		
		M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
1	Kudigere	50	53	113	37	30	67	23	23	49	54	47	101	35	26	61	19	21	40	6	4	10	3	3	6	3	1	4
2	Chikkabilagunji	NO HARIJAN COMMUNITY IN																										
3	Kalasipete	29	41	70	20	19	39	9	22	31	29	41	70	20	19	39	9	22	31	4	7	11	3	6	9	1	1	2
4	Kanlepura	28	28	56	18	19	37	10	9	19	28	28	56	18	19	37	10	9	19	8	10	18	5	6	11	3	4	7
5	Kanle	78	76	154	43	49	92	35	27	62	78	76	154	43	49	92	35	27	62	1	2	3	1	2	3	NONE		
6	Lingadehalli	26	35	61	15	19	34	11	16	27	21	27	48	10	15	35	11	12	23	8	7	15	3	4	7	5	3	8
7	Handigodu	44	48	92	20	35	55	24	13	37	44	48	92	20	35	55	24	13	37	19	24	43	11	23	34	8	1	9
8	Koli Salu	NO HARIJAN COMMUNITY IN																										
9	Beleyooru	48	43	91	26	27	53	22	16	38	38	35	73	20	21	41	18	24	32	4	5	9	-	5	5	4	-	4
10	Bommathi	8	7	15	4	4	8	4	3	7	8	7	15	4	4	8	4	3	7	NONE AFFECTED								
11	M. Manchale Kangodu	14	11	25	9	4	13	5	7	12	9	10	19	6	3	9	3	7	10	3	2	5	1	2	3	2	-	2
12	B. Manchale	30	20	50	15	14	29	15	6	21	30	20	50	15	14	29	15	6	21	NONE AFFECTED								
13	Keladipura	59	71	130	39	43	82	20	28	48	47	58	105	31	35	66	16	23	39	11	10	21	6	9	15	5	1	6
14	Sangla	24	27	51	17	16	33	7	11	18	24	27	51	17	16	33	7	11	18	1	4	5	1	4	5	NONE		
15	Kugwe	34	34	68	17	16	33	17	18	35	27	25	52	13	12	25	14	13	27	4	6	10	4	5	9	NONE		
16	Saidoor	39	44	83	26	25	51	13	19	32	39	44	83	26	25	51	13	19	32	1	3	4	-	3	3	1	-	1
17	Balgodu	34	28	62	23	20	43	11	8	19	32	26	58	23	19	42	9	7	16	2	1	3	-	1	1	NONE		
18	Hodabatte	33	43	76	23	26	49	10	17	27	33	43	76	23	26	49	10	17	27	1	1	2	1	1	2	NONE		
19	Malalagadde	4	9	15	3	5	8	3	4	7	4	9	15	3	5	8	3	4	7	1	1	2	1	1	2	NONE		
20	Othagodu	21	22	46	12	11	23	9	11	20	21	22	46	12	11	23	9	11	20	1	2	3	1	2	3	NONE		
21	Hirethota	NO HARIJAN COMMUNITY IN																										
22	Appemane	NO HARIJAN COMMUNITY IN																										
23	Pura	18	15	33	11	10	21	7	5	12	18	15	33	11	10	21	7	5	12	NONE AFFECTED								
24	Belooru	66	55	121	45	37	82	21	18	39	63	51	144	43	35	78	20	16	36	2	-	2						
25	Manegatta	21	21	42	15	16	31	6	5	11	21	21	42	15	16	31	6	5	11	NONE AFFECTED								

26	Ganganhonda	5	3	8	5	3	8	NONE			5	3	8	5	3	8	NONE			2	1	3	2	1	3	NONE			
27	Karehonda	176	157	335	92	97	189	86	60	146	176	152	328	91	95	186	85	57	142	6	2	8	3	2	5	3	-	3	
28	Khandika	50	43	93	26	27	53	24	16	40	50	43	93	26	27	53	24	16	40	----------NONE AFFECTED----------									
29	Geejagaru	50	38	88	32	22	54	22	16	38	50	38	88	32	22	54	22	16	38	----------NONE AFFECTED----------									
30	Umbali Bylu	----------NO HARIJAN COMMUNITY IN ----------																											
31	Kagodudimba	40	31	71	27	22	49	13	9	22	40	31	71	27	22	49	13	9	22	1	1	2	1	1	2	NONE			
32	Neechadi	38	29	67	15	19	34	23	10	33	24	21	45	11	13	24	13	8	21	-	3	3	-	3	3	NONE			
33	Harokoppa	32	34	66	20	25	45	12	9	21	27	27	54	17	20	37	10	7	17	4	9	13	2	8	10	2	1	3	
34	Bandagadde	86	89	175	52	53	105	34	36	70	37	36	73	23	22	45	14	14	28	2	6	8	2	5	7	-	1	1	
35	Beruve	----------NO HARIJAN COMMUNITY IN ----------																											
36	Kerekoppa	4	4	8	3	1	4	1	1	4	4	4	8	3	1	4	1	1	4	----------NONE AFFECTED----------									
37	Malaliyuru	15	16	31	7	7	14	8	9	17	4	6	10	2	2	4	2	4	6										
38	Mandagalele	37	35	72	24	17	41	13	13	31	37	35	72	24	17	41	13	13	31	-	1	1	-	1	1				

Table No. 13

Prevalence of Handigodu Disease in Non Harijan/Non-Brahmines communitywise

	SURVEYED							EXAMINED							AFFECTED						
	Total	Adults			Children			Total	Adults			Children			Total	Adults			Children		
		M	F	T	M	F	T		M	F	T	M	F	T		M	F	T	M	F	T
1 Edigas	2738	762	146	1508	611	619	1230	2638	739	717	1456	592	590	1182	17	1	9	10	2	5	7
2 Lingayats	590	217	182	396	100	94	194	542	196	171	367	89	86	175	12	2	2	4	3	5	8
3 Vokkaligas	1117	335	308	643	216	258	474	957	288	268	556	178	223	401	25	6	9	15	4	6	10
4 Poojars/Poojary	293	83	76	159	57	77	134	262	71	66	137	52	73	125	1	-	1	1	NONE		
5 Achars	129	41	33	74	26	29	55	68	24	17	41	14	13	27	5	1	-	1	2	2	4
6 Uppars	168	40	48	88	37	43	80	113	28	32	60	25	28	53	1	-	1	1	NONE		
7 Muslims	61	15	16	31	20	10	30	60	14	16	30	20	10	30	----------NONE AFFECTED----------						
8 Madiwal/Madiuala	421	124	117	241	81	99	180	397	118	112	230	74	93	167	3	1	2	3	NONE		
9 Shetty	99	26	28	54	26	19	45	90	24	25	49	23	18	41	1	1	-	1	NONE		
10 Gowdas	113	40	45	85	14	14	28	113	40	45	85	14	14	28	----------NONE AFFECTED----------						
11 Mogaveera	47	17	12	29	11	7	18	41	16	11	27	10	4	14	1	-	1	1	NONE		
12 Barber	30	7	10	17	5	8	13	30	7	10	17	5	8	13	----------NONE AFFECTED----------						
13 Kumhar/Potmaker	80	18	22	40	17	23	40	80	18	22	40	17	23	40	----------NONE AFFECTED----------						
14 Bhandari/Bhandar	46	12	16	28	8	10	18	46	12	16	28	8	10	18	----------NONE AFFECTED----------						
15 Nayaks	32	12	9	21	5	6	11	31	11	9	20	5	6	11	----------NONE AFFECTED----------						
16 Devidiga	104	34	29	63	19	22	41	99	33	29	62	17	20	37	----------NONE AFFECTED----------						
17 Bunts	20	6	6	12	1	7	8	20	6	6	12	1	7	8	----------NONE AFFECTED----------						
18 Bovy	23	9	6	15	5	3	8	23	9	6	15	5	3	8	----------NONE AFFECTED----------						
19 Rama Khasthriya	3	2	1	3		NONE		3	2	1	3		NONE		----------NONE AFFECTED----------						
20 Divaru	35	11	8	19	9	7	16	35	11	8	19	9	7	16	----------NONE AFFECTED----------						
21 Channaya	4	1	1	2	-	2	2	4	1	1	2	-	2	2	2	1	1	2	NONE		
22 Vishnubakta	3	2	1	3		NONE		3	2	1	3		NONE		----------NONE AFFECTED----------						
23 Christian	2	1	1	2		NONE		2	1	1	2		NONE		1	1	-	1	NONE		
24 Nrishars	4	1	1	2	-	2	2	4	1	1	2	-	2	2	----------NONE AFFECTED----------						
25 Badogi	5	1	1	2	1	2	3	5	1	1	2	1	2	3	----------NONE AFFECTED----------						
26 Mahiyalis	1	1	-	1		NONE		1	1	-	1		NONE		----------NONE AFFECTED----------						
27 Daivajna	5	1	1	2	1	2	3	5	1	1	2	1	2	3	----------NONE AFFECTED----------						
28 Dombane	5	1	1	2	1	2	3	5	1	1	2	1	2	3	----------NONE AFFECTED----------						
29 Shastria	4	1	1	2	1	1	2	4	1	1	2	1	1	2	----------NONE AFFECTED----------						
30 Malabars	15	3	3	6	3	6	9	15	3	3	6	3	6	9	----------NONE AFFECTED----------						

31	Goldsmith	39	10	12	22	11	6	17	39	10	12	22	11	6	17	----------NONE AFFECTED----------			
32	S.T.S.	26	5	8	13	8	5	13	26	5	8	13	8	5	13	----------NONE AFFECTED----------			
33	JOGI	26	5	6	11	7	8	15	24	4	6	10	7	7	14	2	-	2	2	NONE
34	Bilava	17	7	3	10	2	5	7	17	7	3	10	2	5	7	----------NONE AFFECTED----------			
35	Gaugamatha	15	5	3	8	3	4	7	15	5	3	8	3	4	7	----------NONE AFFECTED----------			
36	Mager	5	1	1	2	1	2	3	5	1	1	2	1	2	3	----------NONE AFFECTED----------			
37	Konkni	5	1	1	2	2	1	3	5	1	1	2	2	1	3	----------NONE AFFECTED----------			
38	Balgor	6	3	2	5	-	1	1	6	3	2	5	-	1	1	----------NONE AFFECTED----------			
39	Ganiga	7	1	1	2	4	1	5	7	1	1	2	4	1	5	----------NONE AFFECTED----------			
40	Vishwakar	5	2	1	3	-	2	2	5	2	1	3	-	2	2	----------NONE AFFECTED----------			
41	Namdev	4	1	1	2	-	2	2	4	1	1	2	-	2	2	----------NONE AFFECTED----------			
42	Kunchatiga	24	7	5	12	8	4	12	24	7	5	12	8	4	12	----------NONE AFFECTED----------			

Table No. 14

MARITAL PATTERN IN SELECTED VILLAGES AMONGST HARIJANS OF SAGAR TALUK

	Affected Village	Unaffected Village
CHALUVADI	a	b
a) Total No. of villages studied	8	5
b) Total No. of couples living	145	90
c) Couples with bride from affected village	120 (80%)	Nil (0%)
d) Couples with bride from unaffected village	25 (20%)	90 (100%)
CHANANGI	c	d
a) Total No. of villages studied	8	9
b) Total No. of couples living	174	148
c) Couples with bride from affected village	124 (71.3%)	17 (11.5%)
d) Couples with bride from unaffected village	50 (28.7%)	131(88.5%)

a. Handigodu, Beluru, Harokoppa, Ganganhonda, Keladipura, Kanlepura, Mandagalale, Saidoor.
b. Achapura, Islampura, Murughamatta, Khira, Kengattokeri
c. Lingadahalli, Bommathi & Manchale, Balgodu, Beleyooru, Maneghatta, Bandagadde, Kalsipete, Khandika & Geejagaru
d. Chiplli, Hale-ikkeri, Beduroo, Badgodu, Hulimane, Padavagodu, Masura, Mattikoppa, Honnesara

TABLE NO. 15

Dwarf Survey in Sagar Taluk, District Shimoga

S.No.	Name of Hobli	No. of Villages	No. of Hamlets	Dwarfs *
1	Kasba	52	104	10
2	Talaguppa	28	90	8
3	Anandpuram	68	88	10
4	Avinahalli	41	144	5
5	Karur	26	348	2
6	Bharangi	27	200	5
	Total	242	974	40

*Do not include dwarfs idenfified in villages/ hamlets under ICMR survey

Brahmins	4	Vokkaliga		Muslim	5
Lingayat	3	Ediga	8	Christian	3
Jain	1	Chanangi	5	Not known	2
		Chaluvadi	1		
		Adi-Karnataka	1		
		Uppar	1		
		Achar	1		

Table No. 16

Results of water samples analysis (Meerut)

	Ca mg/l	Mg mg/l	F PPM	I ug/l	Cl mEq/l	Na mg/l	K mg/l	Total Hardness mg/l	Calcium Hardness mg/l	Total Acidity mg/l	Total Alk-alkanity mg/l	Cd ug/l	Cu ug/1	Zn ug/1	Mn ug/1
Mean	14.5	2.5	0.3	3.6	6.8	12.9	4.9	39.9	38.0	24.3	36.1	15.61	22.2	84.5	153.8
S.D.	+9.0	+2.4	+0.1	+2.9	+3.7	+8.0	+4.8	+25.4	+23.5	+17.6	+24.8	+17.9	+21.3	131.9	+220.1

Table No. 17

Fluoride, Iodine and Magnesium Content of Water Samples

Region	Fluoride (ug/ml)	Iodine (ug/L)	Magnesium (ug/ml)
Sagar		mean +SD	
1st survey (19)	0.09+0.04	nt	2.25+2.10
2nd survey (38)	0.14+0.04	1.89+3.41	0.67+0.82
Bangalore (10)	0.30+0.15	nt	20.13+10.65
Nalgonda-Rural Area (17)	2.52+1.36	53.3+34.2	9.81+1.96

Number in paranthesis denotes number of samples.
nt=not tested
NIN, Hyderabad

Table No. 18

Heavy Metal content of Water Samples

	Cd	Cr	Cu	Mn	Ni	Pb	Zn
Sagar (57)	-	0.002+ 0.001	0.015+ 0.02	0.056+ 0.136	0.008+ 0.011	0.024+ 0.006	0.08+ 0.15
Bangalore (10)	-	0.006+ 0.001	0.003+ 0.02	0.001+ 0.081	0.055+ 0.111	0.049+ 0.017	0.18+ 0.11
BLG Rural (12)	-	0.011+ 0.008	0.044+ 0.072	0.081+ 0.148	0.005 0.002	0.183+ 0.459	1.37+ 2.90

Values are given as Mean + SD (mg/ml)
Indicates less than detection limit
Number in parenthesis indicates number of samples.
NIN, Hyderabad

Table No. 19

Heavy Metal Content of Air Samples

	Cd	Cr	Cu	Mn	Ni	Pb	Zn
Sagar (19)	0.0013+	0.016+	1.811+	0.118	0.044+	0.055+	4.30+
	0.0006	0.020	1.557	0.102	0.066	0.156	4.48
Bangalore (10)	0.0017+	0.017+	0.741+	0.109+	0.021+	0.069+	1.24+
	0.002	0.009	0.385	0.044	0.011	0.029	1.17
BLG Rural (5)		0.006+	1.382+	0.079+	0.084+	0.039	0.29+
		0.004	1.085	0.065	0.064		0.15

Values are given as Mean + SD (mg/ml)
Number in parenthesis indicates number of samples.
NIN, Hyderabad

Table No. 20

Heavy Metal Content of Diets

	Cd	Cr	Cu	Mn	Ni	Pb	Zn
Sagar (15)	0.1682+ 0.0997	2.879+ 1.602	14.809 17.850	16.759+ 9.173	1.489+ 0.911	2.711+ 3.771	25.62+ 33.12
Bangalore (6)	0.0906+ 0.0471	3.869+ 2.579	5.403+ 1.103	16.858+ 11.60	2.719+ 1.952	1.042+ 0.489	41.53+ 74.39
BLG Rural (11)	0.0498	1.326+ 0.766	3.259+ 1.814	27.087+ 23.586	0.863+ 0.396	1.393+ 0.675	26.23+ 25.98

Values are given as Mean + SD (mg/ml of dry diet)
Number in parenthesis indicates number of samples.
NIN, Hyderabad

Table No. 21

Heavy Metal Content of Leafy vegetables

Leafy vegetables	Cd	Cr	Cu	Mn	Ni	Pb	Zn
Cassa	0.4958	12.71	32.52	303.38	4.96	4.74	53.09
Suji Menash	0.1113	3.37	11.55	27.48	2.48	1.94	22.47
Yelavarigi	o.3559	7.88	13.18	30.54	4.99	3.43	56.83

Mg/gm dry weight on one sample each.
NIN, Hyderabad

Table No. 22

Trace Metal Analysis of Water Samples

Trace metal	Study	Control
Ag	.007	.007
Al	.28	.43
As	.017	.017
B	010	010
Be	017	017
Ca	15.	7.1
Cd	.003	.003
Co	.033	.033
Cr	.056	.066
Cu	.007	.007
F	.10	.10
Fe	.015	.50
Hg	.50	.50
Mg	10.	1.9
Mn	.47	.033
Mo	.033	.033
NOB	11.	.35
Ni	.033	.033
Pb	.033	.033
Sb	.033	.033
Se	.030	.030
Sn	1.7	1.7
Te	.060	.060
Tl	.033	.033
V	.060	.060
W	3.3	3.3
Zn	.010	.010

in ppm

Table No. 23

HAIR CLIPPING ANALYSIS for Trace Metals by Emission Spectroscopy

	CONTROLS							STUDY						
	1	2	3	4	5	6	Mean	1	2	3	4	5	6	Mean
Pb	1.10	0.52	3.92	2.02	0.80	1.03	1.57	2.17	1.58	0.72	1.95	0.85	0.31	1.26
Cd	0.03	0.03	0.05	0.03	0.06	0.04	0.04	0.13	0.06	0.04	0.04	0.04	0.03	0.06
Zn	108	1.8	94	85	99	108	100	100	97	136	101	113	141	115
Cu	13.5	14.1	11.7	24.5	9.9	56	21.6	21.6	-	17.6	14.1	21	12.1	17.3
Mn	64	23	14	46	19	54	37	32	-	46	17	37	24	31
B	4.2	3.2	4.2	4.3	4.4	2.7	4.0	2.6	-	5.7	1.2	2.6	3.1	2.9
Al	190	84	66	104	51	178	112	71	-	131	51	43	59	71
Si	525	82	60	95	53	135	158	75	-	157	80	31	71	83
Ni	1.3	1.2	0.4	3.4	2.4	4.6	2.2	0.8	-	1.4	0.8	4.5	1.5	1.8
Cr	2.5	17	2.6	32	19	6	13.2	7.3	-	2.5	1.3	17	19	9.4
Sr	3.4	3.9	7.3	5.9	5.4	12	6.3	13.7	-	8.1	3.9	6.2	3.6	7.1
Ba	7.7	9.0	6.9	9.2	6.0	18	9.5	33	-	10.6	6.4	4.5	4.0	12.1
Sn	0.21	0.40	0.21	0.46	0.29	0.17	0.29	0.13	-	0.05	0.06	0.15	0.41	0.16

ppm

St. John's Medical College, Bangalore

Table No. 24

DIETARY INTAKE PER DAY (MEAN + SD)

Age Group (Years)	KCal	Protein (g)	Calcium (g)	Magnesium* (mg)	Phosphorus** (mg)	Vitamin A (ug)	Vitamin D** (IU)
0-5	600	14.0	42.6	85.0	+475.0	15.5	1.4
(n=985)	+310	+5.6	+25.1	+62.4	+202.0	+26.5	+5.5
	870	11.7	957.4			259.5	398.6
5-10	840	16.0	85.0	120.0	488.0	9.7	2.0
(n=1218)	+230	+4.5	+33.2	+55.0	+203.0	+21.7	+4.6
	1403	24.06	915.0			340.3	398.0
10-18	1758	54.7*	121.8	243.5	866.6	41.62	3.9
(n=1889)	+520	+10.8	+93.1	+72.8	436.9	31.5	+8.0
	430		878.0			419.0	396.1
18+	****	55.1*	94.4	266.3	974.2	33.0	2.3
(n=6405)	+202	+10.7	81.6	+45.2	+284.7	+25.4	10.5
	805		705.0			717.0	97.7

*Adequate intakes.

**All subject had compensated for their difficient intake of dietary vitamin D through exposure to sunshine (4-8 hours per day)

Deficient intake per day calculated as per 'Dietary Allowances for Indians's Gopalan C and Narsinga Rao B, NIN ICMR, 1985.

Table No. 25

PLASMA BIOCHEMISTRY (Mean +SD)

Age Groups (Yrs)	Subjects	Total Protein g/dl	Ca++ mg/dl	PO4- mg/dl	Alk Ptase KAU/dl	T3 ng/ml	T4 ug/dl	TSH uU/ml	HGH ng/ml	25(OH)D3 ng/ml	1,25 (OH) 2D3 pg/ml	1-34 HPTH pg/ml
5-10	Patients(3)	7.7 +0.0	9.6 +0.0	5.2 0.8	26.8 +3.2	0.8 +0.3	7.9 +1.5	2.8 +0.7	0.6 +0.6	-	-	-
	Normal lab values(80)	9.3 +0.7	9.3 +0.7	4.5 0.2	17.0 +1.4	0.8 +0.1	12.3 +1.3	2.1 +0.6	7.0 +0.0	-	-	-
10-18	Patients(14)	7.3 0.0	9.3 +0.3	6.0 +0.0	24.8 12.2	1.3 +1.3	10.4 +2.6	3.1 +0.9	8.7 +14.5	-	-	-
	Normal lab values(75)	9.4 +0.2	9.4 +0.2	4.0 +0.3	14.3 +1.1	0.6 +0.1	9.3 +2.3	2.9 +0.5	3.7 +2.4	-	-	-
18	Patients(30)	7.5 +0.8	9.1 +0.4	4.3 +0.9	15.6 +9.8	0.7 +0.4	9.5 +3.4	3.4 +0.8	4.3 +7.5	30.4 +5.81	71.0 +18.2	135.4 141.4
	Normal lab values(56)		9.4 +0.3	3.7 +0.3	13.6 +1.5	1.4 0.3	7.2 +1.5	3.7 +0.6	2.5 1.8	26.2 +5.5	33.5 11.5	30.2 +4.5

Table No. 26

URINARY BIOCHEMISTRY*:24-HOUR URINARY EXCRETIONS (MEAN + SD)

Groups (Yrs)	Volume ml	Sp.Gr.	pH	Ca++ (mg)	PO4- (mg)	Mg++ (mg)	Creat. (mg)	17-KS (mg)	17-KGS (mg)	17-OHCS (mg)	Aminoaciduria
5-10	372.0	1022.0	7.6	55.8	99.4	16.6	241.0	1.2	1.0	0.8	Glycine pattern **
(5)	+165.9	+7.5	+1.2	+62.7	+47.9	+3.7	+71.0	+0.0	+0.0	+0.0	
5-18	611.0	1025.0	7.8	91.3	228.0	39.4	423.5	3.5	2.9	2.1	Glycine pattern **
(15)	+240.8	+9.6	1.7	+51.8	175.2	18.9	+174.7	1.2	+0.6	+0.4	
18*	728.0	1024.0	7.8	119.7	255.6	40.0	463.6	3.6	2.9	2.0	Glycine pattern **
(38)	+433.7	+8.0	1.2	+75.1	157.5	17.7	186.4	+1.4	+1.0	+0.7	

*Screening tests for mucopolysaccharides were negative in all the cases
**Normal pattern with predominance of glycine.

Table No. 27

CLINICAL AND RADIOLOGICAL FINDINGS IN 5 PATIENTS STUDIED INDETAIL

	Patient No.	Age (Yrs)	Sex	Clinical	Radiological
1	Baswanappa	22	M	Subnormal stature, pain and stiffness in hips, low back pain, limping, lumbar lordosis, genu valgum.	Platyspondyly, osteorathrosis, multiple radioluscent and lytic areas in femoral head and neck, both sides.
2	Manjappa	25	M	Subnormal stature. pain in hips, stiffness.	Mild degree of platyspondyly, osteoarthrosis, prominent medial condyle.
3	Manjappa	18	M	Dwarf. low back pain, lumbar lordosis, bulging of chest, flexion at hip.	Platyspondyly; hypoplastic, flattened and mushroom shaped femoral heads; hypoplastic and irregular epiphysis of humerus cardiomegaly.
4	Nagraja	18	M	Dwarf, asymptomatic	Platyspondyly, hypoplastic femoral heads and neck, wine-glass pelvis, irregular pubic symphysis, hyoplastic epiphysis of radius and ulna, thick, short and dense metacarpal bones, dense hypoplastic trumpet shaped epiphysis at knees, submetaphyseal band of osteoporosis, coarse cystic trabeculations, prominent rectangular medical condyle of femur.
5	Sidappa	23	M	Dwarf. low back pain, pain in hips, stiffness, limping, scoliosis, lower limbs	Platspondyly, hypoplastic and irregular epiphyses of ileum, femoral head, neck, and acetabulum. Irregular

Table No. 28

ANTHROPOMETRIC MEASUREMENTS OF 5 PATIENTS STUDIED IN DETAIL

Pt. No.	Age (Yrs)	Sex	Wt. (Kg)	U.S. (cm)	L.S. (cm)	Span (cm)	Ht. (cm)	MAC(L) (cm)	H.C. (cm)	Arm Length (cm)	Forearm Length (cm)	Chest Circum. (cm)
1	22	M	42.0	67.0	75.5	154.5	142.5	23.0	57.0	23.0	26.0	77.0
2	25	M	34.5	71.0	74.0	152.0	145.0	24.0	54.5	20.0	24.0	75.0
3	18	M	27.5	62.5	70.0	143.0	132.0	20.0	21.0	18.0	26.0	75.0
4	18	M	29.5	60.0	57.0	134.5	117.0	21.0	57.0	20.0	21.0	71.0
5	23	M	41.0	59.5	61.5	118.0	121.0	23.0	53.5	18.0	20.5	72.0
Mean	21.2		34.9	64.0	67.6	140.4	131.6	22.2	48.6	19.8	23.6	74.0
SD	+3.1		+6.5	+4.9	+8.0	+14.8	+12.5	+1.4	+15.5	+2.0	+2.5	+2.4

Table No. 29

MEAN DIETARY INTAKE PER DAY TAKEN AT THEIR HOME IN SAGAR TALUK

Patient No.		Age (Yrs)	Sex	Kcal	Prot. (g)	Fat (g)	CHO	Ca (mg)	P	Mg (mg)	Vit D (IU)
1	Baswanappa	22	M	1860	40	8.0	407	120	600	150	5
2	Manjappa	25	M	1905	36	9.0	420	95	810	114	5
3	Manjappa	18	M	1896	35	6.0	423	80	720	120	5
4	Nagraja	18	M	1854	38	6.0	412	80	550	112	8
5	Sidappa	23	M	2025	45	9.0	441	111	680	110	6

Lack in dietary intake of vitamin D had been compensated by adequate exposure to sunshine (4-8 hours). Patients 1,2,4,5 had been living in village Handigodu and No. 3 in village Keladipura.

Table No. 30

LABORATORY INVESTIGATIONS: PLASMA BIOCHEMISTRY OF 5 PATIENTS STUDIED IN DETAIL

Pati. No.	Ca	P	Mg	Alk. Ptase	Urea	Na	K	Cl	Blood PLASMA Cd	Cu	Zn	Mn	Ca Balance (mg/day) Home* Diet	Hospital** Diet
	mg/dl			KAU/dl	mg/dl	mEq/l			ug/dl					
1	9.8	4.5	2.8	31.8	18	142	4.5	103	0.38	118	97	1.8	-49	+168
2	10.2	3.6	3.0	10.0	12	137	4.7	101	0.56	104	87	2.8	-70	+196
3	10.5	3.2	2.5	17.7	22	138	4.8	100	0.35	121	86	2.5	-46	+215
4	9.0	4.0	2.5	11.4	20	135	5.0	102	0.39	111	95	2.3	-37	+97
5	9.2	4.8	3.2	10.0	15	140	4.0	98	0.58	97	88	4.1	-26	+196

*Mean intake 98 mg/day

** Mean intake 850 mg/day

Table No. 31

LABORATORY INVESTIGATIONS: METOBOLIC AND ENDOCRINE

Pat No.	T3 ng/ml	T4 ug/dl	TSH mIU/ml	HGH ng/ml	25-OHD ng/ml	1-25 (OH)2D3 pg/ml	1-34 HPTH pg/ml	Chromosomal Karyotyping	Semen Sperm Count million/ml
1	0.76	5.2	UD	1.0	29	65	192	Normal	102
2	0.84	15.0	UD	0.0	25	68	145	Normal	95
3	0.96	4.2	UD	0.0	24	82	275	Normal	86
4	0.64	6.0	UD	0.0	31	55	77	Normal	75
5	1.04	8.2	4.4	0.0	26	48	<4	Normal	130
	0.6-1.2	4.5-12.0	0-10	0-10	10-40	20-65	<120		60-200

Normal range in our Labs

Table No. 32

24 HOUR URINARY EXCRETIONS

Pat. No.	Total Volume ml	Sp.Gr.	pH	Ca mg	PO mg	Mg mg	Cr mg	NH mEq	TA mEq	Aminoaciduria	17-KS mg	17-KGS mg	17-OHCS mg
1	1270	1016	6.0	138.0	398.0	64.0	685.0	17.0	8.3	Glycine pattern	4.5	3.7	2.9
2	948	1024	6.0	146.0	595.0	61.0	611.0	18.0	11.0	Glycine pattern	4.3	3.4	2.4
3	565	1025	6.4	73.0	309.0	36.5	363.5	15.5	10.0	Glycine pattern	2.4	1.8	1.4
4	670	1018	6.6	112.0	281.0	36.5	568.0	13.5	6.7	Glycine pattern	3.0	2.4	2.0
5	495	1020	6.3	130.0	313.0	38.0	550.0	17.8	6.5	Glycine pattern	3.9	2.7	2.2
Mean	790	1021	6.3	120.0	379.0	47.0	555.0	16.4	8.5		3.6	2.8	2.2
SD	+319	+3.9	+0.3	+29.0	128.0	14.0	119.0	+1.9	+1.9		+0.9	+0.8	+0.6