PATTERN OF DISTRIBUTION OF PATIENTS PRESENTING WITH OSTEOGENESIS IMPERFECTA AT A.I.C. CURE CHILDREN'S INTERNATIONAL HOSPITAL, KIJABE

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ABSTRACT

Background: Osteogenesis imperfecta is one of the common diseases encountered at AIC CURE Children's International Hospital (Cure Hospital Kenya). Osteogenesis imperfecta is a rare condition constituting 2% of all cases seen at the hospital. The Cure Hospital runs 15 clinics throughout Kenya, in which osteogenesis imperfecta is frequently encountered .

Objective*:* The study was carried out to determine the tribal and geographical distribution of patients with osteogenesis imperfecta in Kenya.

Design*:* This was a 14 year retrospective review study.

Setting: Cure Hospital, Kenya.

Materials and methods: The medical charts of all patients admitted with Osteogenesis Imperfecta (OI) over a period of 14 years [2000 to 2014] were reviewed.

Results: A total of 80 patients with osteogenesis imperfecta were seen. Fifty seven point five percent of the patients with OI were males and 42.5% were females. Thirty seven point five percent were of Kamba origin while 28.8% were from the Kikuyu tribe. Majority of these patients came from Eastern region of Kenya with 26.25% coming from Machakos and 30 out of the total of 80 patients were from Kamba tribe.

Conclusions: Most of these patients come from Eastern region of Kenya. Majority of patients with OI were of Kamba origin followed by the Kikuyu tribe. A larger epidemiological study needs to be carried out to more conclusively determine the relative prevalence and genetic patterns of osteogenesis imperfecta in Kenya.

INTRODUCTION

Osteogenesis Imperfect (OI) is a disease which is included in the group of the osseous dysplasias having a heterogeneous genetic character and whose basic defect is an alteration in the synthesis of Procollagen type I. This leads to serious fragility in skeletal structures as well as in exoskeletal structures, causing multiple fractures and deformities. A genetic study of osteogenesis imperfecta in Victoria, Australia confirmed that there are at least four distinct syndromes at present called osteogenesis imperfecta (1,2). It is also associated with low bone mass (3). It is an inherited disorder with an estimate incidence of 1 in 100,000 live births (4).

Osteogenesis imperfecta is characterized by bone fragility as a cardinal manifestation, accompanied by short stature, dentinogenesis imperfecta, hyper laxity of ligaments and skin, blue sclerae and hearing loss (5) It is a genetically transmitted disease and thus it is very important to identify epidemiological patterns geographical distribution and identify the particular tribes that are affected.

The Cure Hospital Kenya runs 15 clinics throughout Kenya as shown in Figure 1. Osteogenesis imperfecta is frequently encountered and constitutes 2% of all cases seen at the hospital. The study was carried out to document the local geographical distribution of this disease as seen at the Cure Hospital. There is no data available about distribution of osteogenesis imperfecta in Kenya and the region. A study on the relative frequency of patients presenting at the hospital in terms of tribe and where they come from could provide valuable information about paediatric orthopaedic conditions that are known to be genetically transmitted.

MATERIALS AND METHODS

Charts for all patients admitted at Cure Hospital with osteogenesis imperfecta were reviewed for the period between January 2000 and December 2014. Our patients presented with the classic features of osteogenesis imperfecta. Most patients had multiple fractures, long bone deformities and bowing, short stature, blue sclerae and dentinogenesis. The patients required multiple procedures to treat the frequent

and recurrent fractures and deformities. The patients presented from different parts of the country having being screened from our mobile clinics that are spread across the country.

RESULTS

There were 80 patients in total with 57.5% males and 42.5% being females. The eldest patient was 30 years old while the youngest was 3 years.

Table 1
Distribution of patients according to their ages

Age (years)	Frequency	(%)
0-5	3	3.8
6-10	20	25.0
11-15	25	31.3
16-20	13	16.3
21-25	12	15.0
26-30	7	8.8
Total	80	100

Table 2
Distribution of disease according to the tribes

Tribe	Frequency	(%)
Kamba	30	37.50
Kikuyu	24	30.00
Luhya	6	0.08
Kisii	4	0.05
Kalenjin	3	0.04
Luo	2	0.03
Giriama	2	0.03
Turkana	2	0.03
Meru	3	0.04
Others (Boran,Somali)	4	0.06
Total	80	100

Table 3
Distribution according to counties

Region	Frequency	(%)
Machakos	21	26.25
Kiambu	14	17.50
Embu	9	11.25
Nairobi	8	0.10
Kitale (Trans Nzoia)	7	0.09
Nakuru	4	0.05
Kisii	3	0.04
Meru	3	0.04
Mombasa	2	0.03
Eldoret (Uasin Gishu)	2	0.03
Kisumu	2	0.03
Kericho	2	0.03
Siaya	1	0.01
Mandera	1	0.01
Isiolo	1	0.01
Total	80	100

Figure 1

Map of Kenya showing mobile clinics locations

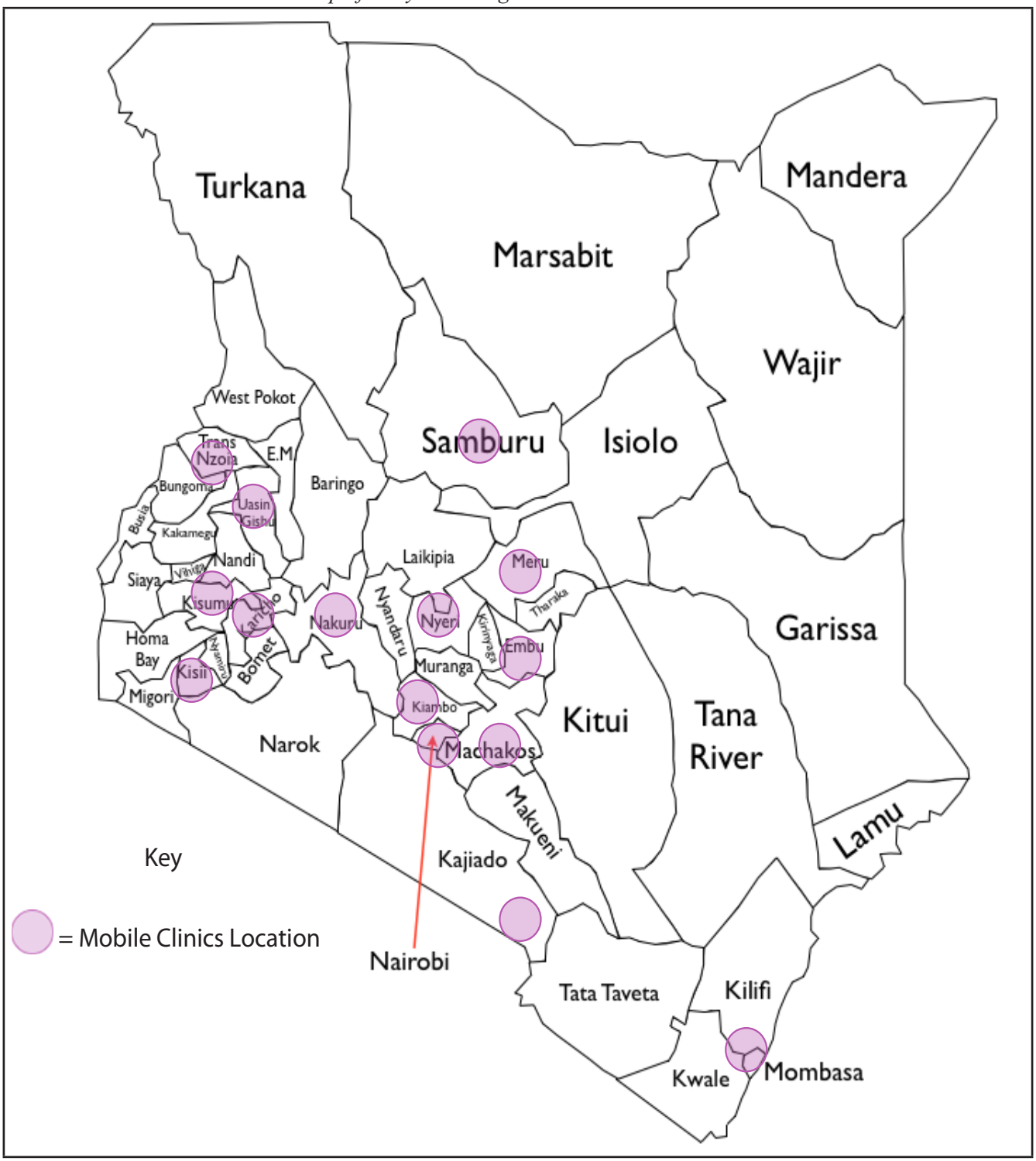
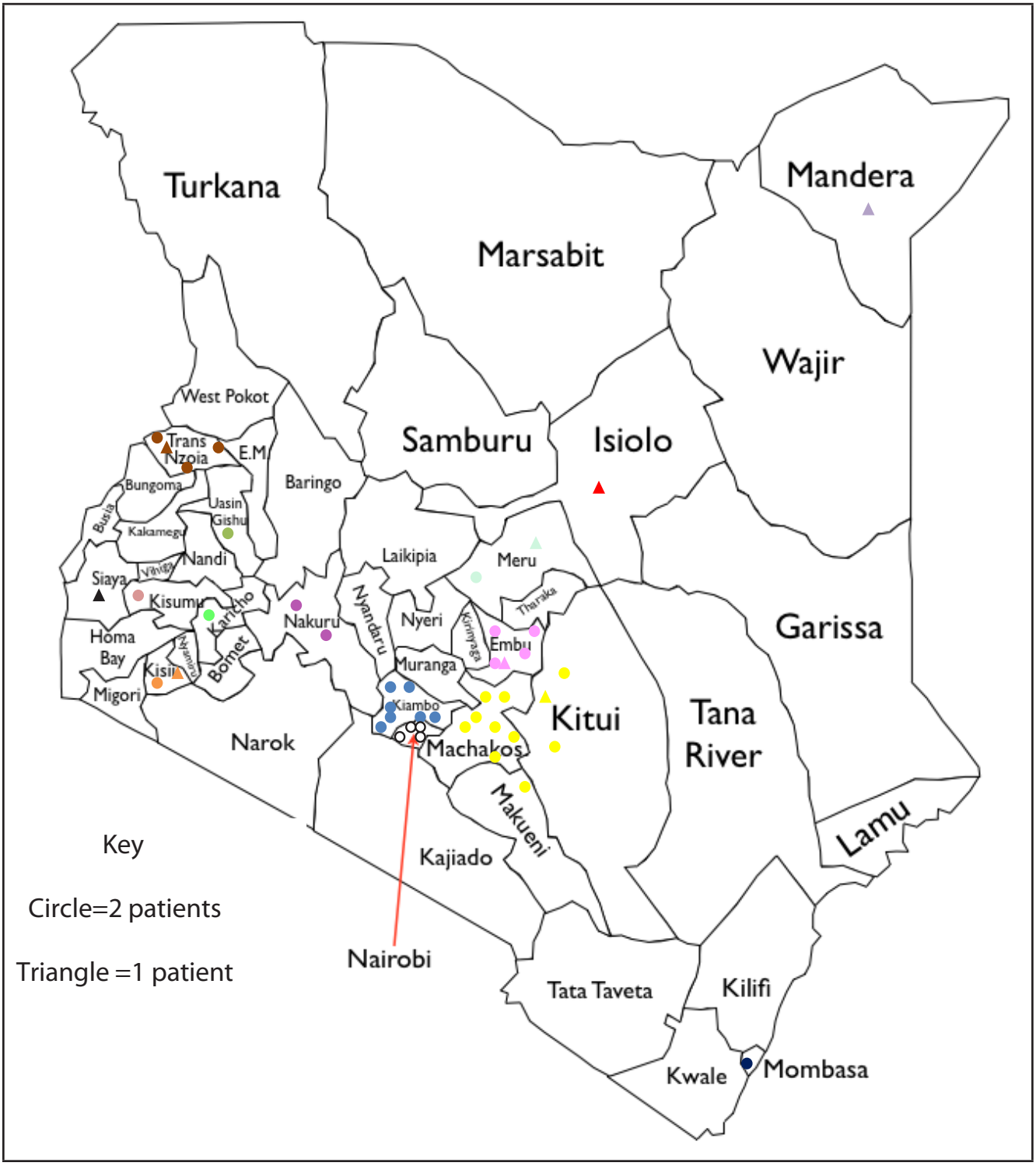


Figure 2

Map of Kenya showing counties and distribution of OI



DISCUSSION

Osteogenesis Imperfecta (OI) is a clinically and genetically heterogeneous brittle bone disorder that results from defects in the synthesis, structure, or post-translational modification of type I procollagen. Dominant forms of OI result from mutations in *COL1A1* or *COL1A2*, which encode the chains of the type I procollagen heterotrimer. The mildest form of OI typically results from diminished synthesis of structurally normal type I procollagen, whereas moderately severe to lethal forms of O.I. usually result from structural defects in one of the type I procollagen chains. (2,6). Osteogenesis imperfecta is a genetic disorder of connective tissue characterized by bone fragility and alteration in synthesis and post-translational modification of type I collagen. Children with osteogenesis imperfecta can suffer from frequent

fractures and limb deformities, resulting in impaired ambulation. Osteopenia and thin cortices complicate orthopaedic treatment in this group (7).

In a survey of Black patients with osteogenesis imperfecta attending the Baragwanath Hospital, Johannesburg, the severe autosomal recessive OI type III (Sillence classification) was recognized in 21 patients, of whom 18 lived in the Johannesburg area. By contrast only 5 had the ostensibly common mild autosomal dominant OI type I. The estimated minimum population frequency is 0.6 per hundred thousand for OI type III in this group and 0.1 per hundred thousand for OI type I. These figures are the reverse of those calculated for White Australians, where the ratio between OI type I and III is of the order of 7 to 1. This anomalous situation has important genetic and practical implications (8).

Little data is available about osteogenesis imperfecta in Black African children. This defect was diagnosed in monozygotic twins from Rwanda who presented with multiple fractures, in particular of the femur, when they began to walk. Osteogenesis imperfecta was confirmed by lower limb deformity, presence of wormian bones in the skull, blue sclera and tooth defects. In addition to the fact that it is uncommon to encounter this condition in monozygotic twins, this case is interesting for several reasons. Was osteogenesis imperfecta in these patients type I, frequent, or type III, exceptional? More importantly, this case stresses the high prevalence of type III in Black Africans which could constitute a hot-bed in the world (9).

The only epidemiological study from Africa is a survey of institutions for crippled persons in Zimbabwe, 58 patients with osteogenesis imperfecta were identified; 42 had the rare OI type III (Sillence classification). The Shona and Ndebele people, who comprise the major tribal groups in Zimbabwe, both had a similar and relatively high gene frequency for this disorder. Both tribes were derived from common progenitors, but until 150 years ago had been geographically separated for 2 millennia. Subsequently, they have remained culturally and socially distinct. The implications are that the mutation for osteogenesis imperfecta [Sillence classification type III in Africa] occurred at least 2,000 years ago (10).

Of interest to note was the high number of patients coming from the Eastern region (37.54%). The Kamba tribe was also noted to be mostly affected (35.7%). This may point to a genetic predisposition to the disease just as the other studies pointed out like the Shona and Ndembele tribes of Zimbabwe (10).

This study concentrated on patients who had been admitted for a surgical treatment at the hospital because information about them was at the hospital. The hospital through its network of outpatient clinics had served many more patients with osteogenesis imperfecta as outpatients. Inclusion of these patients could have strengthened the information in the study. Some tribes live in remote parts of the country and access to medical care is adversely affected by geographical distance, cultural barriers, illiteracy and poor economic conditions; these factors could result in under-representation of the prevalence of osteogenesis imperfecta within the tribes.

CONCLUSIONS

Majority of patients with OI seen at the Cure Hospital Kenya are of Kamba origin followed by the Kikuyu tribe. Most of these patients come from Eastern region of Kenya with majority coming from Machakos county. These patients present with multiple long bone fractures and deformities requiring multiple orthopaedic procedures.

A larger epidemiological study needs to be carried out to further determine the patterns of distribution and inheritance characteristics of patients with osteogenesis imperfecta in Kenya.

REFERENCES

1. Sillence, D.O., Sen A. and Danks, D.M. Genetic heterogeneity in osteogenesis imperfecta**.** *J Med Genetics.* 1979; **62**:101-116.
2. Kelley, B.P., Malfait F., Bonase L., Baldridge D., Homan E., *et al*. Mutations in FKBP10 cause recessive osteogenesis imperfecta and Bruck syndrome. *J Bone Miner Res*. 2011; **26**(3): 667-672.
3. Lingaraju, N.P., Vijayalakshmi, N.P.J. and Sheshadri, P. Osteogenesis imperfecta/lobstein syndrome associated with dentinogenesis imperfecta**.** *J Contemp Dental Practice*. 2013; **14**(1):140-142.
4. Ward, L.M., Rauch, F., Travers, R., Chabot G., Azouz, E.M., *et al*. Osteogenesis imperfecta type VII: an autosomal recessive form of brittle bone disease. *Bone*. 2002; **31:** 12–18.
5. Peng, H., Zhang, Y., Long, Z., Rhao, D., Guo, Z., *et al*. A novel splicing mutation in COL1A1 gene caused type I osteogenesis imperfecta in a Chinese family. *Genetics*. 2012; **502**(2):168-171.
6. Yasemin, A., Hrispima, A., Natalia, C., Eda, U., Koray, B., *et al.* Mutations in the Gene Encoding the RER Protein FKBP65 cause autosomal-recessive osteogenesis imperfecta. *Amer J Human Genetics*. 2010; **86**(4):555-559.

7. Lin, D., Zhai, W., Lian, K. and Ding, Z. Results of a bone splint technique for the treatment of lower limb deformities in children with type I osteogenesis imperfecta. *Indian J Orthoped.* 2013; **47**:377-381.
8. Beighton, P. and Versfeld, G.A. On the paradoxically high relative prevalence of osteogenesis imperfecta type III in the black population of South Africa. *Clin Genetics*. 1985; **27**(4):398-401.
9. Armstrong, O., Karayuba, R., Ngendahayo, L. and Habonimana, E. Osteogenesis imperfecta in monozygotic twins in Burundi. *Med Trop*. 1994; **54**(1):59-62.
10. Viljoen, D. and Beighton, P. Osteogenesis imperfecta type III: an ancient mutation in Africa? *Amer J Med Genetics*. 1987; **27**(4): 907-912.