Clinico-epidemiological Study of Congenital Ichthyosis in a Tertiary Care Center of Eastern India

Arghyaprasun Ghosh, Rahul Ahar¹, Gobinda Chatterjee², Neha Sharma², Shruti Alhad Jadhav²

Abstract

Background: Congenital ichthyoses comprises various specific genetic diseases and can range from mild to very severe presentation. Furthermore, these may be associated with various syndromes. There is scanty data regarding the demographic profile and clinical features of patients with congenital ichthyosis in India. Aims and Objectives: The aim is to evaluate the epidemiology and clinical characteristics of various types of congenital ichthyoses. Materials and Methods: The study was conducted for 1 year from April 2013 to March 2014. Patients were evaluated for epidemiological profile and clinical features. Results: During the study of 1 year, 106 patients of congenital ichthyoses were identified. The most common of the various ichthyoses was ichthyosis vulgaris, followed by lamellar ichthyosis, X-linked recessive ichthyosis. One case of Netherton syndrome and one of ichthyosis hystrix were also identified. Conclusion: Various types of congenital ichthyoses present with different clinical features which range from mild to severe. These present with significant psychological stress to both patients and their families. Furthermore, all these diseases have significant implications of transmission to their offspring.

Key Words: Atopy, congenital ichthyoses, Eastern India, Netherton Syndrome

Introduction

Congenital ichthyosis is a group of genetically inherited disorders of keratinization caused by the specific genetic defect. These disorders are more common in the winters when the suffering patients are especially psychologically disturbed. According to the 2009 first consensus classification, ichthyosis is divided into nonsyndromic and syndromic. Harlequin ichthyosis, lamellar ichthyosis (LI), and congenital ichthyosiform erythroderma (CIE) fall under autosomal recessive congenital ichthyosis. The keratinopathic ichthyosis due to keratin mutations includes epidermolytic ichthyosis (EI) and superficial EI.[1] Fortunately, the most common of these, the ichthyosis vulgaris (IV) is relatively mild and easily amenable to emollients. However, the more severe ones like EI (formerly bullous ichthyosiform erythroderma [BIE]) and LI pose difficulties in the treatment of their associated features of fibrous digital bands threatening autoamputation of the fingers, ectropion, and eclabium. While the knowledge of these conditions helps treat them by simple means whenever possible and thus avoid unnecessary medications. Furthermore, intensive therapy in the form of high-dose oral retinoids can promptly be started to relieve more severe features associated with BIE and LI. Their inheritance pattern is especially important to find the chances of transmission of the disorder to the offspring.

Materials and Methods

This is an institution based, cross-sectional, descriptive study undertaken at the outpatient department (OPD) of the Department of Dermatology, Venereology, and Leprosy of a tertiary care set up in Kolkata. Cases were recorded in a prestructured pro forma from April 2013 to March 2014 after obtaining permission from the institutional ethics committee. Patients presenting with features consistent with congenital ichthyosis and willing to give written informed consent were included.
in the study. Patients unwilling to take part in the study were excluded from the study. Laboratory investigations including complete blood count, liver function test, renal function test, and lipid profile were done in selected cases only. History and clinical examination findings were recorded. A punch biopsy was taken from atypical and doubtful cases. Digital photographs were taken.

Results

Over the 1 year duration of the study, a total of 106 cases of congenital ichthyoses were identified and examined in the dermatology OPD. Of these, 79 (74.54%) were IV, 10 (9.43%) were X-linked recessive ichthyosis (XLRI) [Figure 5], 10 (9.43%) were LI [Figure 6], 3 (2.84%) were EI/BIE, 1 (0.94%) ichthyosis hystrix (IH), 1 (0.94%) was Netherton syndrome (NS) [Figure 7], and 2 (1.88%) were Conradi-Hünermann-Happle syndrome (CHHS) [Figure 8].

**Demographic profile**

Maximum number of patients presented in the age group of 0-10 years (39, 36.8%) [Table 1 and Figure 1]. Total number of male patients were 69 (65%) and females were 37(35%) [Table 2 and Figure 2]. Most of the patients were student (43, 40.56%) [Table 3 and Figure 3]. Fifty seven patients were Hindus (53.8%) and 49 (46.2%) were Muslims. Also patients with rural background were

---

**Table 1: Age distribution of the patients in the study**

| Age (years) | Number of patients |
|-------------|--------------------|
| 0-10        | 39                 |
| 11-20       | 29                 |
| 21-30       | 17                 |
| 31-40       | 11                 |
| 41-50       | 6                  |
| 51-60       | 3                  |
| 61-70       | 0                  |
| 71-80       | 1                  |

**Table 2: Sex distribution of patients with congenital ichthyoses (males:females)**

| IV | XLRI | LI | EI/BIE | IH | NS | CHHS |
|----|------|----|--------|----|----|------|
| 49:30 | 10:0 | 5:5 | 3:0    | 1:0 | 1:0 | 0:2  |

IV: Ichthyosis vulgaris, XLRI: X-linked recessive ichthyosis, LI: Lamellar ichthyosis, BIE: Bullous ichthyosiform erythroderma, EI: Epidermolytic ichthyosis, IH: Icthysis hystrix, NS: Netherton syndrome, CHHS: Conradi-Hünermann-Happle syndrome

**Table 3: Occupational variability in the study population**

| Students (%) | Skilled workers (%) | Housewives (%) | Unskilled workers (%) | Others (%) |
|--------------|---------------------|----------------|-----------------------|------------|
| 43 (40.56)   | 11 (10.38)          | 15 (14.15)     | 14 (13.21)            | 23 (21.7)  |

**Table 4: Demographic profile of the patients of congenital ichthyoses in the study**

| Parameter | IV | XLRI | LI | BIE | IH | NS | CHHS |
|-----------|----|------|----|-----|----|----|------|
| Male:female | 49:30 | 10:0 | 5:5 | 3:0 | 1:0 | 1:0 | 0:2  |
| Hindu:Muslim | 37:42 | 8:6 | 2:6 | 4:6 | 2:1 | 1:0 | 1:0 |
| Rural: urban | 37:42 | 5:5 | 6:4 | 3:0 | 1:0 | 1:0 | 2:0 |
| APL: BPL | 62:17 | 7:3 | 4:6 | 3:0 | 0:1 | 0:1 | 2:0 |

**Figure 1: Age distribution of the patients in the study**

**Figure 2: Sex distribution of patients with congenital ichthyoses (males:females)**

**Figure 3: Occupational variability in the study population**

---

Ghosh, et al.: Study of congenital ichthyosis in Eastern India
Clinical profile of patients of congenital ichthyoses

Clinical features of IV are described [Table 5]. Keratosis pilaris (KP) was present in only 5 (6.3%) such patients.

Clinical features of patients with XLRI are described [Table 6]. Atopy was present in 5 (50%) patients. Sweating was impaired in 3 (30%) patients and heat intolerance was present in 7 (70%) patients. Eye involvement and undescended testis were not found in any patient. One patient gave history of surgery for inguinal hernia.

In patients with LI, atopy was present in 4 (40%) patients [Table 7]. Impaired sweating and heat intolerance were present in 6 (60%) patients. Ectropion was present in 3 (30%) and exposure keratitis in 1 (10%) patient.

In patients with BIE/EI, impaired sweating and heat intolerance were present in 2 (66.7%) patients and nail involvement in form of thickening and roughening was present in 1 (33.3%) patients [Table 8].

One (0.94%) patient each of IH and NS and two (1.88%) patients of CHHS were also seen within the duration of the study.

Discussion

Male patients constituted 65.1% of the study population. A higher percentage of male patients may be because, first, female patients with congenital ichthyoses, who
belong to rural areas tend not to seek medical advice because of the mild nature of the disease, and second, because XLRI which constituted 9.43% of all patients in our study presents only in males.

Seventy-eight (73.58%) patients were above the poverty line and 28 (26.42%) patients were below poverty line. Although most patients attending the Dermatology OPD at our hospital are not rich, still these values may be because the poverty line has been set at Rs. 32 for villages and Rs. 47 for cities per day. This corresponds to 29.5% of Indian population living below poverty line.\[6\] Corneal opacities or dots and testicular maldescent were not found in any patient. These findings are in contrast to the reported rate of 24%–100% for corneal opacities\[4-7\] and 11.84% for testicular maldescent.\[8\] This suggests that these features might not be as common as have been mentioned in the literature or they may be less common in Indian patients. Lack of corneal opacities may also be because only two patients were above the age of 20 years. However, one patient gave a history of being operated for inguinal hernia at the age 3-49
\[\text{Range} \quad 3-49\]

\[\text{Mean}\pm\text{SD} \quad 18.3\pm14.870\]

\[\text{Median} \quad 13\]

\[\text{Age of onset (months)} \]

\[\text{Range} \quad 0.5-7\]

\[\text{Mean}\pm\text{SD} \quad 2.375\pm3.092\]

\[\text{Median} \quad 1\]

\[\text{Prolonged labor} \]

\[\text{Present}:\text{absent}:\text{history not available} \quad 4:4:2\]

\[\text{Family history} \]

\[\text{Present}:\text{absent} \quad 6:4\]

\[\text{Marriage} \]

\[\text{Consanguineous}:\text{nonconsanguineous} \quad 1:9\]

\[\text{Atopy} \]

\[\text{Present}:\text{absent} \quad 5:5\]

\[\text{Progression} \]

\[\text{Improving}:\text{increasing}:\text{no change} \quad 2:7:1\]

\[\text{Sweating} \]

\[\text{Impaired}:\text{not impaired} \quad 3:7\]

\[\text{Heat intolerance} \]

\[\text{Present}:\text{absent} \quad 7:3\]

\[\text{Flexures} \]

\[\text{Involved}:\text{not involved} \quad 1:9\]

\[\text{Eye involvement} \quad \text{Nil}\]

\[\text{Undescended testis} \quad \text{Nil}\]

\[\text{Hernia} \]

\[\text{Present}:\text{absent} \quad 1:9\]

SD: Standard deviation

Table 6: Clinical features of X-linked recessive ichthyosis patients found in the study

| Patient profile               | Findings                        |
|------------------------------|---------------------------------|
| Age at presentation (years)   |                                 |
| \[\text{Range} \quad 3-49\]   |                                 |
| \[\text{Mean}\pm\text{SD} \quad 18.3\pm14.870\] |                                 |
| \[\text{Median} \quad 13\]    |                                 |
| Age of onset (months)         |                                 |
| \[\text{Range} \quad 0.5-7\]   |                                 |
| \[\text{Mean}\pm\text{SD} \quad 2.375\pm3.092\] |                                 |
| \[\text{Median} \quad 1\]     |                                 |
| Prolonged labor               |                                 |
| \[\text{Present}:\text{absent}:\text{history not available} \quad 4:4:2\] | |
of 5 year. This goes with the fact that hernia is more common than testicular maldescent.[9]

In patients with LI, there was no such patient in which parents or relatives other than sibling were affected. Hence, there was no patient of “autosomal dominant LI” in our study. This inheritance pattern has never been found in India although it has been reported from Germany, France, and Sweden.[10] Interestingly, 4 (40%) patients were atopic. However, we could not find atopy as a feature of LI in literature.

Although it has been mentioned that NBIE/CIE is more common than LI,[3] we did not find any patient of NBIE/CIE in our study.

BIE/EI was diagnosed in 3 patients. All patients were males. Two were of PS 2 type and one was of NPS 2 type. Both of the PS 2 patients presented with generalized hyperkeratotic scales all over the body with accentuation of scaling in the flexural area. Severe palmoplantar keratoderma was present in both patients and in one patient, there was a severe constriction band around the fifth toes of both feet, threatening self-amputation. He was treated with oral retinoids mainly in winters to prevent the digit loss. In both patients, the scaling was increasing with age. Both had impaired sweating and heat intolerance. We could not find impaired sweating as a feature of BIE in literature.

One (0.94%) patient each of IH and NS and two (1.88%) patients of CHHS were also seen within the duration of the study. IH: Ichthyosis hystrix, NS: Netherton syndrome, CHHS: Conradi-Hünermann-Happle syndrome.

**Conclusion**

Different epidemiological and clinical features of different types of congenital ichthyosis are described and compared.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information.

---

**Table 7: Clinical features of lamellar ichthyosis patients found in the study**

| Patient profile | Findings |
|----------------|----------|
| Age of presentation (years) | 3-23 |
| Range | Mean±SD | Median |
| Collodion membrane | Present:absent:history not available | 4:5:1 |
| Family history | Present:absent | 2:8 |
| Marriage | Consanguineous:nonconsanguineous | 3:7 |
| Atopy | Present:absent | 4:6 |
| Progression | Improving:increasing:no change | 4:5:1 |
| Keratoderma (palms) | None:mild:moderate:severe | 3:4:1:2 |
| Keratoderma (soles) | None:mild:moderate:severe | 3:3:2:2 |
| Sweating | Impaired:not impaired | 6:4 |
| Heat intolerance | Present:absent | 6:4 |
| Flexures | Involved:not involved | 5:5 |
| Eye involvement | Ectropion in 3 (30%) cases, exposure keratitis in 1 (10%) case |

SD: Standard deviation

**Table 8: Clinical features of epidermolytic ichthyosis/bullous ichthyosiform erythroderma patients in the study (n=3)**

| Patient profile | Findings |
|----------------|----------|
| Erythroderma at birth | Present:absent:cannot comment | 1:0:2 |
| Blister at birth | Present:absent:cannot comment | 0:1:2 |
| Family history | Present:absent | 1:2 |
| Marriage | Consanguineous:nonconsanguineous | 0:3 |
| Atopy | Present:absent | 0:3 |
| Progression | Improving:increasing:no change | 0:3:0 |
| Keratoderma (palms) | None:mild:moderate:severe | 1:0:0:2 |
| Keratoderma (soles) | None:mild:moderate:severe | 1:0:0:2 |
| Constriction bands | Present:absent | 2:1 |
| Sweating | Impaired:not impaired | 2:1 |
| Nails | Involved:not involved | 1:2 |
| Heat intolerance | Present:absent | 2:1 |
| Flexural accentuation | Present:absent | 3:0 |

One (0.94%) patient each of IH and NS and two (1.88%) patients of CHHS were also seen within the duration of the study. IH: Ichthyosis hystrix, NS: Netherton syndrome, CHHS: Conradi-Hünermann-Happle syndrome.
to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

### What is new?
- Incidence of keratosis pilaris was less in patients with IV.
- Significant number of patients with XLRI and LI had atopy.
- Both patients with PS2 type of BIE/EI had impaired sweating and heat intolerance.
- Nail dystrophy with thickening and roughening was seen in patient with BIE/EI.

### References

1. Phiske M. Ichthyosis and ichthyosiform disorders. In: Majid I, editor. IADVL Recent Advances in Dermatology. 1st ed. New Delhi: The Health Sciences Publisher; 2016. p. 36-47.
2. Singh MK. New Poverty Line: Rs. 32 in Villages, Rs. 47 in Cities. The Times of India. Available from: [http://www.timesofindia.indiatimes.com/india/New-poverty-line-Rs-32-in-villages-Rs-47-in-cities/articleshow/37920441.cms](http://www.timesofindia.indiatimes.com/india/New-poverty-line-Rs-32-in-villages-Rs-47-in-cities/articleshow/37920441.cms). [Last accessed on 2014 Jul 07].
3. Judge MR, McLean WH, Munro CS. Disorder of keratinization. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology. 8th ed. Singapore: Wiley-Blackwell; 2010. p. 19.1-19.122.
4. Sever RJ, Frost P, Weinstein G. Eye changes in ichthyosis. JAMA 1968;206:2283-6.
5. Costagliola C, Fabbrocini G, Illiano GM, Scibelli G, Delfino M. Ocular findings in X-linked ichthyosis: A survey on 38 cases. Ophthalmologica 1991;202:152-5.
6. Okano M, Kitano Y, Yoshikawa K, Nakamura T, Matsuzawa Y, Yuasa T, et al. X-linked ichthyosis and ichthyosis vulgaris: Comparison of their clinical features based on biochemical analysis. Br J Dermatol 1988;119:777-83.
7. Lykkesfeldt G, Høyer H, Ibsen HH, Brandrup F. Steroid sulphatase deficiency disease. Clin Genet 1985;28:231-7.
8. Lykkesfeldt G, Høyer H, Lykkesfeldt AE, Skakkebaek NE. Steroid sulphatase deficiency associated with testis cancer. Lancet 1983;2:1456.
9. Paige DG, Emilion GG, Bouloux PM, Harper JI. A clinical and genetic study of X-linked recessive ichthyosis and contiguous gene defects. Br J Dermatol 1994;131:622-9.
10. Toribio J, Fernández Redondo V, Peteiro C, Zulaica A, Fabeiro JM. Autosomal dominant lamellar ichthyosis. Clin Genet 1986;30:122-6.