

## Frequency of Genodermatoses Among Iraqi Patients

Haider R. Al-Hamami\*, Adil A. Noaimi\*\*, Makram M. Al-Waiz\*\*,  
Abdulkaleq S. Al-Kabraty\*\*

### ABSTRACT:

#### BACKGROUND:

Genodermatoses are hereditary skin disorders or anomalies which can be grouped into three categories: chromosomal, single gene and multifactorial. Most genodermatoses show single gene or Mendelian inheritance (autosomal dominant, autosomal recessive or X-linked recessive genes).

#### OBJECTIVE:

To assess the frequency of genodermatoses among Iraqi patients in outpatients Dermatology and Venereology comparison with other countries.

#### PATIENTS AND METHODS:

This case series descriptive epidemiological study included eighty three patients (57 males and 26 females) with genodermatoses. They consulted the out patient clinic/ Department of Dermatology and Venereology Baghdad Teaching Hospital from

April 2005 through April 2006. Their ages ranged from 2 months-60 years (Median 10 years), With various genetic diseases.

Full history, dermatological and clinical examinations were done to establish the clinical diagnosis of genodermatoses regarding all demographic points related to these disorders.

#### RESULTS:

The frequency of genodermatoses among outpatient attendant in Dermatology and Venereology Department was 83/ 20000 (0.42%).

This study had shown that the most common genodermatoses were; ichthyosis: 21 (25.3 %) patients and epidermolysis bullosa which contain 16 (19.3 %) patients when taken together they constituted 37 (44.6%) patients of the total, neurofibromatosis 8 (9.6 %), hereditary palmoplantar keratoderma 6 (7.2%), darier's disease 5 (6 %) and xeroderma pigmentosa 4 (4.8 %).

Positive family history of the same disease was obtained in; 8 (38.1 %) patients with ichthyosis, 4 (66.6 %) in hereditary palmoplantar keratoderma, 2 (12.5 %) in epidermolysis bullosa and all patients with Hailey-Hailey disease had positive family history of the same condition.

Consanguinity was positive in; 13 (61.9 %) patients of ichthyosis, 12 (75 %) epidermolysis bullosa, 2 (33.3 %) hereditary palmoplantar keratoderma and (100 %) patients with xeroderma pigmentosa

#### CONCLUSION:

Genodermatoses are frequently encountered among Iraqi dermatological outpatients and more common in families with positive consanguinity and were comparable to other countries.

**KEYWORDS:** genodermatoses, iraqi patients, frequency.

### INTRODUCTION:

Genodermatoses are hereditary skin disorders or anomalies. Genetic disorders are often grouped into three categories; chromosomal, Single gene and multifactorial<sup>(1)</sup>.

Chromosomal disorders can be either numerical such as trisomy and monosomy or structural resulting from translocations, Deletions and duplications<sup>(1)</sup>.

\* Department of Dermatology and Venereology, College of Medicine, University of Baghdad.

\*\*Department of Dermatology and Venereology, College of Medicine, University of Baghdad.

\*\*\*Department of Dermatology and Venereology, Baghdad Teaching Hospital.

Most genodermatoses show single gene or mendelian inheritance (autosomal dominant, Autosomal recessive or x- linked recessive genes).<sup>(2)</sup>

The inheritance of genetic diseases, abnormalities or traits is described by both the type of chromosome, the abnormal gene resides on (autosomal or sex chromosome), and by whether the gene itself is dominant or recessive<sup>(2)</sup>.

Genodermatoses are variable in their onset and severity, Some developed since birth while others developed later in life<sup>(3)</sup>.

In the world, many works were done to estimate the frequency of genodermatoses in different societies.

No previous study in Iraq reporting these genodermatoses among Iraqi population, So the present work is designed to determine the frequency of genodermatoses among Iraqi patients and to be compared with other countries.

### **PATIENTS AND METHODS:**

This case series descriptive epidemiological study was conducted at the outpatient clinic of Dermatology and Venereology - Baghdad Teaching Hospital during April 2005 to April 2006.

Eighty three patients with genodermatoses consulted the clinic during this period. A detailed history from each patient was recorded regarding the following points:-Age, sex, place of birth and residence, occupation and marital state. Also patient present complain, time of onset, seasonal variation and aggravating factors. Family history including pedigree, consanguinity and positive family history of same genetic skin disease.

Full dermatological and clinical examination was performed looking for;

- Cutaneous manifestations which include type of skin lesions, site of predilection, associated features, size and number of lesions. Searching for mucous membrane, dental, hair and nail involvement.
  - For confirmation and sorting of genetic disorders in these patients a search for extracutaneous manifestations associated with the diseases were done including:-Central nervous and cardiovascular systems, eyes, throat examination, Musculoskeletal system
- According to the genetic disorder, some patients were subjected to different investigation like skull X-ray, chest X-ray, serum zinc and skin biopsy if needed to confirm the diagnosis; resort the type of disease and to determine the severity of the disease.

### **RESULTS:**

Eighty three patients with various genetic skin diseases were studied, 57 (68.7 %) patients were males and 26 (31.3 %) patients were females. The gender of patients were males outnumbered females (♂:♀ratio 2.1: 1) their ages at presentation to our department ranged from 1 month- 60 years (median 10 years).

The total number of patients consulting the Department of

Dermatology and Venereology -Baghdad Teaching Hospital during this period was 20000 patients, therefore the frequency of patients with genodermatoses is calculated to be 83/20000 which equals to 0.42%(prevalence in outpatient of Dermatology and Venereology Department) .

The most common genodermatoses were; ichthyosis 21 (25.3 %) patients and epidermolysis bullosa 16 (19.3 %) patients, When taken together, They constituted (44.6 %).

Neurofibromatosis 8 (9.6 %) and all of them were of type 1, hereditary palmoplantar keratoderma 6 (7.2 %), darier's disease 5(6 %), xeroderma pigmentosa 4 patients (4.8 %), Regarding the frequency of other genodermatoses were illustrated in table 1.

Epidermolysis bullosa (EB) was diagnosed in 16 patients out of 20000 outpatients (0.08 %),three quarter of cases with epidermolysis bullosa had epidermolysis bullosa simplex (75 %) while the remaining quarter of them had epidermolysis bullosa dystrophica(25%).

About of forty-three percent of patients with ichthyosis presented as ichthyosis vulgaris in 42.9% and non bullous ichthysiform erythroderma(23.8 %), (19 %) as X- linked ichthyosis and (14.3 %) as lamellar ichthyosis.

Half of patients with hereditary palmoplantar keratoderma presented as Mal-de-meleda, A third as Unna- Thost and (16.7 %) as Papillon-Lefever syndrome.

In the present study, 8 (0.04 %) cases of neurofibromatosis were diagnosed among 20000 outpatients consultation. Xeroderma pigmentosa occurs with frequency of 0.02 %.Lipoid proteinosis was reported in 3 cases per 20000 (0.015 %), while acrodermatitis enteropathica was found in 2 cases of per 20000 (0.01 %), the age of onset was from 6 months to 2 years, both coming from rural areas, dermatitis was present in 100 % and diarrhea in 50 %.

Regarding epidermodysplasia verruciformis, 3 cases per 20000(0.015 %) patients were reported, 2 of them came from Samara city and 1 case from Diayla City. No malignancy was recorded. Three cases of ectodermal dysplasia per 20000 (0.015 %) patients were reported; all of them were of anhidrotic type.

The time of onset in most of the patients with genodermatoses was at birth as in epidermolysis bullosa, ichthyosis and neurofibromatosis, while the other genodermatoses started in early or late childhood as in xeroderma pigmentosa, Fabry's disease and Darier's disease except Hailey- Hailey disease began in the second decade of life.

The family history was positive in 29(34.9 %) patients, 8(38.1%) had ichthyosis, 4(66.66 %) with hereditary palmoplantar keratoderma, 2(12.5%) had epidermolysis bullosa, all patients (100 %) with Hailey-Hailey had positive family history. Family history was not recorded in patients with

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acrodermatitis enteropathica. The family history in patients with other genodermatoses is illustrated in table 1.

Regarding the consanguinity, it was positive in 41 (49.4%) patients of the total number of patients: In epidermolysis bullosa was positive in three quarters

of patients, in ichthyosis positive in (61.9 %), In xeroderma pigmentosa, all patients were positive for consanguinity, it is apparent that the consanguinity was strongly positive in genodermatoses with autosomal recessive inheritance( Table -2).

**Table 1: Frequency distribution genodermatoses according to diagnosis, gender and family history.**

Genodermatoses	Patients						Family history			
	♂		♀		Total		-ve		+ve	
	No.	%	No.	%	No.	%	No.	%	No.	%
Ichthyosis	16	28.07	5	19.23	21	25.3	13	24.07	8	27.58
Epidermolysis bullosa	12	21.05	4	15.38	16	19.2	14	25.92	2	6.89
Neurofibromatosis	4	7.01	4	15.38	8	9.6	6	11.11	2	6.89
Hereditary PPK	4	7.01	2	7.69	6	7.2	2	3.70	4	13.79
Darier disease	5	8.77	0	0	5	6.02	4	7.40	1	3.44
Xeroderma pigmentosa	4	7.01	0	0	4	4.81	2	3.70	2	6.89
Ectodermal dysplasia	1	1.75	2	7.69	3	3.6	1	1.85	2	6.89
Epidermodysplasia verruciformis	2	3.50	1	3.84	3	3.6	1	1.85	2	6.89
Hailey-Hailey disease	1	1.75	2	7.69	3	3.6	0	0	3	10.34
Lipoid Proteinosis	2	3.50	1	3.84	3	3.6	1	1.85	2	6.89
Pseudoxanthoma elasticum	0	0	2	7.69	2	2.4	2	3.70	0	0
Acrodermatitis enteropathica	2	3.50	0	0	2	2.4	2	3.70	0	0
LWNH	1	1.75	1	3.84	2	2.4	2	3.70	0	0
Fabry's disease	1	1.75	0	0	1	1.2	1	1.85	0	0
Klippel-Trenaunay syndrome	0	0	1	3.84	1	1.2	1	1.85	0	0
Mucopolysaccharidosis	1	1.75	0	0	1	1.2	1	1.85	0	0
Tuberous sclerosis	0	0	1	3.84	1	1.2	0	0	1	3.44
Pachonychia congenital	1	1.75	0	0	1	1.2	1	1.85	0	0
Total	57	99.92	26	99.95	83	100	54	99.95	29	99.93

\*Mantel- Haen Szell  $\chi^2$  (Ns) P value >0.05

**Table 2: Distribution of patients according to consanguinity and diagnosis.**

Genodermatoses	Family History			
	-ve		+ve	
	No.	Column%	No.	%
Ichthyosis	8	19.04	13	31.70
Epidermolysis bullosa	4	9.52	12	29.26
Neurofibromatosis	6	14.28	2	4.87
Hereditary Palm Plantar keratoderma	4	9.52	2	4.87
Darier disease	4	9.52	1	2.43
Xeroderma pigmentosa	0	0	4	9.75
Ectodermal dysplasia	1	2.38	2	4.87
Epidermodysplasia verruciformis	3	7.14	0	0
Hailey-Hailey disease	3	7.14	0	0
Lipoid Proteinosis	1	2.38	2	4.87
Pseudoxanthoma elasticum	1	2.38	1	2.43
Acrodermatitis enteropathica	1	2.38	1	2.43
Linear and whorled nevoid hypermelanosis	2	4.76	0	0
Fabry's disease	1	2.38	0	0
Klippel-Trenaunay syndrome	1	2.38	0	0
Mucopolysaccharidosis	1	2.38	0	0
Tuberous sclerosis	0	0	1	2.43
Pachonychia congenital	1	2.38	0	0
Total	42	100	41	100

\* Mantel- Haen Szell Chi-square (Ns) P value >0.05

### DISCUSSION:

Genodermatoses are diseases that are encountered in general medical practice, the true incidence of which is not documented before in Iraq. The present work showed that the proportion of patients with genodermatoses was 83 / 20000 which are equal to 0.42%.

The two most common diseases which both comprised 44.6 % of total number of cases were ichthyosis and epidermolysis bullosa and these results are comparable to had been mentioned by Sharquie and AlKhafaji<sup>(4)</sup>.

Comparing the incidence of genodermatoses in the present work with those reported in other countries, It found that ichthyosis vulgaris was diagnosed in 0.045 % patients out of a total of 20000 outpatients while X-linked ichthyosis (0.02%), non – bullous ichthysiform erythroderma and lamellar ichthyosis (0.04 %). Griffith, Leigh and Marks, found that the estimated incidence of ichthyosis vulgaris was (0.4%); X- linked ichthyosis was (0.01%) of British population and the estimated incidence of non-bullous ichthysiform erythroderma and lamellar ichthyosis is (0.001%) of general population<sup>(5)</sup>. This means that the incidence of ichthyosis vulgaris is more in British population than in Iraq, While the incidence of non bullous ichthysiform erythroderma and lameller ichthyosis is lower in British population than in Iraq.

In the present study, the commonest type of ichthyosis was ichthyosis vulgaris (42.9 %) and this disagrees with an Iraqi study performed in 1997 which showed that X- linked recessive ichthyosis was the commonest type (38.6 %) and the incidence of ichthyosis vulgaris was lower(20.5%)<sup>(6)</sup>.

This work showed that, epidermolysis bullosa(EB) was diagnosed in 0.08 % patients out of 20000 outpatients while the incidence of this disease varies in different countries, for example the National Epidermolysis bullosa Registry report in US stated that 50 cases occur per one million (0.005%) live births. In Norway are 54 cases per million live births. In Japan are 7.8 cases per million (0.0007 %) live births and in Croatia are 9.6 cases per million (0.0009 %) live births<sup>(7)</sup>. This means that Iraqi population had higher incidence of EB in comparison with other world countries.

The commonest type of EB was of the simplex (75%) while dystrophic constitute(25%) and this agrees with an Iraqi study performed in 2003 which showed that the simplex constitute (50 %) of cases while dystrophic constitute (32.5 %) of cases<sup>(8)</sup>.

In the current study the frequency of neurofibromatosis were 0.04 % among 20000

outpatients consultation, jennirer and thomas showed that worldwide neurofibromatosis occurs in approximately (0.04 %- 0.03 %) of live births<sup>(9)</sup>.

This is comparable to results of the present study.

Robbins, et al found that xeroderma pigmentosa occurs with frequency of approximity 0.0004 % in Europe and USA<sup>(10)</sup>. Neel et al found that the frequency of xeroderma pigmentosa has been reported to be higher in Japan approximately (0.002 %)<sup>(11)</sup>, while in this work 0.02 % was diagnosed. This means that the incidence of XP is higher in Iraq and this goes with Sharquie's and Mancy's results, which showed that the incidence of XP in Al- Ramadi City was 0.005%<sup>(12)</sup>.

Internationally lipid proteinosis is considered to be rare, no precise incidence was reported. Worldwide, approximately 300 cases are reported in the literature<sup>(13)</sup>. In this study 3 cases per 20000 (0.015 %). In this work, 2 cases of acrodermatitis enteropathica per 20000 (0.01 %) were recorded, the age of onset was from 6 months to 2 years, Both coming from rural areas, Dermatitis was present in 100 %, Diarrhea in 50 %, and this agrees with Sharquie et al, Who showed that the age of onset of acrodermatitis nteropathica in Iraqi patients was from 2 months to 2 years and most of them came from rural areas, Dermatitis recorded in 100 % and diarrhea in 27.2 %<sup>(14)</sup>. internationally: an estimated 1 in 500000 (0.0002 %) people in Denmark are affected<sup>(15)</sup>. Thus the incidence of acrodermatitis enteropathica is higher in Iraq than western countries.

Another Iraqi study showed that the frequency of acrodermatitis enteropathica among Iraqi infants was 0.4 %<sup>(16)</sup>.

Regarding epidermodysplasia verruciformis, internationally: the largest series reported in the literature included 195 cases, mainly in Eastern Europe, poland and Latin America, The reported frequency of malignant changes range from 30-60 %<sup>(17)</sup>. In current study 3 cases per 20000 (0.015 %) patients were reported, 2 of them came from Samara City and 1 case from Diayla City. No malignancy was recorded in this work. Sharquie et al study record that in Iraq, there are two foci for EV in Samara (North of Baghdad) and Diayla where the disease seems to be common among their families, although sporadic cases could be seen from other Iraqi areas<sup>(17)</sup>. Also this study reported three cases of EV with invasive periorbital squamous cell carcinoma and urgently needed eye enucleation as radical therapy for this lesion in these three cases<sup>(17)</sup>.

Another Iraqi study by Sharquie et al report that patients with kidney transplantation had high frequency of viral warts (50 %) and skin malignancy mainly squamous cell carcinoma and basal cell carcinoma were seen in exposed parts of the body (9.2 %) and these might simulate inherited EV so that deserve the term acquired EV<sup>(18)</sup>.

In current study, 3 cases of ectodermal dysplasia per 20000 (0.015 %) patients were reported; all of them were of anhidrotic type. In the US the prevalence of anhidrotic ED is estimated to be 1 case per 100000 (0.001 %) births. Internationally: collectively, the prevalence of ED is estimated at 7 cases per 10000 (0.07 %) births<sup>(19)</sup>so, it is more common Worldwide than Iraq.

About 35 percent of patients have positive family history of the same genetic disease. In Hailey – Hailey disease, all cases had positive family history and this goes with Don, carney et al study who showed that in Hailey – Hailey disease the family history was positive in approximately two third of patients<sup>(20)</sup>. In xeroderma pigmentosa, family history was noted in 50 % of our cases, sharquie and mancy, showed that family history was noted in 72 % of cases<sup>(12)</sup>. In this study, 38.1 % of patients with ichthyosis had positive family history while it was positive in 92.9 % of patients in previous Iraqi study done in 1997<sup>(6)</sup>. In this study, 12.5 % of patients with epidermolysis bullosa had positive family history, while Al-Mosawy HN showed that the family history of EB in Iraq was positive in 47.5 % of patients<sup>(8)</sup>. In this work, family history was not recorded in patients with acrodermatitis enteropathica while Sharquie et al study showed that family history was positive in 27.2 % of Iraqi patients<sup>(14)</sup>.

Regarding the gender of patients, males outnumbered females (♂:♀ratio 2.1: 1). This difference may be attributed to that some genodermatoses are x-linked and they occur exclusively in males as in X- linked ichthyosis.

During this work it was found that the consanguinity was recorded in 41 (49.4 %) cases and it was more obvious in diseases of autosomal recessive inheritance as xeroderma pigmentosa and epidermolysis bullosa dystrophica in which all patients had positive consanguinity because both parents were more likely to carry the same defective gene and express the disease in their children. In this study, consanguinity was positive in 61.9 % of patients with ichthyosis, while in previous Iraqi study, The consanguinity was positive in 82.1 % of cases<sup>(6)</sup>. In epidermolysis bullosa, the consanguinity was recorded in 75 % of patients,

While Al-Mosawy showed that it was positive in 90 % of cases<sup>(8)</sup>. In xeroderma pigmentosa, consanguinity was positive in 100 % of cases, while Sharquie and Mancy, showed that consanguinity was positive in 84 % of Iraqi patients with XP<sup>(12)</sup>.

### CONCLUSION:

Genodermatoses are frequently encountered among Iraqi dermatological outpatients and more common in families with positive consanguinity and most of them were comparable to other countries.

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