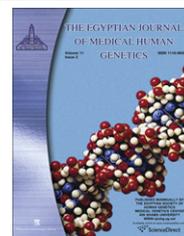




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ORIGINAL ARTICLE

## Clinico-epidemiologic features of oculocutaneous albinism in northeast section of Cairo – Egypt

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**Abstract** *Background:* Oculocutaneous albinism (OCA) is a genetically heterogeneous group of disorders characterized by the absence or reduced pigmentation of the skin, hair and eyes. To assess the clinico-epidemiologic features of different forms of OCA among Egyptian patients, we performed a retrospective study to determine the frequency, types, clinical presentation and associated genomic errors in albino patients and their relatives consulting the Genetics Clinic, Pediatric Hospital, Ain Shams University, Cairo, Egypt.

*Methods:* We used the outpatients index files to identify diagnosed cases of albinism referred from the dermatologic and ophthalmologic departments with different genodermatoses over 43 year period. We used specifically designed data collection protocol forms to extract epidemiological and clinical data from the patients medical records. These were entered into a computer database and analyzed using standard statistical software.

*Results:* The occurrence rate of albinism in our study was 20.4% of genodermatoses patients and 1 per 5843 patients attending the Pediatric hospital. Consanguineous marriage was reported among parents of 66.37% of patients and positive family history was reported in 46.01% of patients. Complete OCA was detected in 48.59% of patients, partial albinism in 41.59% of patients and

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syndromic albinism was detected in 7.96%. Associated genomic errors were detected in 36.28% of our albino patients and seventy one multiple mutant genomic errors were defined among relatives of thirty seven index families of oculocutaneous albinism patients.

*Conclusion:* To the best of our knowledge, this preliminary study is the first report of its kind from Egypt. The high rate of parental consanguinity among the parents of our Egyptian albino patients may account for the frequency of this genodermatosis in Egypt.

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## 1. Introduction

Albinism, derived from the Latin, *albus*, meaning white, is a heterogeneous group of inherited disorders of melanin biosynthesis characterized by a generalized reduction in pigmentation of hair, skin and eyes [1].

Albinism may be isolated oculocutaneous albinism (OCA), ocular or syndromic. OCA is considered isolated if it involves only tissues that are normally pigmented. The four known types of OCA (OCA1 to OCA4) are autosomal recessive disorders associated with mutations of specific genes, TRY [2], OCA2 (P) [3], TYRP1 [4–6] and MATP [7], respectively. However, other genes yet unidentified probably exist [8]. In ocular albinism (OA), the clinical manifestations are limited to the eyes and can be caused by mutations in OA1 gene located on the X-chromosome, however, in autosomal recessive ocular albinism (AROA), can be caused by mutations in OCA genes [9–11]. In Southern Africa, brown OCA (BOCA) maps onto the OCA2 locus on chromosome 15q [4]. In addition, OCA is a phenotypic component of at least three syndromic disorders: Hermansky–Pudlak syndrome (HPS), which can result from mutations in eight known genes, most frequently HPS1 and HPS4; Chediak–Higashi syndrome (CHS), which results from mutations in LYST (CHS1); and Griscelli syndrome (GS), which can result from mutations in three known genes (MYO5A; RAB27A, and MLPH) [12]. Syndromic forms of albinism are associated with defects in the packaging of melanin and other cellular proteins. As such they are distinct from OCA, which are associated with defects in the production of melanin [13].

The clinical spectrum of OCA varies with OCA1A being the most severe type characterized by complete lack of melanin production throughout life (tyrosinase negative, the critical enzyme required in melanin biosynthesis pathway), while the milder forms OCA1B, OCA2, OCA3 and OCA4 show some pigment accumulation over time [8] (tyrosinase positive), there by producing some red-yellow photomelanin pigment that gives rise to sandy colored hair and light brown irises [9]. Clinical manifestations of OA include various degrees of congenital nystagmus, iris hypopigmentation and translucency, reduced pigmentation of the retinal pigment epithelium, foveal hypoplasia, reduced visual acuity and refractive errors, color vision impairment and prominent photophobia. Misrouting of the optic nerves is a characteristic finding, resulting in strabismus and reduced stereoscopic vision [1]. Syndromic OCA such as Chediak–Higashi and Hermansky–Pudlak syndrome also manifest with extrapigmentary defects consisting of leucocyte, platelet, pneumocyte and reticular cell dysfunction. Griscelli syndrome can also manifest with immunodeficiency and neurologic defects [14].

Herein, we conduct a retrospective study to determine the frequency, types, clinical presentation and associated genomic

errors in albino patients and their relatives in the Genetics Clinic, Pediatric Hospital, Ain Shams University. This hospital is located in the northeast section of Cairo (the capital of Egypt). It has a high standard of health care, so nearly all patients in this area attend this hospital for consultation. Also patients come nearly from all governorates of Egypt to take good health care. So, the frequency and characteristics of albinism in this hospital will represent that in the general population to a great extent.

## 2. Subjects and methods

The present study comprised 553 index patients with genodermatoses who were registered at Genetics Clinic, out of 660,280 attending the pediatric hospital, Ain Shams University, at the interval 1966–2009.

All the patients were referred either through the ophthalmologic or dermatologic clinic for genetic counseling. They were subjected to the following studies: detailed family history, index pedigree design and clinical assessment of index patients and their families.

We compiled data on six skin and hair parameters (skin color, pigmentation pattern, color of scalp hair, eye brows, and eye lashes, freckles and birthmarks), and eight eye and vision parameters (photophobia, visual acuity, refractive value, nystagmus, iris translucency, fundus pigmentation, foveal hypoplasia and misrouting of the optical pathways).

Since detailed ophthalmic and/or dermatologic data could not be obtained on some of the old registered patients, the clinical criteria to classify patients as complete oculocutaneous albinism (OCA1A) were the presence of white hair and skin throughout life. The group of partial oculocutaneous albinism (OCA1B) patients included those who initially had white scalp hair at birth but developed pigment in the first decade of life [15].

## 3. Results

### 3.1. Occurrence rate

Of 553 new genodermatoses patients presenting to the Genetics unit, and 660,280 patients attending the Pediatric hospital, during the period of the study, 113 patients (20.4%) had clinically confirmed diagnosis of albinism. The occurrence rate was 20.4% of genodermatoses patients attending the Genetic unit, and 1 per 5843 patients attending the Pediatric hospital, Ain Shams University, Cairo, Egypt.

### 3.2. Epidemiological profile

Of the 113 patients, 62 (54.86%) were males and 51 (45.13%) were females giving a male to female ratio of 1.2:1. All patients

were of Egyptian nationality and their ages ranged from 1 month to 25 years. Consanguineous marriage was reported among the parents of 75 patients (66.37%). Fifty-two out of the 113 patients (46.01%) had a positive family history of albinism (one or more of their family members, particularly siblings, had albinism as the index patient).

### 3.3. Clinical findings (Table 1)

#### 3.3.1. Clinical phenotypes

Oculocutaneous albinism was detected in 104 patients (92.04%) of whom, fifty five patients (48.67%) had complete oculocutaneous albinism with white hair color, pinkish skin, red pupils, reduced visual acuity, nystagmus and photophobia and forty seven patients (41.59%) had partial oculocutaneous albinism with white blond skin, light brown hair, reduced visual acuity, nystagmus, photophobia, blue eyes. Ocular albinism was detected in 2 patients (1.76%) with reduced visual acuity, nystagmus, photophobia, blue eyes.

Syndromic oculocutaneous albinism was detected in 9 cases (7.96%): 2 cases (1.76%) had Hermansky–Pudluk syndrome; 2 cases (1.76%) had Cross syndrome and five cases (4.42%) had Chediak–Higashi syndrome.

#### 3.3.2. Other medical associations

We reported mental retardation in 19 cases (16.8%), seizures in 14 cases (12.38%), Down syndrome in 2 cases (1.76%) and deafmutism in 4 cases (3.53%).

#### 3.3.3. Multiple mutant genomic errors (Table 2)

Seventy one multiple mutant genomic errors were defined among relatives of thirty seven index families (32.74%) of oculocutaneous albinism.

## 4. Discussion

There are no published reports in the medical literature about the incidence of OCA and only few reports deal with the pigmentary disorders in Egypt [16,17]. Our study shows that the occurrence rate of OCA was 20.4% of genodermatoses patients attending the Genetics unit, and 1 per 5843 patients attending the Pediatric hospital, Ain Shams University, Cairo, Egypt. OCA is considered to be a rare autosomal recessive genodermatoses with a worldwide incidence of 1:17,000 [9]. The prevalence of albinism from several studies in South Africa, Tanzania and Nigeria ranged from as low as 1 in 15,000 in the East Central state of Nigeria to as high as 1 in 1000 in the Tonga Tribe of Zimbabwe [18–20] where it is considered a public health issue. In our clinical observations, the frequency of OCA in Egypt seems to be higher than that reported in the medical literature and falls in a midway position between the low and high ranges reported in various regions of Africa.

Prevalence of the different forms of albinism varies considerably worldwide, partly explained by the different founder mutations in different genes and the fact that it can be difficult clinically to distinguish between the different subtypes of albinism among the large normal spectrum of pigmentation. OCA2 is the most prevalent form worldwide [21]. However, in our series OCA1 was the most prevalent type. All types of OCA and ocular albinism in our study had similar ocular findings, including nystagmus, hypopigmentation of iris, reduced

visual acuity and sometimes a degree of color vision impairment.

In our study, albinism associated with systemic pathology such as HMP, Cross syndrome and Chediak–Higashi syndrome was reported in 2%, 2% and 5% of our patients, respectively. The relationship of albinism and the systemic manifestations that occur in HPS, CHS and appears to be related to the cellular machinery in the ribosomes involved with vesicles and lysosome transport. Specifically the link between immunodeficiencies and albinism involves the use of secretory vesicles and lysosomes by the immune system [22].

In this study, there was a slight male preponderance, with a male to female ratio of 1.2:1. However, it is reported that the incidence of these albino diseases are equal in both sexes [4]. We could not find any reason to account for this male preponderance, but perhaps there is a predominance of males over females in this region of Egypt [23]. Our study showed forty six percent of patients had a positive family history and a high proportion of patients with consanguineous parents (66.37%) compared to 38% in the general population [24]. This high consanguinity rate may account for the high occurrence rate of autosomal recessive genodermatoses such as OCA in this region.

Genealogic analysis of pedigrees of index patients with oculocutaneous albinism revealed an apparently high incidence of other genetic anomalies which manifested simultaneously or segregated randomly among many of proband's relatives. The identification of isolated albinism as well as isolated sensory neural deafness or mental deficiency among certain index kindreds, could advocate the possibility of linkage of mutant gene loci mediating both types of anomalies.

Deafmutism was reported in 7.27% of our patients with complete OCA1. Hereditary hearing impairment is frequently found associated with pigmentary disorders in genetic diseases such as Waardenburg syndrome, Tietz-Smith syndrome and piebaldism. Nevertheless, in none of these syndromes are total OCA and only partial albinism, ocular or cutaneous reported. Linkage analysis with markers close to the four known OCA loci excluded linkages to OCA1, OCA2 and OCA3 and homozygosity in markers near OCA4 locus was observed. The combined occurrence of deafness and albinism was due to mutations in two different genes, showing autosomal recessive inheritance and they resulted by chance from consanguineous matings [25].

Mental retardation and seizures were also reported in 30.91% and 25.45% of our patients with complete OCA. The albino were found to be more intellectually mature than the controls but the control group showed slightly more diffuse body image boundary differentiation than the albino group [26]. However, White et al. [27] reported a 20 year old man with tyrosinase-negative OCA, mental retardation, epilepsy, sensory neural deafness, ataxia and Barter syndrome and Budisteanu et al. [28] present a case of oculocutaneous albinism in a child with associating multiple malformations (pre-axial polydactyly, small penis, cardiac malformation) and psychomotor retardation. Other disorders reported in the literature include meningomyelocele [29], and hydrocephalus, megalocornea, retinal coloboma and cerebral anomalies [30].

The association of albinism with chromosomal abnormalities like Down syndrome is considered co-incidental. However there is a report about the occurrence of ocular albinism in a female with dup X chromosome [31].

**Table 1** Summary table of the clinico-epidemiological features of 113 patients with albinism.

Clinico-epidemiologic data	Complete OCA No. &%	Partial OCA No. &%	OA No. &%	Hermansky–Pudlak No. &%	Cross syndrome No. &%	Chediak–Higashi No. &%
Patients No.	55 (100%)	47 (100%)	2 (100%)	2 (100%)	2 (100%)	5 (100%)
Egyptian Nationality	55 (100%)	47 (100%)	2 (100%)	2 (100%)	2 (100%)	5 (100%)
Sex: Male	29 (52.73%)	25 (53.19%)	2 (100%)	2 (100%)	1 (50%)	3 (60%)
Positive parental relationship	37 (67.27%)	30 (63.83%)	–	2 (100%)	2 (100%)	4 (80%)
Positive family history	26 (47.27%)	21 (44.68%)	1 (50%)	2 (100%)	–	2 (40%)
White hair color	55 (100%)	–	–	–	–	–
Pinkish skin	55 (100%)	–	–	–	–	–
White, blond	–	47 (100%)	2 (100%)	2 (100%)	2 (100%)	–
Light brown hair	–	47 (100%)	2 (100%)	2 (100%)	2 (100%)	–
Silvery sheen to the hair and skin	–	–	–	–	–	5 (100%)
Red pupils	55 (100%)	–	–	–	–	–
Reduced visual acuity	55 (100%)	47 (100%)	2 (100%)	2 (100%)	2 (100%)	5 (100%)
Nystagmus	55 (100%)	47 (100%)	2 (100%)	2 (100%)	2 (100%)	5 (100%)
Photophobia	55 (100%)	47 (100%)	2 (100%)	2 (100%)	2 (100%)	5 (100%)
Blue eyes	–	47 (100%)	2 (100%)	2 (100%)	2 (100%)	5 (100%)
Prolonged bleeding	–	–	–	2 (100%)	–	–
Immune deficiency	–	–	–	–	–	5 (100%)
Neurologic complications	–	–	–	–	–	5 (100%)
MR	17 (30.91%)	–	–	–	2 (100%)	–
Microphthalmia	–	–	–	–	2 (100%)	–
Seizures	14 (25.45%)	–	–	–	–	–
Deafmutism	4 (7.27%)	–	–	–	–	–
Down syndrome	2 (3.64%)	–	–	–	–	–
Albinism index families with definable MMGE	20 (36.36%)	16 (34.04%)	–	–	1 (50%)	–

**Table 2** Multiple mutant genomic errors defined among relatives of 37/113 albinism index families.

MMGE	No.	%
<b>Definable errors</b>	43	60.56
<i>Single gene errors</i>	18	25.35
Optic atrophy	3	4.23
Squint	2	2.82
Congenital blindness	1	1.41
Congenital cataract	1	1.41
Insulin dependent diabetes mellitus	3	4.23
Polydactyly	1	1.41
G6PD deficiency	1	1.41
Epidermolysis bullosa	1	1.41
Deafmutism	4	5.63
Rubeinstein Tybi synd.	1	1.41
<i>Chromosomal errors</i>	1	1.41
Down syndrome	1	1.41
<i>Multifactorial errors</i>	24	33.80
Congenital heart disease	1	1.41
Bronchial asthma	1	1.41
Cleft palate	1	1.41
Seizures	9	12.68
Non Insulin dependent Diabetes mellitus	10	14.08
Hypertension	2	2.82
<b>Non definable errors</b>	28	39.43
Mental deficiency	12	16.90
Speech defect	7	9.86
Infertility	5	7.04
Vetiligo	1	1.41
Hydrocephalus	1	1.41
Short stature	1	1.41
Talipes equinovarus	1	1.41
<b>Sum of traceable errors</b>	71	100.00

Lifespan in patients with OCA is not limited, and medical problems are generally not increased compared to those in the general population. However, skin cancers may occur and regular skin checks should be offered. Development and intelligence are normal. Persons with OCA have normal fertility [21]. Most of our albino patients, attending our clinic were in the age range of one month to 25 years. Other publications in Africa report a relatively greater number of individuals with albinism in the younger age groups (below 30 years). In the East Central state of Nigeria, 89% of identified people with albinism were in the age range of 0–30 years, while another study reported that 77% were under the age of 20 in the same Nigerian state. A mean age of 17.8 years was reported in Soweto, South Africa. Also in Cameroon, Nigeria and Tanzania, observations indicate a low number of people with albinism in age groups above 30 [18].

In albino population, ocular problems are ubiquitous. In some studies, visual difficulties have been reported to occur in 100% of people with albinism. Due to the lack of retinal pigment required for the normal development of the visual system these individuals experience photophobia, myopia and other visual problems including nystagmus and strabismus. Aside from the visual handicaps, UV exposure is highly detrimental to the hypopigmented skin. Lack of melanin predisposes this population to severe skin damage. The majority of these lesions are in the most sun-exposed parts of the body such as the face, ears, neck and shoulders. Skin lesions include sunburns, blisters, solar elastosis/keratosis, epelides, lentiginosis,

and superficial ulcers. Ultimately, squamous cell, and less frequently basal cell carcinomas may occur [18,21].

In addition to their health concerns, people with albinism must also deal with psychological and social challenges. In Nigeria, one study collected written accounts of people with albinism. These individuals stated that they tended to be more withdrawn from social situations to avoid being noticed. They were more emotionally unstable and had less assertive personalities than people without albinism. Also, they considered their society to be generally unkind and rejecting, even though they did have close friends. Much of the social discrimination appears to stem from the communities' lack of education about albinism's etiology. Furthermore, their family members may also experience discrimination from the community [18].

In conclusion, albinism, especially in Africa including Egypt due to extreme sun exposure, is a condition that requires further attention than in the past. In Egypt we need more progress in terms of medical and social care and we hope to further increase the awareness of albinism throughout the country in the future.

### 5. Conflict of interest

The authors declare no conflict of interest.

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