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Original Research Article

Congenital Ichthyoses in Pediatric Age Group

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Abstract

Background: A collection of monogenetic cornification illnesses collectively known as congenital ichthyosis occasionally manifests as systemic symptoms. Anomalies related to skin inflammation can include abnormal keratinocyte kinetics, abnormal stratum corneum thickness, or abnormal scale production in terms of quality or quantity. Anhidrosis, ectropion, pruritus, and fragile skin are occasionally linked to uncommon forms of ichthyoses. Correct clinical diagnosis of an ichthyosis patient is necessary before prognostications, treatment recommendations, and genetic counseling can be provided. However, due to clinical variability, a precise diagnosis may be difficult to reach in some cases. Ichthyoses are a diverse set of illnesses caused by aberrant differentiation and desquamation of the epidermis along with deficiencies in keratinization or cornification. Congenital ichthyosis nomenclature and nosology have developed over time, resulting in a bewildering patchwork of words and categorization schemes.

Aim: To study the clinical presentation of various types of congenital ichthyosis in the pediatric age group.

Material and Method: A cross-sectional observational study was carried out in the pediatric department. Based on clinical patterns, 30 instances of ichthyosis in total were included in the study. For comparative research, the entire number of new patients who visited the department at that time was enrolled. A predetermined format for the questionnaires was used to extract the history. Concerns were raised regarding the following: blistering of the skin, seasonal fluctuation, shedding of skin on a cyclical basis, age of onset, duration, itching, reduced perspiration and heat intolerance, and history of collodion infant.

Results: Of the thirty individuals who had congenital ichthyosis, seventy-seven percent had ichthyosis vulgaris, and fifteen percent had lamellar ichthyosis. Sjogren-Larsson syndrome and bullous ichthyosis form erythroderma (BIE) each made up 6% of the total, while non-bullous ichthyosis form erythroderma (NBIE) made up 9%. In both sexes, the prevalence of ichthyosis vulgaris was nearly equal. Females had a higher incidence of lamellar ichthyosis. In NBIE, the distribution of sexes was equal. In cases of ichthyosis vulgaris, 25% of patients had a history of second- or third-degree consanguineous marriage, while 75% of patients did not have any such history. In lamellar ichthyosis, NBIE, Sjogren–Larsson syndrome, and Netherton's syndrome, all the patients had consanguineous parents. In ichthyosis vulgaris 40% of patients had a family history of ichthyosis. In lamellar ichthyosis, a positive family history was present in 20% of patients.

Conclusion: Numerous distinct forms of ichthyoses possess distinguishing characteristics and are dependable in their diagnosis. However, due to significant clinical heterogeneity, a precise diagnosis may be difficult to reach in some patients and families. Generally speaking, diagnosis is aided by knowing if ichthyosis is inherited or acquired, present at birth or later in life, and confined to the skin or a component of a multisystem condition. Other helpful clinical findings include blistering, the kind and distribution of scale, the existence or absence of erythroderma, and any related abnormalities of the skin adnexa. To identify the inheritance pattern, a complete family history is necessary.

Keywords: Congenital ichthyosis, Collodion baby and Ichthyosis Vulgaris.

Introduction

The ichthyoses are a diverse collection of illnesses defined by a widespread scaling of the skin of variable severity. They are also known as disorders of keratinization or disorders of cornification. The majority of ichthyoses are inherited, however cancer, autoimmune or viral diseases, and dietary deficiencies can also lead to the development of acquired variants. The identification of causative mutations in over 50 genes encoding structural proteins or enzymes involved in a wide range of cellular functions, from deoxyribonucleic acid

(DNA) repair to skin barrier homeostasis, has shed light on the molecular basis and pathophysiology of the majority of inherited ichthyoses. [1,2]

Congenital ichthyosis encompasses a heterogeneous group of hereditary skin disorders all of which are present at birth. [3] Following the newborn stage, the afflicted children exhibit extensive scaling, varying degrees of erythema, or, in the case of epidermolysis hyperkeratosis (EHK), blisters and very thickened skin all over the body. [4] The diagnosis of lamellar ichthyosis (LI), Netherton's syndrome (NS), EHK, or Harlequin ichthyosis (HI) is typically confirmed by clinical examinations in conjunction with DNA testing. For now, there is no treatment for ichthyosis. The treatment is lifelong and consists of baths, daily topical emollient treatments, and oral acitretin for extremely severe symptoms. [5,6]

A particular type of genetic abnormality causes a range of keratinization illnesses known as congenital ichthyosis. Winter is a common time for these diseases to occur since the individuals who suffer from them are more psychologically disturbed. The 2009 first consensus categorization categorizes ichthyosis into two groups: non-syndromic and syndromic. Autosomal recessive congenital ichthyosis includes Harlequin ichthyosis, lamellar ichthyosis (LI), and congenital ichthyosis from erythroderma (CIE). Epidermolysis ichthyosis (EI) and superficial EI are two types of keratinopathic ichthyosis caused by keratin mutations. [7] Thankfully, ichthyosis vulgaris (IV), the most prevalent of these, is quite mild and readily treated with emollients. The most severe ones, such as LI and EI (previously known as bullous ichthyosis form erythroderma [BIE]), provide challenges in the treatment of the fibrous digital bands that risk finger autoamputation, ectropion, and eclabium. Understanding these illnesses enables one to treat them as simply as possible, without the need for needless medicine.

Generally speaking, diagnosis is aided by knowing if ichthyosis is inherited or acquired, manifested at birth or later in life, and if it affects only the skin or is a component of a multisystem condition. Other helpful clinical findings include blistering, the kind and distribution of scale, the existence or absence of erythroderma, and any related abnormalities of the skin adnexa. To identify the inheritance pattern, a complete family history is necessary. Correct clinical diagnosis of an ichthyosis patient is necessary before prognostications, treatment recommendations, and genetic counseling can be provided. [8] Quality of life (QoL) studies in adults with ichthyosis have shown that their skin disease has affected them negatively and that the most problematic period has been their childhood. [8,9] Many skin diseases in children have been associated with impaired QoL. [10,11] There are few QoL data available for kids with congenital ichthyosis. The current study looked at the quality of life (QoL) of Swedish children who had various kinds of congenital ichthyosis as well as the effect the disease had on the families of those affected children. To identify the inheritance pattern, a complete family history is necessary. Making prognosis and treatment decisions for an ichthyosis patient requires establishing an accurate clinical diagnosis. [12] Recent advances in molecular genetics have provided tools to categorize ichthyosis based on their underlying genetic defect which helps in offering genetic counseling. [13]

Material and Methods

This cross-sectional observational study was conducted at the Department of Pediatrics**.** A total of 30 cases of ichthyosis were enrolled in the study based on clinical patterns. The total number of new patients who attended the department during the period was enrolled for comparative studies. In eliciting the history, a set pattern of questionnaires was followed. Enquiries were made concerning symptoms, age of onset, duration, itching, diminished sweating and heat intolerance, history of collodion baby, blistering of the skin, seasonal variation, cyclical shedding of skin, photosensitivity, and photophobia.

History: In eliciting the history, a set pattern of questionnaires was followed (as given in the proforma). Inquiries were made about symptoms, age of onset, duration, history of collodion baby, blisters, seasonal variation, repeated skin infection, and atopy. History regarding the involvement of other systems like the central nervous system, and the skeletal system was taken. History regarding the involvement of other systems such as the central nervous system (CNS), and the skeletal system was taken. History of any maternal illness and medication during the antenatal period, prematurity, and prolonged labor was elicited. Patients' developmental history and family history of similar lesions in the parents and siblings were elicited. History regarding the consanguineous marriage of parents was recorded. A detailed general examination was conducted with specific reference to the CNS and skeletal system.

Clinical Examination: A careful and detailed dermatological and systemic examination with necessary investigations was conducted methodically. Patients up to fourteen years of age were examined for distribution and nature of scales, presence of erythroderma, and blisters along with a note of associated disorders if any. Referral to other specialties like neurology and ophthalmology were done to confirm or to rule out associated features of some syndromes as and when suspected. Measurement of head circumference was performed and evidence of short stature,

microcephaly, cataract, and gait were noted. On dermatological examination, skin lesions were examined, and the nature of scales whether polygonal or lamellar, the color of scales, and whether loose or adherent were noted along with the distribution of scales with sparing of certain areas. The presence of blisters, erythroderma, lichenification, ectropion, eclabion, eczematization, and impetiginization was noted. Hair and nails were examined for alopecia, brittle hair, and nail dystrophy. Palms and soles were examined for hyper-linearity, palmoplantar keratoderma, sclerodactyly, and digital contractures

Laboratory Investigations: A routine hematological investigation was done in all cases. Apart from routine hematological examination, skin biopsy and microscopic examination of hair were done wherever indicated. Referral to other specialists such as neurologists and ophthalmology was done to confirm or rule out associated features of some syndromes as and when suspected.

Inclusion Criteria:

- Patients presenting with features consistent with congenital ichthyosis and willing to give written informed consent were included in the study.

Exclusion Criteria:

- Acquired ichthyosis
- Malnutrition
- Congenital hypothyroidism
- Acquired immune deficiency syndrome

Statistical Analysis: All the data were compiled and analyzed statistically and inference was drawn. Statistical analysis was done using SPSS version 22.0 was used to analyze the data. To compare the proportions Chi-square test was applied.

Result

Out of 200 patients who attended the dermatology outpatient department, the total number of patients with congenital ichthyosis was 30.

Table 1: Relative incidence of different types of congenital ichthyoses

Clinical types	Number of cases (%)
Ichthyosis vulgaris	18 (60)
Lamellar ichthyosis	5 (16.6)
NBIE	3 (10)
BIE	1 (3.3)
Netherton's syndrome	1 (3.3)
Sjogren–Larsson syndrome	2 (6.6)

Out of 30 patients with congenital ichthyosis, ichthyosis vulgaris constituted 70% of cases followed by lamellar ichthyosis 15%. Non-bullous ichthyosis form erythroderma (NBIE) constituted 9% followed by bullous ichthyosis form erythroderma (BIE) and Sjogren–Larsson syndrome each constituted 6%. The incidence of ichthyosis vulgaris was almost equal in both sexes. The incidence of lamellar ichthyosis was higher in females. Equal sex distribution was seen in NBIE.

Table 2: Age of onset of congenital ichthyoses

Types of Ichthyosis	Birth	3 months	6 months	1 year
Ichthyosis Vulgaris	-	12	12	1
Lamellar Ichtyosis	4	-	-	-
NBIE	2	-	-	-
BIE	1	-	-	-
Sjogren–Larsson syndrome	2	-	-	-
Netherton's syndrome	1	-	-	-

All except two cases of ichthyosis vulgaris had an age onset from 3 to 6 months. Lamellar ichthyosis, NBIE, BIE, and other ichthyosis form syndromes had the age of onset since birth.

Table 3: Evolution of collodion babies

Collodion babies	Number of babies (%)
Lamellar ichthyosis	4 (66.6)
NBIE	2 (33.3)

Table 3 shows that out of 6 collodion babes, 66.6% of cases evolved into lamellar ichthyosis, and 33.3% evolved with NBIE. In ichthyosis vulgaris, 75% of patients had no history of consanguineous marriage of patients, and 25% of the patient's history of second-and third-degree consanguineous marriage was present. In lamellar ichthyosis, NBIE, Sjogren–Larsson syndrome, and Netherton's syndrome, all the patients had consanguineous parents. In ichthyosis vulgaris 40% of patients had a family history of ichthyosis. In lamellar ichthyosis, a positive family history was present in 20% of patients.

Discussion

In our study, the incidence of ichthyosis vulgaris was 1 in 170 which complies with that of the study by Wells and Kerr1966 which showed the

incidence of ichthyosis vulgaris. maybe as common as 1 in 250. [14] The age of onset of ichthyosis vulgaris was around 3-6 months in 98% of patients. In lamellar ichthyosis, NBIE, and BIE the age of onset of the disease was from birth. This complies with that of the description of the age of onset of the disease given by Traupe et al.2014 [15], in the guide to clinical diagnosis of ichthyosis.7 In Van Gysel et al.2002 [16] studies of follow-up to 17 cases of collodion babies, 60-80% of the infants developed NBIE and lamellar ichthyosis.

In Van Gysel et.al 2002 [16] study of follow-up of 17 cases of collodion babies, 60-80% of the infants developed non-bullous ichthyosis from erythroderma and lamellar ichthyosis. In this study of 13 cases of collodion babies, 70% of the patients developed lamellar ichthyosis and 30% of the patients developed non-bullous ichthyosis from erythroderma. Thus, the ratio of non-bullous ichthyosis form erythroderma Vs bullous ichthyosis form erythroderma was 1:2.

A study by Kuokanen 1969 [17] showed an association of atopy in 37-50% of patients which was 6.5% in our study. 76% of patients with ichthyosis vulgaris had no history of their parents' consanguineous marriage, while 24% of patients had a history of second- or third-degree consanguineous marriage. Third-degree consanguineous marriage was found in 55% of patients with lamellar ichthyosis, whereas second-degree consanguineous marriage was found in 44% of patients. That of autosomal recessive inheritance is adhered to by this.

Netherton's syndrome is caused by second-degree consanguineous marriage, which is consistent with autosomal recessive inheritance. Of the patients with ichthyosis vulgaris, 41% had a family history of the condition. One household with two affected siblings had a positive family history with lamellar ichthyosis. Given that the condition is inherited autosomally dominantly, there is a 25% chance of having further affected children, as this instance illustrates. There was no history of ichthyosis in the BIE family. Given that the condition is inherited autosomally dominantly, it can be assumed that the patient's new keratin gene mutation occurred.

Gencoglan et al.2012 [18] mentioned the hypopyon lacunae with surrounding septa in lymphangioma circumscriptum. Hypopyon formation can be attributed to the red corpuscles settling down due to gravity and lymph floating over them in the upper half.

Behera et al.2017 [19] in their study observed multiple yellow dots against a pinkish-gray background. Here, yellow dots correspond to follicular hyperkeratosis and sebum whereas a pinkish-gray background corresponds to proliferating blood vessels and melanin incontinence. Shinkuma et al.2015 [20] observed reddish-brown strands with white lines in between in shagreen patches which we did not find in our patient.

In one study, the mother of an ichthyosis patient described her frustration about the shedding of her son’s skin in their home. In that study, it was found that parents of children (n=2) with ichthyosis also have an extra financial burden. This is in line with the findings in the present study concerning housework and the fact that the expenditure had an impact on their QoL. [21] In a study comprising 30 children with different forms of EB, [22] the total CDLQI scores were much higher than the total CDLQI scores in this study. However, this study's findings confirm that ichthyosis impairs children's quality of life more than other skin conditions. To evaluate how ichthyosis affects quality of life in comparison to other congenital and chronic disorders, general questionnaires and several additional studies are required. [23]

The existence of symptoms, which mostly involved changing the patient's physical appearance, as well as the severity of the disease and the majority of incapacitating disease consequences had an impact on the quality of life (QoL) of family members. All in all, our findings highlight the importance of providing patients and their families with psychological and socioeconomic support in order to ensure optimal worldwide care. Lastly, among the patient-reported outcomes assessed in clinical trials should be the measurement of the impact of the secondary disease on "the greater patient."

Conclusion

Numerous distinct forms of ichthyoses possess distinguishing characteristics and are dependable in their diagnosis. However, due to significant clinical heterogeneity, a precise diagnosis may be difficult to reach in some patients and families. Generally speaking, diagnosis is aided by knowing if ichthyosis is inherited or acquired, present at birth or later in life, and confined to the skin or a component of a multisystem condition. Other helpful clinical findings include blistering, the kind and distribution of scale, the existence or absence of erythroderma, and any related abnormalities of the skin adnexa. To identify the inheritance pattern, a complete family history is necessary. Correct clinical diagnosis of an ichthyosis patient is necessary before prognostications, treatment recommendations, and genetic counseling can be provided.

References

1. Moeschler JB, Shevell M; American Academy of Pediatrics Committee on Genetics. Clinical genetic evaluation of the child with mental

retardation or developmental delays. Pediatrics. 2006;117:2304-16.
2. Elias PM, Menon GK. Structural and lipid biochemical correlates of the epidermal permeability barrier. Adv Lipid Res. 1991; 24:1-26.
3. Traupe H. The ichthyoses: a guide to clinical diagnosis, genetic counseling, and therapy. Berlin; New York: Springer Verlag;1989.
4. DiGiovanna JJ, Robinson-Bostom L. Ichthyosis - Etiology, diagnosis, and management. A Clin Dermatol. 2003;4:81-95.
5. Vahlquist A, Gånemo A, Virtanen M. Congenital ichthyosis: an overview of current and emerging therapies. Acta Derm Venereol. 2008;88:4-14.
6. Ganemo A, Virtanen M, Vahlquist A. Improved topical treatment of lamellar ichthyosis: a double-blind study of four different cream formulations. Br J Dermatol. 1999;141:1027-32
7. Phiske M. Ichthyosis and ichthyosis form disorders. In: Majid I, editor. *IADVL Recent* Advances in Dermatology. New Delhi: The Health Sciences Publisher; 2016;1:36–47.
8. Ganemo A, Lindholm C, Lindberg M, Sjoden PO, Vahlquist A. Quality of life in adults with congenital ichthyosis. J Adv Nursing. 2003; 44: 412-9.
9. Ganemo A, Sjoden PO, Johansson E, et al. Health-related quality of life among patients with ichthyosis. Eur J Dermatol. 2004;14:61-6.
10. Ganemo A, Svensson A, Lindberg M, Wahlgren CF. Quality of life in Swedish children with eczema. Acta Derm Venereol. 2007; 87:345-9.
11. Holm EA, Wulf HC, Stegmann H, Jemec GB. Life quality assessment among patients with atopic eczema. BrJ Dermatol. 2006;154:719-2 5.
12. Pietrusinski M, Stanczyk-Przyluska A, Chlebna-Sokól D, Borkowska E, Kaluzewski B, Borowiec M, et al. Identification and clinical consequences of a novel mutation in the gene for transglutaminase 1 in a patient with lamellar ichthyosis. Clin Exp Dermatol. 2015; 40:921-3.
13. Richard G. Molecular genetics of the ichthyoses. Am J Med Genet C Semin Med Genet. 2004;131:32-44.
14. Wells RS, Kerr CB. Clinical features of autosomal dominant and sex-linked ichthyosis in an English population. Br Med J. 1966; 1:947-50.
15. Traupe H, Fischer J, Oji V. Non-syndromic types of ichthyoses - An update. J Dtsch Dermatol Ges. 2014;12:109-21.
16. Van Gysel D, Lijnen RL, Moekti SS, de Laat PC, Oranje AP. Collodion baby: A follow-up study of 17 cases. J Eur Acad Dermatol Venereol. 2002;16:472-5.
17. Kuokkanen K. Ichthyosis vulgaris. A clinical and histopathological study of patients and their close relatives in the autosomal dominant and sex-linked forms of the disease. Acta Derm Venereol Suppl (Stockh). 1969;62:1-72.
18. Gencoglan G, Inanir I, Ermertcan AT. Hypopyon-like features: New dermoscopic criteria in the differential diagnosis of cutaneous lymphangioma circumscriptum and haemangiomas? J Eur Acad Dermatol Venereol 2012; 2 6:1023-5.
19. Behera B, Kumari R, Gochhait D, Sathya AB, Thappa DM. Dermoscopy of adenoma sebaceum. J Am Acad Dermatol. 2017; 76:86-8.
20. Gundalli S, Ankad BS, Ashwin PK, Kolekar R. Dermoscopy of shagreen patch: A first report. Our Dermatol Online. 2015;6:331-3.
21. Basra MK, Finlay AY. The family impact of skin diseases: the Greater Patient concept. Br J Dermatol. 2007;156:929-37.
22. Horn HM, Tidman MJ. Quality of life in epidermolysis bullosa. Clin Exp Dermatol. 2002;27:707-10.
23. Beattie PE, Lewis-Jones MS. A comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. Br J Dermatol. 2006;155:145-51.